Cats’ Internal Exposure to Selected Brominated Flame Retardants and Organochlorines Correlated to House Dust and Cat Food


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ABSTRACT: Pet cats may be used as a biomarker for assessing exposures to organohalogen compounds (OHCs) adsorbed to household dust in home environments. This study explores two exposure routes of OHCs, ingestion of OHCs (i) via house dust and (ii) via cat food. House dust from 17 Swedish homes and serum from the participating families’ pet cats were collected, and cat food was purchased matching the diet reported. Paired samples of cat serum, house dust, and cat food were analyzed for brominated flame retardants/natural products (polybrominated diphenyl ethers (PBDEs), decabromobiphenyl (BB-209), decabromodiphenylethane (DBDPE), 2,4,6-tribromophenol (2,4,6-TBP), OH-PBDEs) and organochlorines (polychlorinated dibenzo-47 (PCP)). Significant correlations were found between serum and dust samples from the living rooms for BDE-47 (p < 0.035), BDE-99 (p < 0.035), and BDE-153 (p < 0.039), from the adult’s bedroom for BDE-99 (p < 0.019) and from all rooms for BDE-99 (p < 0.020) and BB-209 (p < 0.048). This is the first time a correlation between cat serum levels and household dust has been established, finding that supports the hypothesis that dust is a significant exposure route for cats. Serum levels were also significantly correlated with concentrations found in cat food for 6-OH-BDE47 (p < 0.035), 2,4,6-TBP (p < 0.020) and BB-209 (p < 0.007). DBDPE was found in high concentrations in all dust (median 154 pmol/g) and food samples (median 0.7 pmol/g lw) but was below detection in serum samples, suggesting low or no bioavailability for DBDPE in cats.

1. INTRODUCTION

Brominated flame retardants (BFRs) are industrial chemicals produced to fire-protect construction materials, indoor decorations, furniture, textiles, electronics, and electrical appliances.1,2 One of the major classes of BFRs are the polybrominated diphenyl ethers (PBDEs).3 PBDEs are not chemically bound to the product material, so they are prone to migrate into the environment and adsorb to particles such as household dust.4 Unlike the legacy POPs, where dietary intake is an important route of exposure, BFRs also have indoor dust as a significant source of exposure via inhalation and hand-to-mouth activities, a special concern for small children and cats.5,6,11 An exposure assessment study on PBDE burdens in Americans found that the food intake of PBDEs explained less than 20% of the total body burden and that 82% of the body burden of PBDEs could be accounted for through house dust exposure.12 This large contribution from indoor dust is proposed as an explanation for the elevated levels of PBDEs in serum observed in North Americans.12,13 In adults, the lower brominated PBDE congener is generally considered to be from dietary sources, whereas the higher brominated PBDEs, such as the BDE-209, are mainly associated with dust as an exposure source.3 However, for small children, dust has been shown to also be an exposure route for the lower brominated PBDEs.7,8,14 The exposure route of both low and high brominated PBDEs from dust in small children are also seen in pet cats, which is a likely explanation for the overall higher PBDE concentrations found in pet cats compared to adults from the same region/country.9,10,15 Another possibility of the elevated levels in pet cats could be the reduced activity in phase 1 metabolic reactions, which would facilitate a higher accumulation of these lipophilic compounds in cats compared to humans.16

Other BFRs addressed here are decabromobiphenyl (BB-209), decabromodiphenylethane (DBDPE), hexabromobenzen-
zene (HBB), and a brominated intermediate currently used in the BFR production and natural product (i.e., 2,4,6-tribromophenol; 2,4,6-TBP) all of which are reviewed and assessed by EFSA 2010-2012. In 1976, the US stopped production of BB-209, but BB-209 continued to be produced in Europe (France) until 2000. DDBDE was introduced as a replacement for decabromodiphenoxy ether (BDE-209) and has been on the market for more than 20 years.20 HBB is an alternative flame retardant used to replace PentaBDE formulations. The flame retardant is used in paper, textiles, plastics, and electronics; it has also been detected in various matrices in the environment.21

Due to the extensive application of BFRs in products, materials, and everyday goods (contributing up to 30% of the mass of these products, materials, and goods), many of the BFRs are now ubiquitous environmental contaminants.22−24 The scientific community is concerned that their reported persistence, bioaccumulation, long-range transport, and the lack of better understanding of their toxicity is troublesome.25 PBDEs, among others, are of concern since they may target the endocrine system.26 In humans, PBDEs are metabolized via phase I and II enzymes to form hydroxylated PBDEs.27 This metabolic pathway implies formation of monohydroxylated OH-PBDEs, where oxidation can result in a 1,2-bromine shift. Hydroxylated metabolites of BDE-47 (i.e., 5-OH-BDE47, 6-OH-BDE47, and 2,4-dibromophenol) have been demonstrated in in vitro incubations of human hepatic microsomes, where CYP2B6 was identified as the major enzyme involved in the biotransformation.28,29 Furthermore, PBDEs may also undergo debromination, which is the major route for the higher brominated PBDEs, such as BDE-209, leading to the formation of PBDE congeners that possess higher bioavailability.27,30 Another proposed phase I metabolism pathway for PBDEs is cleavage of the ether bond (i.e., hydrolysis) to form a simple polybrominated phenol and a brominated catechol.31 In contrast to the anthropogenic formed OH-PBDEs and brominated phenols, there are naturally occurring OH-PBDEs (i.e., 2′-OH-BDE68, 6-OH-BDE47, and brominated phenols (2,4-DBP and 2,4,6-TBP)) that are well-known natural products produced by, for example, algae and sponges in marine environments.32 Of particular concern is the abundant 6-OH-BDE47 as it has endocrine-disrupting properties and can disrupt oxidative phosphorylation in the electron transport chain.33,34

One major concern regarding the toxicity of OH-PBDEs involves their capacity to mimic the structure of the native hormone thyroxin (T4) and by that competitively bind to important T4-transport proteins such as transthyretin (TTR).35 Thyroid hormone disrupting compounds (THDCs) with a binding potency to TTR has recently been reviewed.36 The majority of the TTR binding chemicals were aromatic, halogenated, and hydroxylated compounds. These compounds are typical metabolites of BFRs as well as products of organochlorines regulated under Stockholm Convention: polychlorinated biphenyls (PCBs) and organochlorine pesticides such as 1,1-bis(4,4′-dichlorodiphenyl)-2,2,2-trichloroethane (4,4′-DDT), 1,1-bis(4,4′-dichlorodiphenyl)-2,2-dichloroethene (4,4′-DDE), hexachlorobenzene (HCB), and pentachlorophenol (PCP). A review article of organic contaminants in settled house dust reported 485 chemicals, including a wide range of compound groups such as PBDEs, PCBs, organophosphate esters, per- and polyfluoroalkyl substances (PFAS), polycyclic aromatic hydrocarbons (PAHs), chlorinated phenols, and pesticides.36,37

In this study, correlation between cats’ internal and external exposure by paired analyses of serum, cat food (matched after each cat’s food requirements according to the cat owners), and settled house dust was investigated. Several previous studies have analyzed cat blood for BFRs,11,15,38−41 PCBs,15,38−42 and pesticides.38−40 Cats are renowned for developing feline hyperthyroidism, an endocrine disorder tentatively linked to environmental factors. A recently published study reports that higher serum concentrations for BDE-99, BDE-153, and BDE-183 in pet cats may be associated with hyperthyroidism in cats.15 The study also reported BB-209 to be present in all cat serum samples, at levels similar to BDE-209, which is intriguing as the production and application of this flame retardant ceased in Europe in 2000.41

The long reaching goal of the project (www.aces.su.se/missee/) is to identify mixtures of THDCs in indoor environments that may lead to hormone-related diseases and disorders. Cats’ exposure to house dust is assumed to be more similar to small children than to adults, so the internal exposure in cats is assumed to mirror that of small children assuming similar bioavailability for chemicals accumulated in dust.

2. MATERIALS AND METHODS

2.1. Samples. 2.1.1. Cat Serum. Seventeen families in the Stockholm/Uppsala region participated in the study. Samples were collected between August 2013 and March 2014. The requirements of the participating families included having a healthy adult pet cat (>1 year of age) and at least one child (<10 years of age) living at home. The constellation of the participating families and the description of their cats are listed in Table S1. On average, the families had two children living at home and more than one cat. The majority of the cats were domestic (shorthair) cats (57%) and most of the families lived in free-standing houses (53%). The majority of the cats (86%) spent more than 50% of their time indoors. The cat’s health was checked by a simple clinical examination before the blood was sampled, and their thyroid status was evaluated by measuring the levels of total serum T4 and thyroid stimulating hormone (TSH). All the cats were clinically healthy, and none of the cats were on medication.

In total, blood was drawn from 28 unsedated pet cats in their home environment. Blood was taken from the cephalic vein in the right foreleg using a 0.8 mm (21 G) needle connected to a plain evacuated tube with a clotting activator (BD Vacutainer, BD, Plymouth, UK). Serum was obtained by letting whole blood coagulate at ambient temperature for at least 30 min. Next, the sample was centrifuged for 5 min (3000 °C) before analysis. The study was performed after obtaining permission from the Swedish Board of Agriculture and Uppsala Ethical Committee on Animal Studies (No. 31-10466/12).

Mean density of cat serum was experimentally determined to be 1.042 g/mL (n = 20, SD = 0.008, and CV = 0.77%). If the cats were siblings, they were living in the same household, and were feed the same diet, their serum samples were pooled to increase the sample volumes. In total, 10 individual and 9 pooled serum samples were analyzed and reported here.

2.1.2. House Dust. Dust samples were vacuumed from three different rooms, i.e., the living rooms and children’s and parents’ bedrooms of the participating families to separate point...
sources which can differ between the rooms. The dust sampling was performed at the same occasions as when the blood samples were collected from the cats. Dust was collected using a Duststream dust collector (Indoor Biotechnologies Ltd., Wiltshire, United Kingdom) containing a disposable filter (mesh size 40 μm) and attached to a household vacuum cleaner tube. The collected dust samples were so-called still standing dust, from surfaces that were least disturbed by daily activity (e.g., outdoor activities and/or containing food crumbs). Typical sampling areas were book shelves, TV furniture, electronics, window benches, on top of hanging and standing lamps, wall strips, on top of sofas and armchairs, and around beds. Sampling of human and cat hair as well as large gravel or other nondust particles was avoided. The sampling volume varied greatly between houses and rooms, from 40 mg up to almost 800 mg, depending on the family’s lifestyle, house conditions, and the last time the room was cleaned. The participants were instructed not to clean the room for at least 3 days before sampling. All but three dust samples (D12, D14, and D16) were sampled from one room. For these three samples, pooled dust (living room and children’s and parents’ bedrooms) was used to extract enough material for analysis. The samples were sieved through a 1 mm metallic strainer, stored in aluminum foil, and kept at -20 °C until analysis.

2.1.3. Cat Food. Cat food, dry (n = 16) and wet (n = 12), was selected and purchased based on what the cat owners reported in the questionnaire. The major cat food brands were chosen, with most samples coming from Mjau, Royal Canin, and Pussi (Table S2).

2.2. Chemicals and Analysis. Experimental details regarding clinical analysis (i.e., determination of thyroid hormone levels (T₄, TSH) and blood lipids (cholesterol and triglycerides)) and the chemical analysis (i.e., extraction and cleanup procedures of serum, cat food, and house dust, instrumental analysis, and quantification) are given in the Supporting Information.

2.3. QA/QC. Two solvent blanks (1% KCl (w/v), 5 mL) were run in parallel with the 19 serum samples to control any potential background contamination. Cat serum and cat food analysis were carried out in a cleanroom to keep contributions from dust to a minimum, whereas the dust sample analyses were performed in a common laboratory. Along with each batch of cat serum samples (n = 19), two human plasma samples (bought from Karolinska University Hospital in Solna, Sweden in 2006) (5 mL) were analyzed in parallel as quality control (QC). For dust analysis, five standard reference material (SRM) samples from NIST (Organic contaminants in house dust, SRM 2585) and 10 solvent blanks were analyzed along with the dust samples. For cat food analysis, a pool of cat food homogenate (Whiskas in gravy with Salmon in pouch) was used as QC sample. One QC sample (10 g) and one solvent blank were extracted along with each batch of cat food (n = 6).

The extraction and cleanup method used here has previously been fully evaluated regarding the analysis of polybromophenols and OH-PBDEs in cat serum, and the accuracy regarding PBDE analysis was evaluated by the analysis of standard reference material (Organic contaminants in nonfortified human serum, SRM 1957) from NIST and is reported elsewhere. The quality of the dust analysis was evaluated with SRM material, Organic contaminants in house dust (SRM 2585). The in-house measured values (n = 5) for the ten PBDEs ranged between 81% and 106% of the certified NIST values (Figure S1), except for BDE-206 which was 58% of the certified NIST value. Both BDE-206 and BDE-209 are challenging to determine, which is for example reflected in the elevated relative standard deviation for BDE-209 (33%).

In general, LOQ was determined as the smallest quantifiable peak for the batch of samples analyzed and sample LOD was then set to LOQ/3. However, if the compound to be analyzed was present in the blank, LOD was set to the average amount determined in the blanks and LOQ was set to three times the value of LOD. The average amount of the blanks (if present) was subtracted from the quantified amount in the sample. For the statistical calculations, if a peak was >LOD and <LOQ, it was given the value LOQ/√2, and levels <LOD were considered to be zero.

2.4. Statistics. Due to heteroskedasticity of the data, possibly containing outliers potentially exerting a strong leverage effect on the regression line, the nonparametric Mann-Kendall trend test based on the Kendall’s tau coefficient (τ) was used to measure the association between serum concentrations in cats and matched for dust and food samples. As a robust alternative to ordinary regression lines, the Kendall-Theil Robust line (i.e., the median slope among all lines through pairs of two-dimensional sample points) is shown in the figures. For comparison, the determination coefficient (r²), a parametric regression test, was added in the correlation plots. Since Kendall’s tau coefficient (τ) is more robust and gives more reliable results than the determination coefficient (r²), a significant correlation was only considered if both of these tests were significant (p < 0.05). In addition, only positive correlations between serum and dust/food concentrations were assumed; therefore, one-tailed tests were applied. A significance level of 5% was applied in the statistical analysis (α = 0.05).

Principal component analysis (PCA) was performed on the four most abundant compounds in dust (BDE-47, BDE-99, BDE-209, and DBDPE) to study a potential difference in concentration and congener pattern between the living room and children’s and parents’ bedrooms. Before the PCA-scores were plotted, they were scaled to 100% and centered as follows: the percentage of each compound (log-transformed concentration relative to the sum) in each serum sample was calculated and then centered by log-ratio transformation before the PCA analysis to avoid a possible bias due to the compositional nature of the data. The eigenvector loadings were added to the PCA plot as vectors showing the magnitude of the relative concentrations for each compound. The Hotelling’s 95% confidence ellipses for the center of gravity for each group were also calculated and plotted (i.e., the ellipse in which 95% of all equally sized samples from the same populations is expected to fall within). A Hotelling’s T squared test, including the individual compounds, was used to check for significant differences in compound composition between the two groups. The significant level was set to 5% (α = 0.05).

3. RESULTS

3.1. Brominated and Chlorinated Contaminants in Cat Serum. The concentrations of the brominated analytes (pmol/g lipid weight (lw)) and quantification frequency (%) in 19 cat serum samples are reported in Table S3A, and the chlorinated compounds are reported in Table S3B. All results are reported on a molar basis to promote correct comparisons on concentrations of contaminants independent of molecular mass of the analyte.
Among the neutral compounds, five PBDEs (BDE-47, -99, -153, -183, and -209), BB-209, two PCBs (CB-138 and CB-153), 4,4′-DDT, and 4,4′-DDE could be quantified. 4,4′-DDE was found at the highest median concentration (42 pmol/g lw), followed by BDE-209 (32 pmol/g lw), 4,4′-DDT (30 pmol/g lw), CB-153 (28 pmol/g lw), and BB-209 (24 pmol/g lw). 2′-MeO-BDE68 was the only methoxylated PBDE detected in cat serum, and it was only found in two of the samples (2.6 and 3.2 pmol/g lw).

Three brominated phenols (2,4,6-TBP, 2′-OH-BDE68, and 6-OH-BDE47) and one chlorinated phenol (PCP) were determined in the cat serum. Highest median concentration was reported for 2,4,6-TBP (73 pmol/g lw) and was quantified in 37% of the samples, and PCP (68 pmol/g lw) and 6-OH-BDE47 (58 pmol/g lw) were found in 7% and 100% of the samples, respectively.

Only BDE-183, BDE-209, and 6-OH-BDE47 were found in 100% of the samples. BB-209 was found in 89% and 4,4′-DDE was found in 84% of the samples. 6-OH-BDE47 was the dominating phenol, and for comparison to other studies, we give the median concentration on a weight basis: 125 pg/g serum (min 42 pg/g serum, max 1206 pg/g serum). Although the conventional way of reporting phenolic compounds, not associated with the blood lipids, is on a fresh weight basis, we report all levels on a lipid weight basis to compare the exposure profile from cat food and house dust.

Nine of 19 cat serum samples were pooled which made it irrelevant to correlate the levels versus gender; only 4 individual cats were females. The age could be tested though, as the pooled cat serum samples came from siblings of the same age. Only serum lipid content (p < 0.05), CB-138 (p < 0.02), CB-153 (p < 0.02), and DDE (p < 0.004) increased significantly with age of the cats.

3.2. Brominated Contaminants in House Dust. Eighteen PBDE congeners (BDE-28, -47, -66, -99, -100, -153, -154, -183, -194, -196, -197, -198, -201, -202, -206, -207, -208, and BDE-209), BB-209, HBB, and DBDPE were detected in dust samples from the cat owner’s homes. Dust samples were taken from the living room and the children’s and parents’ bedrooms, and the concentrations (pmol/g dw) are given in Table S4A,B. The quantification frequency was 100% for the majority of the PBDEs, but BDE-154, -183, -194, -196, -197, -198, -201, and -202 had detection frequencies ranging between 56% and 98%.

Median concentrations of BB-209 were > LOD and only quantified (>LOQ) in 27% of the dust samples. The highest median concentrations were found in BDE-209 and DBDPE (262 and 154 pmol/g dw) followed by BDE-47 and BDE-99 (32 and 27 pmol/g dw, respectively).

The relative distribution pattern and concentration differences among the different rooms for the four most abundant flame retardants are visualized by principal component analysis (PCA) in Figures 1 and S2. The PCA-plot in Figure S2 shows equal distribution of the compounds among the various investigated rooms within a household. Looking at concentration differences, there was a tendency toward higher levels of brominated flame retardants in the dust from the living rooms compared to the dust from the children’s and parents’ bedrooms. However, this difference was not significant since the Hotelling’s confidence ellipses (showing the 95% confidence interval) for the living rooms and the two bedrooms were not fully separated (Figure 1). This result could possibly be due to a few extreme values, occasionally measured for the bedrooms, disturbing the disparity. All data points were included in the statistical analysis, so no extreme values were considered outliers and excluded. The indicated higher levels found are reasonable as many of these compounds are associated with electronics which are found at a higher extent in the living rooms.

3.3. Brominated and Chlorinated Contaminants in Cat Food. The concentrations of the brominated analytes (pmol/g lw) and quantification frequency (%) in dry and wet cat food samples are reported in Table S5A, and the chlorinated compounds are reported in Table S5B. Among the neutral compounds, five PBDEs (BDE-47, -99, -153, -183, and -209), BB-209, DBDPE, two MeO-PBDEs (2′-MeO-BDE68 and 6-MeO-BDE47), two PCBs (CB-138 and CB-153), HCB, 4,4′-DDT, and 4,4′-DDE were quantified in the dry and wet cat food samples. 4,4′-DDE was present in the highest median concentration (4.2 pmol/g lw), quantified in 96% of the cat food samples. The second highest median concentrations were measured for CB-138 (2.2 pmol/g lw), followed by BDE-209 (1.9 pmol/g lw), CB-153 (1.3 pmol/g lw), and 6-MeO-BDE47 (1.0 pmol/g lw). BB-209 was quantified in 43% of the samples in a median concentration of 0.05 pmol/g lw, ranging from <LOD to 2.4 pmol/g lw. DBDPE was found in 100% of the analyzed cat food samples in a median concentration of 0.7 pmol/g lw. The quantification frequencies of 2′-MeO-BDE68 and 6-MeO-BDE47 were 78% and 89%, respectively, and the median concentrations were 0.4 and 1.0 pmol/g lw, respectively.

Three brominated phenols (i.e., 2,4,6-TBP, 2′-OH-BDE68, 6-OH-BDE47, and PCP) were determined in both dry and wet cat foods. The quantification rates of 2,4,6-TBP, 2′-OH-BDE68, and 6-OH-BDE47 were 81%, 24%, and 76%, respectively. The highest median concentration was present in 2,4,6-TBP (2.9 pmol/g lw), followed by PCP (1.5 pmol/g lw) quantified in 70% of the samples and the two hydroxylated PBDEs (6-OH-BDE47 (0.03 pmol/g lw) and 2′-OH-BDE68 (<LOD pmol/g lw)).

Interestingly, 4,4′-DDT was mainly detected in the dry cat food as well as the higher brominated BDE-138, BDE-209, and BB-209. In contrast, the phenolic compounds were found in a higher quantification frequency and at higher concentrations in the wet cat food.
3.4. Correlation between Cat Serum and External Exposure.

The serum, dust, and food samples were matched as described in Table S6, and a summary of mean and median concentrations of some brominated compounds was analyzed in cat serum, house dust, and cat food (Table 1).

Five PBDE congeners (BDE-47, -99, -153, -183, and -209) and BB-209 were present in both cat serum and house dust for comparison. The serum concentrations were age adjusted for the persistent neutral compounds to ensure equal comparison among cats of different ages. Cat serum concentrations were compared to dust concentrations from the living room, the children’s and parents’ bedrooms, and the sum of all rooms. A significant correlation was found between cat serum and dust from the living rooms (p < 0.035), parents’ bedrooms (p < 0.019), and compared to all rooms (p < 0.020) for BDE-99 (Figure 2) and the living rooms for BDE-47 (p < 0.035) and BDE-153 (p < 0.039) (Figures S3 and S4, respectively). However, BDE-47 had a detection frequency of 26% in serum, so care should be taken when expressing the correlation as significant for this congener.

For BB-209, no significant correlation was found between serum concentrations and the living room nor any other rooms, but when combining all the rooms, a significant correlation (p < 0.048) was measured between serum and house dust (Figure S5). Three PBDE congeners (BDE-47, -99, and -209), BB-209, two PCBs (CB-138 and CB-153), 4,4′-DDT, 4,4′-DDE, PCP, 2,4,6-TBP, 2′-OH-BDE68, and 6-OH-BDE47 were present in the cat serum and cat food that were compared. A significant correlation between serum levels and cat food was found for (A) BB-209 (p < 0.007), (B) 2,4,6-TBP (p < 0.035), and (C) 6-OH-BDE47 (p < 0.002) (Figure 3).

Table 1. Summary of Concentrations of Some Brominated Compounds Analyzed in Cat Serum, House Dust, and Cat Food from 17 Swedish Households

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<th>Compound</th>
<th>Cat Serum (pmol/g lipid)</th>
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*Compound not analyzed.

4. DISCUSSION

4.1. Cats’ Exposure to BFRs via Dust. This study investigates cats’ exposure sources to BFRs and organochlorines. The levels of PBDEs in dust quantified here are in agreement with levels reported in dust from Stockholm houses and apartments. Cats have been used as models for indoor exposure of BFRs and organochlorines to look for possible correlations between house dust concentrations and the health status of cats. However, this is the first time a correlation can be statistically confirmed between cat serum and house dust, a result likely dependent on this study’s use of paired samples. This study also explored differences in concentrations between different rooms within a household. Interestingly, most of the correlations were found between serum and the living rooms, but serum concentrations showed poor correlation with dust from the bedrooms. This can be due to a higher concentration found in the living rooms as indicated in Figure 1 or to the possibility that these cats spend more time in the living rooms. Furthermore, when adding the dust concentration from all rooms, the correlation between serum

Figure 2. Concentrations of BDE-99 in cat serum and house dust (paired samples) from the living room, children’s and parents’ bedroom, and the sum of all rooms: n = number of cats; r² = coefficient of determination; τ = Kendall’s tau. If p < 0.05 for both r² and τ, a correlation was considered significant.
and dust for BDE-47 and BDE-153 was lost, possibly due to dilution effects.

The concentrations of lower PBDE congeners in pet cats in Sweden are within the same range as pet cats in the UK,38 1 order of magnitude lower than pet cats in Australia,9 and 200–400 times lower than in pet cats in the US.40 The concentration of BDE-209 has only been determined in pet cats from the US40 and in stray cats in Japan,41 with reported median level of 290 and 60 pmol/g lw, respectively, compared to 32 pmol/g lw determined in this study. The concentration range most probably reflects the different standards for protection against flammability in the different countries.22 The observation of no correlation between serum concentrations of BDE-209 and dust or food is likely explained by the short half-life of BDE-209.50 Also, the BDE-99 and BDE-209 congener profile is significantly different between humans and cats, indicating different exposure sources for these compounds. The BDE-47/-99 ratio has frequently been used to demonstrate an exposure to PBDEs, but it may also be formed through the metabolism of HCB.54

In cat serum, 6-OH-BDE47 (58 pmol/g lw) is the most common analyte with its presence in all samples. Only one more OH-PBDE (i.e., 2′-OH-BDE68) was detected in cat serum but only in 21% of the samples. High concentrations of 6-OH-BDE47 have previously been reported in Japanese stray cats (213 pmol/g lw), Swedish pet cats (135 pmol/g lw), and UK cats (4.0 pmol/g lw).15,39,41 The origin of 6-OH-BDE47 and 2′-OH-BDE68 found in the cat serum is most likely explained by food as a source rather than formed through PBDE metabolism. In a recent publication, it was demonstrated that cat liver microsomes have a very low capacity to oxidatively transform BDE-47 to hydroxylated metabolites.14,55 S-OH-BDE47, which was the major metabolite following 3-OH-BDE47, constituted 0.27% and 0.055% of total transformed BDE-47. 6-OH-BDE47 was only formed in trace amounts, i.e., 0.005% of total BDE-47. These findings demonstrate differences in metabolic capacity between cats and humans. Incubation of BDE-47 in human liver microsomes has previously shown 6-OH-BDE47 and 5-OH-BDE47 to be the major metabolites of human CYP450 induced metabolism.16,28

The natural occurrence of OH-PBDEs is well-known.32,56 OH-PBDEs and simple polybrominated phenols are produced naturally in the marine environment by marine plants and may enter the food chain by seafood.57,58 This is a possible route for naturally produced compounds to end up in cat food. This observation further strengthens the hypothesis of food as a source rather than formed through PBDE metabolism.

4.2. Cats’ Exposure to BFRs and Halogenated Phenolic Compounds via Food. In manufacturing cat food, it is mandatory that the raw material of the flavor must constitute at least 4% by weight. Commonly, a batch of cat food consists mainly of abattoir offal (e.g., lung, heart, liver, kidney, and throat) from mainly chicken (which is neutral in taste) but also from pig and cattle. Flavor is added during the final step of production. Hence 92–96% of the cat food from the same producer is very similar across the various flavors. Dry food is prepared in similar ways with a common batch boiled and then dried. Despite similar content, differences could be seen between dry and wet cat food. The higher brominated compounds, BDE-183 and BDE-209, could only be found in dry food, a finding also observed in another study.10 BB-209 was mainly found in dry food, although at low concentrations. Phenolic compounds, on the other hand, were mainly found in wet food and at a higher concentration than in dry food.

The highest concentrations of the phenolic compounds found in cat food relates to 2,4,6-TBP followed by PCP. Both compounds have a potency to bind to the transport protein for thyroxin and thereby disrupt the thyroid hormone balance, implicating a possible health effect on the cats.35 PCP has been reported at high concentrations in pet cat samples from Japan, Pakistan, and UK,38,39,42 but in this study, the concentrations are only one-fifth of these concentrations. In the past, PCP was used to preserve wood, but it may also be formed through the metabolism of HCB.54

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supports the evidence for this hypothesis since their food is likely influenced by fish from the Pacific Ocean, where 6-OH-BDE47 was first identified. 62

6-OH-BDE47 could be detected in 76% of the cat food in this present study, although at low levels. 6-MeO-BDE47 could be detected in 89% of the cat food samples but not in any cat serum samples. An earlier study of pooled cat serum indicated quantitative levels of 2-MeO-BDE68 in cat serum. 59

BB-209 was quantified in almost all cat serum samples (89%) and at levels (median 24 pmol/g lw) similar to BDE-209 (median 32 pmol/g lw) and the highly persistent CB-153 (28 pmol/g lw). BB-209 was reported in cat serum from two earlier studies 55,56 and in settled dust from a Swedish smelter facility that recycles electronic scrap. 60 It is evident that the flame retardant is being circulated even though its commercial production stopped in 2000. 1,22 However, BB-209 may still be detected in meat and fish samples for human consumption is more similar to the ratio generally found in humans, indicating adult human exposure to BDE-47 and BDE-99 to be a food source.

The correlation of 6-OH-BDE47 between cat serum and cat food supports the hypotheses of food as an exposure source of the natural produced 6-OH-BDE47. Metabolic capacity for BDE-47 in cats as demonstrated by cat liver microsomes is very low, and 6-OH-BDE47 is formed in negligible amounts (0.005% of BDE-47). Both house dust and cat food have been linked as a source of BB-209, although other sources need to be identified. About 35% of the cats had detectable levels of the flame retardant in their blood although not in their food or in the dust samples from the homes.

DBDPEs are present at relatively high levels and in all dust and cat food samples but not detected in the cat serum. This intriguing result could be interpreted as DBDPE having low bioavailability in cats and/or rapid metabolism. A low uptake following oral uptake is an observation recently reported in rats. 61 DBDPE has been reported in serum and milk from nursing women in Canada, although only in 5.9% and 8.6% of the samples 63 and not at all in Norwegian women. 64 Elevated levels of DBDPE were reported in chicken eggs and chicken from a recycling site in China. 65 DBDPE was reported in 90% of shellfish samples along the French coastlines 66 and at similar concentrations to PBDEs in fish from several rivers in Spain. 67 Considering the extensive application of DBDPE and its persistence and ubiquitous contamination worldwide. All cat samples contained BDE-209, whereas PCBs (CB-138 and CB-153 used as a marker) were only quantified in 63% of the cat samples. The concentrations of PBDE and PCB congeners were within the same order of magnitude and did not differ significantly. This study has confirmed the feasibility of using cats as models for indoor exposure to BFRs via dust, an exposure pathway especially important for children at a sensitive stage of development.

**ASSOCIATED CONTENT**

**Supporting Information**

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.6b05025.

Additional experimental details (clinical and chemical analysis including determination of thyroid hormone levels (T4 and TSH), blood lipids (cholesterol and triglycerides), chemicals, extraction, and cleanup of serum, house dust, and cat food, instrumental analysis, and quantification) and additional figures and tables (PDF)

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**Notes**

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