


# Cat serum contamination by phthalates, PCBs, and PBDEs versus food and indoor air

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**Abstract** A wide variety of endocrine disrupting compounds (EDCs) with semi-volatile properties are emitted to indoor air and, thus, humans might get exposed to these compounds. Pet cats spend the major part of their lifetime at home and might integrate indoor contamination so that they could mirror the human exposure. Three classes of EDCs, polybromodiphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), and phthalates (PAEs), were simultaneously considered and quantified in the serum of cats (*Felis silvestris catus*) living in the Paris area (France). The main compound concentrations by decreasing importance order were as follows: for PAEs, di-*n*-butyl phthalate (79,900 ng L<sup>-1</sup>) next di-*iso*-butyl phthalate

(53,200 ng L<sup>-1</sup>), di-*iso*-nonyl phthalate (43,800 ng L<sup>-1</sup>), and di-ethylhexyl phthalate (32,830 ng L<sup>-1</sup>); for PCBs, CB153 (1378 ng L<sup>-1</sup>) next CB52 (509 ng L<sup>-1</sup>), CB101 (355 ng L<sup>-1</sup>), CB110 (264 ng L<sup>-1</sup>), and CB118 (165 ng L<sup>-1</sup>); and for PBDEs, BDE 153/154 (35 ng L<sup>-1</sup>) next BDE47 (10.7 ng L<sup>-1</sup>). Total serum concentrations as mean ± standard deviation were 107 ± 98 μg L<sup>-1</sup> for ∑9PAEs, 2799 ± 944 ng L<sup>-1</sup> for ∑19PCBs, and 56 ± 21 ng L<sup>-1</sup> for ∑9BDEs. The three chemical groups were found in cat food: 0.088 ng g<sup>-1</sup> for ∑9BDEs, 1.7 ng g<sup>-1</sup> for ∑19PCBs, and 2292 ng g<sup>-1</sup> for ∑9PAEs and in indoor air: 0.063 ng m<sup>-3</sup> for ∑9BDEs, 1.5 ng m<sup>-3</sup> for ∑19PCBs, and 848 ng m<sup>-3</sup> for ∑9PAEs. Contaminant intake by food ingestion was approximately 100-fold higher than that by indoor air inhalation.

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**Highlights** 1. Phthalates, polychlorinated biphenyls, and polybromodiphenyl ethers were quantified in cat serum, food, and indoor air.  
2. Cat serum contamination levels were similar to those found in other European countries.  
3. Relationships between contaminants in cat serum versus indoor air or cat food were shown.  
4. Food intake was the prevailing contamination pathway.

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## Introduction

A wide variety of endocrine disrupting compounds (EDCs) with semi-volatile properties are found in a number of daily consumption products, leading to continuous emissions towards the atmosphere. Indoor volatilization of those compounds strongly increased over the last decades (Rudel and Perovich 2009). Assuming that humans spend approximately 95 % of their lifetime indoor, they are exposed subsequently through the respiratory tract to a large variety of chemicals occurring in the ambient air (Wormuth et al. 2006). In fact, human contamination may occur through breathing gas or particles sized below 1 μm, and also by ingestion of contaminated food that represents the prevailing intake pathway (Fournier et al. 2014; Mizukawa et al. 2013). However, methods of air sampling do not give information about peak

or maximal exposures because their collection time is limited to a few hours or days.

In urban environments, pet cats that remain predominantly indoor might integrate contaminants from the breathing of ambient air and the ingestion of settled dust, particularly through their licking habits. Consequently, they might mirror human exposure to indoor pollutants (Enriquez and Manet 2013). The use of such domestic animals for monitoring the exposure and its subsequent health issues should be helpful for knowledge improvement of public health challenges (Dirtu et al. 2013; Rabinowitz and Conti 2013; Schmidt 2009). However, its pertinence needs to be checked.

As a matter of fact, a wide range of EDCs have been detected in cat tissue and serum (Bellingham et al. 2013). The incidence of cats with feline hyperthyroidism increased clearly since the 1980s and represents today the most current endocrinopathy in that species. A possible involvement of polybrominated diphenyl ethers (PBDEs) in this pathology was suggested (Norrgran et al. 2012). Also, a strong incidence of hyperthyroidism in humans was also reported (Dye et al. 2007). Indeed, humans with very low thyrotropin blood concentrations ( $<0.5 \text{ mU L}^{-1}$ ) displayed high blood levels of polychlorinated biphenyls (PCBs) and of free thyroxine and triiodothyronine, supporting the hypothesis of a novel sporadic subclinical form of hyperthyroidism related to PCBs (Langer et al. 2007). In addition, an anti-estrogenic effect of PCBs by inhibition of the sulfo-conjugation of 17- $\beta$  estradiol was shown (Sharpe and Irvine 2004). Another chemical group, the phthalic acid esters (PAEs), were reported to affect multiple biochemical processes in wildlife as well as humans. These include alterations of reproductive physiology, damages to sperm quality, early onset of puberty in females, abnormalities of reproductive tract, infertility, and adverse outcomes of pregnancy, neurodevelopment, and allergies (Mankidy et al. 2013). Recent studies also indicated thyroid disrupting effects (Boas et al. 2010). These three chemical groups were currently identified in indoor air (Rudel and Perovich 2009). Besides, low dose exposure to mixtures of xenobiotics might induce unexpected adverse effects, whether additive, antagonistic, or synergistic adverse effects. The underlying molecular mechanisms of these cocktail effects at the molecular scale could contribute to the etiology of these diseases (Bellingham et al. 2012).

Since the population of pet cats is growing in France (i.e., 11.4 vs. 7.4 million dogs), the survey of cats through their serum or fur might be some help to both vet practitioners and toxicologists. Cats might be a useful sentinel species for the assessment of human exposure to indoor contamination and could allow the examination of endocrine disruption occurrence (Betts 2007; Potera 2007). Moreover, the presence of toxic chemicals in pets sounds as a cautionary warning for children that display a higher susceptibility to pollutants.

The current study is the first investigation in France of EDCs in pet cat blood and of the exploration of their

relationships with contamination of cat food and indoor air. Since pets share their indoor environment with humans, they might also share similar exposure sources. In that context, our objective was to assess pet cat exposure to three EDC groups currently found in food and indoor air, PAEs, PCBs, and PBDEs, through their blood serum concentrations considered to mirror their systemic impregnation. Compound concentrations were determined in cat serum, cat food, and indoor air. The respective parts played by ambient air and food as pollutant vectors were investigated.

## Materials and methods

### Sampling

#### Cats

Male cats were healthy laboratory animals, utilized as breeding stallion at the CERCA (Centre d'Etudes en Reproduction Canine Assistée) at the Ecole Nationale Vétérinaire d'Alfort (ENVA, Maisons-Alfort, 94700, France). They were kept free to move in close space equipped with litters and sawdust trays. Their food was uniform with pellets and they had free access to tap water. They did not receive any treatment. Two young cats aged 5.5 months (no. 1 and 2) and six adults (no. 3 to 8) were studied. Blood samples were collected in the morning after a 12-h fasting. They were stored at ambient temperature for 15 min to allow the formation of a clot containing the cellular elements. Then, the blood samples were centrifuged ( $900\times g$  for 5 min) prior to analyses.

#### Air

Indoor air was sampled for three successive periods of 2 weeks at the University Pierre et Marie Curie (75005, Paris) to explore the relationships between indoor air concentrations and serum concentrations of cats living in an indoor environment. The whole sampling method was the subject of a separate publication (Alliot et al. 2014). Briefly, the particulate phase was sampled onto a quartz fiber filter (porosity  $2.2 \mu\text{m}$  supplied by Whatman) and the gaseous phase onto XAD-2 resin (20–60 mesh). Thirteen grams of XAD-2 (Sigma-Aldrich, Saint-Quentin Fallavier, France) was used into two brass cartridges (13 mm diameter; 10 cm length). The filter was put into an open aluminum filter holder (Ecomesure, Janvry, France) and used under total suspended particle mode. In that disposal, the gaseous phase included fine particles with  $\text{Ø} < 2.2 \mu\text{m}$ . The sampler was connected to a sampling pump (Busch, model SV1005GP) equipped with a paddle dryer combined to a timer and an air flow meter (Hivolin, Germany). The air speed through the system was  $<170 \text{ cm s}^{-1}$  and a volume from 139 to  $154 \text{ m}^3$  of air was sampled.

## Food

The EDC concentrations of two varieties of food pellets used for cat feeding were determined. Analyses were performed as duplicates.

## Chemicals

Silica gel (40–63  $\mu\text{m}$ , 200  $\text{m}^2 \text{g}^{-1}$ ), neutral alumina (32–63  $\mu\text{m}$ , 200  $\text{m}^2 \text{g}^{-1}$ ), and C18 sorbents (40–63  $\mu\text{m}$ , 500  $\text{m}^2 \text{g}^{-1}$ , carbon load 18 %, end capped) were supplied by Interchim (Montluçon, France) and Florisil was supplied by Merck (150–250  $\mu\text{m}$ , 300  $\text{m}^2 \text{g}^{-1}$ , via VWR, Fontenay-sous-Bois, France). Acidic silica (44 % sulfuric acid, *w/w*) was prepared by mixing neutral silica gel (previously baked at 400 °C) with sulfuric acid (98 %). Sorbents used for column clean-up were baked at 400 °C (4 h) and stored at 150 °C before use. Gas chromatography quality solvents (Merck, Suprasolv) and sulfuric acid (>98 %, nitrogen analysis grade) were supplied by VWR. Helium and nitrogen (99.999 %) were supplied by Air Liquide (Paris, France).

A mixed solution of six PAE standards in isooctane (dimethyl phthalate, DMP; diethyl phthalate, DEP; di-*n*-butyl phthalate, *Dn*BP; butylbenzyl phthalate, BBP; diethylhexyl phthalate, DEHP; di-*n*-octyl phthalate, *Dn*OP) was purchased from Supelco (via Sigma-Aldrich, St. Quentin Fallavier, France). Di-*iso*-butyl phthalate (DiBP), di-*iso*-nonyl phthalate (DiNP), and di-*iso*-decyl phthalate (DiDP) were purchased from LGC (Dr Ehrenstorfer standards). A mixture of DEP D<sub>4</sub> and DEHP D<sub>4</sub> at 2000  $\text{ng mL}^{-1}$  in isooctane was used as IS and benzyl benzoate (Supelco) as SrS.

Mixed native PCB standard solutions and individual congeners were purchased from LGC Standards (Molsheim, France):

- Seven key isomer mix containing CB28, CB52, CB101, CB118, CB138, CB153, and CB180 each one at 10  $\mu\text{g mL}^{-1}$  in isooctane
- World Health Organisation (WHO) coplanar and mono-ortho PCB Mix containing CB77, CB81, CB126, and CB169 for non-ortho PCBs; CB105, CB114, CB118, CB123, CB156, CB157, CB167, and CB189 for mono-ortho PCBs, each one at 10  $\mu\text{g mL}^{-1}$  in isooctane.

CB30 and CB107 were used as ISs since they are not present in formulations or in environmental samples (Schulz et al. 1989). A working solution was prepared at a final concentration of 100  $\text{ng mL}^{-1}$  each one in isooctane (CB30 IS for CB28, CB52, CB101, CB105, and CB110 quantifications; CB107 IS for the other PCBs).  $^{13}\text{C}_{12}\text{CB194}$  was used as SrS for IS recovery determination.

Mixed native PBDE standard solutions were purchased from Cambridge Isotope Laboratories (via LGC Standards,

Molsheim, France). A BDE mixture contained BDE28, BDE47, BDE99, BDE100, BDE181, and BDE183, each one at 1  $\mu\text{g mL}^{-1}$ ; BDE153 and BDE154, each one at 2  $\mu\text{g mL}^{-1}$ ; and BDE209 at 5  $\mu\text{g mL}^{-1}$ .  $^{13}\text{C}_{12}\text{BDE47}$ ,  $^{13}\text{C}_{12}\text{BDE153}$ , BDE181 (each one at 50  $\mu\text{g mL}^{-1}$  in nonane), and  $^{13}\text{C}_{12}\text{BDE209}$  (50  $\mu\text{g mL}^{-1}$  in toluene) (Wellington Laboratories) were used as internal standards (ISs). A working solution was prepared in toluene, containing each IS at 0.5  $\mu\text{g mL}^{-1}$ , except  $^{13}\text{C}_{12}\text{BDE209}$  at 1.85  $\mu\text{g mL}^{-1}$ .  $^{13}\text{C}_{12}\text{BDE47}$  was used as IS for tri- to penta-BDEs, while  $^{13}\text{C}_{12}\text{BDE153}$  was used as IS for hexa- to hepta-BDEs and  $^{13}\text{C}_{12}\text{BDE209}$  was used to quantify BDE209. Chlorobiphenyl 209 (CB209; Sigma-Aldrich, St Quentin Fallavier, France) and bromobiphenyl 209 (BB209; Wellington Laboratories) were used as syringe standards (SrS) to determine IS recoveries.  $^{13}\text{C}_{12}\text{BDE47}$  and  $^{13}\text{C}_{12}\text{BDE153}$  were quantified against CB-209, while  $^{13}\text{C}_{12}\text{BDE209}$  was quantified against BB209.

## Extraction

The ISs were added to serum prior to extraction. Four liquid/liquid extractions by solvents of increasing polarity were carried out to 2 mL of serum. The first one was carried out with the addition of 3 mL hexane then ultrasonic treatment for 20 min, and after centrifugation (1000 $\times$ g for 5 min), the supernatant was collected. This operation was repeated three times successively with 5 mL of hexane/dichloromethane (50:50, *v/v*), then 3 mL of dichloromethane and, last, 1 mL of dichloromethane. The four supernatants were gathered and then concentrated to 500  $\mu\text{L}$  under a nitrogen stream.

For food, 2 g of pellets was finely crushed and then extracted following the same procedure as serum samples.

For indoor air samples, extractions were previously described (Alliot et al. 2014). XAD-2 resin was extracted on polypropylene cartridge by percolation/depression of 100 mL of dichloromethane (DCM) on a Visiprep system (Supelco) with low speed. A mixture of the ISs in acetone was deposited on the XAD-2 resin 1 h before extraction. The quartz fiber filters were extracted three times by 10 mL hexane/acetone (1:1) with an ultrasonic treatment for 20 min. They were spiked with the IS mixture 1 h before extraction. One blank was realized for three samples under the same conditions corresponding to a clean XAD-2 resin and a clean filter (matrix blank). In addition, one solvent blank was integrated to each analytical sequence. After extraction, the methodology used was similar for both gas and particle extracts.

## Fractionation and purification

The extracts were fractionated upon 1 g Florisil cartridge. After loading the extracts, PCBs and PBDEs were eluted with 2  $\times$  5 mL of hexane/dichloromethane (80:20, *v/v*) and then PAEs were eluted with 2  $\times$  5 mL of hexane/diethyl ether

(80:20, v/v). The two fractions were concentrated to 500  $\mu\text{L}$  under a nitrogen stream.

The PCB-PBDE fractions were purified on a multi-layer column consisting, from bottom to top, of 1 g of neutral alumina (activated at 150 °C for 12 h), 1 g of silica (activated at 150 °C for 12 h), and 1 g  $\text{H}_2\text{SO}_4$  impregnated silica (40 %, w/w). Columns were conditioned with 20 mL of hexane/dichloromethane (80:20, v/v), followed by 20 mL of hexane. After extract loading, 20 to 30 % of PCBs were eluted with 20 mL of hexane (fraction A) and PBDEs, and the remaining PCBs (70 to 80 %) were eluted with 15 mL of hexane/dichloromethane (80:20, v/v) (fraction B). Fraction A was kept at  $-20$  °C until analysis. Fraction B was concentrated to  $<1$  mL and then transferred to an injection vial with 25  $\mu\text{L}$  of iso-octane as solvent keeper. Finally, fraction B was concentrated to approximately 40  $\mu\text{L}$  and PBDEs were analyzed. Then, fractions A and B were combined and PCBs were analyzed.

## Analyses

The different SrSs were added to the final extracts prior to analyses (Table Supplementary Material SM 1).

PAE analyses were performed by GC/MS with a 7890A GC coupled to a 5975A MS (Agilent Technologies, Massy, France). The chromatographic characteristics were splitless injector 290 °C, column ZB-7HG (30 m, 250  $\mu\text{m}$  ID, 0.25  $\mu\text{m}$  film thickness), helium (carrier gas—1 mL  $\text{min}^{-1}$ ), and electronic impact detector (70 eV). The oven conditions were 50 °C for 1 min, then 30 °C/min to 280 °C and, next, 15 °C/min to 310 °C for 4 min. Analytical conditions for GC/MS and GC/MS/MS are described in Table SM 2.

The injection volume was 1  $\mu\text{L}$  for the three methods. Sample quantification was carried out by calculating the response factor for each compound relative to its corresponding IS, and concentrations were obtained using a linear regression analysis of relative responses versus relative concentrations.

PCB and PBDE analyses were performed by GC triple quadrupole mass tandem (EI, 70 eV) with an Agilent 7890A GC coupled to a 7000B triple quadrupole MS (Agilent Technologies, Massy, France). The chromatographic characteristics for PCBs were splitless injector 280 °C, injection volume = 1  $\mu\text{L}$ , column ZB-5MS SGE (50 m  $\times$  220  $\mu\text{m}$   $\times$  0.25  $\mu\text{m}$  film thickness), helium (carrier gas—40 psi), and electronic impact detector (70 eV). The oven conditions were 80 °C for 2 min, 30 °C/min to 170 °C, and 3 °C/min to 300 °C, for 3 min. The chromatographic characteristics for PBDEs were splitless injector 280 °C, column Rtx-5Sil MS (15 m  $\times$  250  $\mu\text{m}$   $\times$  0.1  $\mu\text{m}$  film thickness), helium (carrier gas—1.8 mL  $\text{min}^{-1}$ ), and electronic impact detector (70 eV). The oven conditions were 102 °C for 0.8 min, 25 °C/min to 185 °C, 15 °C/min to 270 °C, 5 °C/min to 285 °C, and 30 °C/min to 315 °C, for 3.1 min.

## Method quality controls

Most PAEs get fragmented into characteristic ions such as  $m/z$  149, except DMP ( $m/z$  163), and their fragmentation patterns allow a sensitive and selective detection in the Selected Ion Monitoring (SIM) mode. For PCBs and PBDEs, the Multiple Reaction Monitoring mode (MRM) separates masses in two stages, making the instrument significantly more selective than a single quadrupole system. As a result, even components that could not be analyzed by conventional scan or SIM modes could be easily identified and quantified particularly in case of complex matrices.

The column separation obtained with the three methods was suitable with an accurate quantification (Fig. SM 1). In terms of linearity and of dynamic range, the performance was checked by setting a range of increasing concentrations for the different compounds. The calibration curves were linear from 32.5 to 8000 ng for PAEs, from 0.2 to 200 ng for PCBs, and from 2 to 500 pg for PBDEs, and the correlation coefficients were  $>0.997$  ( $p < 0.001$ ).

Three laboratory blanks were run for each series simultaneously with sample treatment (Table SM 3). Sample measurements were corrected by the concomitant procedural blanks for all compound families. The PAE ubiquity raises real difficulties for treatment and analysis processes that require careful controls of blank concentrations. Also, special care was taken for solvent quality and glassware cleaning procedures to avoid sample contamination.

The instrument detection limits (IDLs) were considered for the less concentrated standard solution for each compound as the concentration with a signal/noise ratio of 3, peak to peak (Table SM 4). The IDLs ranged respectively from 0.06 to 15 pg for PAEs, from 0.03 to 0.17 pg for PCBs, and from 0.24 to 7.5 pg for PBDEs (Table SM 4).

The limit of quantification (LOQ) was considered as the concentration (ng  $\text{L}^{-1}$ ) with a signal/noise ratio of 9, peak to peak. The LOQs were determined as triplicates (Table SM 4). The LOQs displayed low limits of quantification for all compounds, except PAEs, related to the lower sensibility of single MS detection as compared to that with tandem MS/MS (Table SM 3). However, LOQs remained compatible with serum concentrations and allowed PAE quantification in a sample volume of 2 mL.

Recoveries determined for the ISs by the use of SrSs ranged from 65 to 90 % (Table SM 5).

## Expression of results and statistics

Results were expressed as nanograms per liter for serum concentrations, as nanograms per square meter for indoor air concentrations, and as nanograms per gram for food contents.

PAEs were expressed as individual compounds and as the sum of total PAEs ( $\Sigma$ 9PAEs). PCBs were expressed as the

sum of seven PCB indicators ( $\sum$ PCBi) of the European Norm: CB28, CB52, CB101, CB118, CB138, CB153, and CB180 ( $\sum$ PCBi); as the sum of 12 dioxin like-PCBs ( $\sum$ PCB-DL): CB77, CB81, CB126, and CB169 for non-ortho PCBs and CB105, CB114, CB118, CB123, CB156, CB157, CB167, and CB189 for mono-ortho PCBs; and as the sum of total PCBs ( $\sum$ 19PCBs). PBDEs were expressed as individual compounds and as the sum of total PBDEs ( $\sum$ 9PBDEs).

Total indoor air concentrations were considered by adding the gaseous and the particulate phases, the ultrafine particles ( $<1 \mu\text{m}$ ) displaying the ability to reach the blood flow through the alveoli barrier (Rundell et al. 2007).

Inputs from food intake were estimated by the cat pellet daily consumption: 55 g. Inputs from indoor air breathing were estimated by the air volume inhaled daily:  $1.3 \text{ m}^3$ , corresponding to a tidal volume of 30 mL and a respiratory frequency of  $30 \text{ cycles min}^{-1}$  (Lafarge 2001).

Relationships between cat serum and indoor air concentrations or food contents were explored using the ratios serum/air and serum/food.

When the concentration in a sample was below the LOQ, the LOQ was divided by two and used for the mean calculation (Decree July 08 (2010)).

## Results and discussion

### Indoor air and cat food contamination

#### *Indoor air contamination*

The three families of compounds were found in the indoor air. The global trend of indoor air contamination by decreasing importance order was PAEs > PCBs > PBDEs. A similar sequence order in indoor air environments of different European countries was reported (Rudel and Perovich 2009). PAE concentration was  $848 \text{ ng m}^{-3}$  as  $\sum$ 9PAEs. DiNP and DiBP were the main compounds with concentrations of 263 and  $248 \text{ ng m}^{-3}$ , respectively, followed by DEP next DnBP and last DEHP (Fig. 1). Similarly, in the indoor air from 30 French dwellings, a concentration of  $682 \text{ ng m}^{-3}$  as  $\sum$ 8PAEs was found, DiBP being the major compound up to  $356 \text{ ng m}^{-3}$  (Blanchard et al. 2014).

Total PCB concentration was  $1.5 \text{ ng m}^{-3}$  with a predominance of low molecular weight congeners such as CB28 ( $0.18 \text{ ng m}^{-3}$ ) and CB52 ( $0.86 \text{ ng m}^{-3}$ ) (Fig. 1). Our study showed a similar congener pattern to that found in the air of apartments from urban areas of Italy (Menichini et al. 2007). The concentrations were within the same order of magnitude as those observed in homes and offices in the UK and Canada, from 2003 to 2006 (Hazrati and Harrad 2006; Zhang et al. 2011). PCBs were banned in dispersive uses in France in 1975 (Decree of 8 July 1975) and restricted to in-service

equipment by a second decree in February 1986. Finally, in February 2003, a decree recommending the elimination of all equipment containing PCBs before the end of 2010 came into force. However, an unknown stock of PCBs is persisting: buried landfills and other waste-handling facilities as well as diffuse sources such as electrical wiring and paints (Diamond et al. 2010). More recently, new “non-Aroclor” PCBs were detected in paints as by-products of diarylide yellow (Rodenburg et al. 2010) and other pigment production (Anezaki et al. 2015).

Total PBDE concentration was  $0.071 \text{ ng m}^{-3}$ . BDE209 ( $0.041 \text{ ng m}^{-3}$ ) then BDE47 ( $0.020 \text{ ng m}^{-3}$ ) were the major compounds, followed by BDE99/100 ( $0.008 \text{ ng m}^{-3}$ ) (Fig. 1). These results are consistent (1) with a previous study in indoor air in France, with a total PBDE concentration of  $0.017 \text{ ng m}^{-3}$ , the main compounds being BDE209 then BDE47 and BDE99 (Blanchard et al. 2014; Moreau-Guigon and Chevreuil 2014), and (2) with data from Germany (Fromme et al. 2009) and from Sweden (Thuresson et al. 2012).

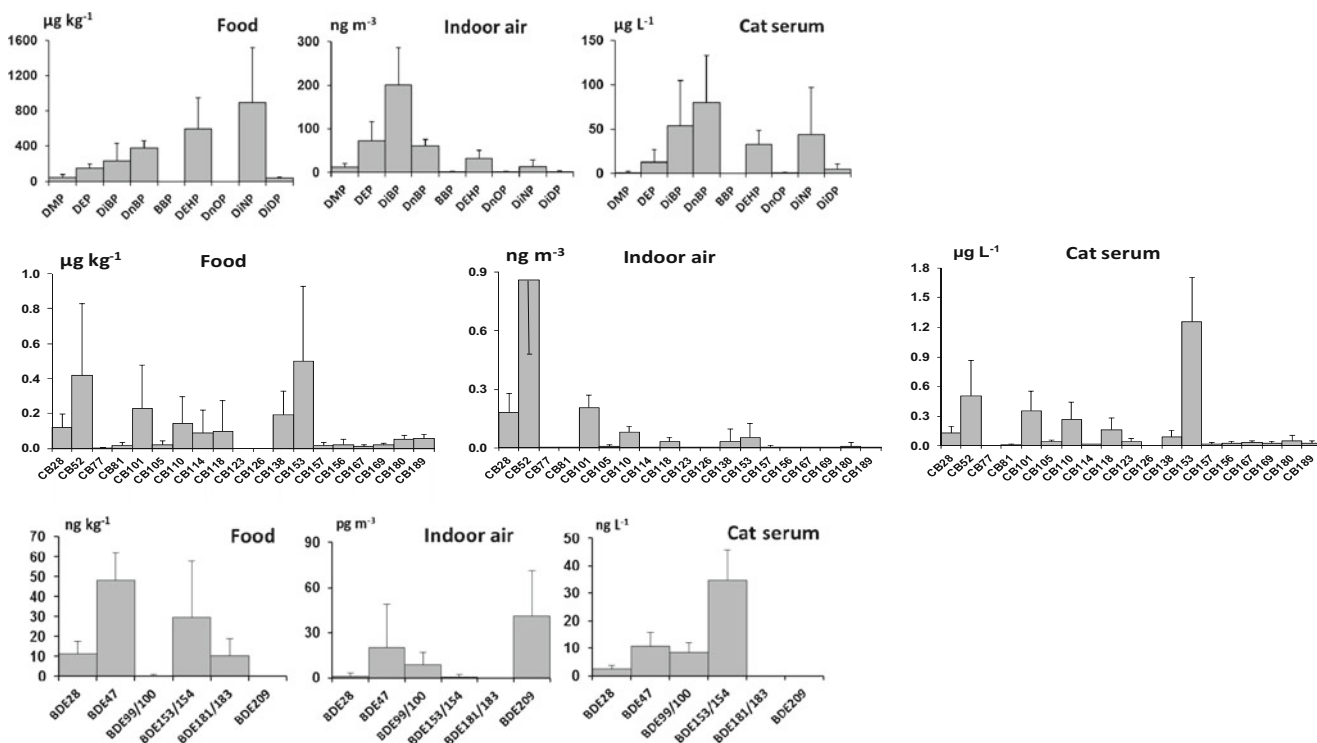
For nearly all compounds, except BDE47, BDE99/100, BDE 209, and the high molecular weight PAEs (DEHP, DiNP, and DiDP), the distribution in the bioavailable phase was prevailing (>65 %). PCBs were almost exclusively in the bioavailable phase (>90 %), with a decreasing ratio from low to high molecular weight congeners (Fig. 2). Semi-volatile organic compounds like PBDEs and PCBs bound to fine particles, display a higher bioavailability than those bound to coarse particles as they can cross the alveoli barrier, and have a longer pulmonary residence time (Kim et al. 2014). In that way, Rundell et al. (2007) reported that breathed fine particles ( $\text{Ø}=0.2$  to  $1 \mu\text{m}$ ) could be translocated from lung alveoli to the systemic circulation.

#### *Food contamination*

Many of the compounds studied were present in commercial food. The average compound concentrations in cat food were  $2292 \text{ ng g}^{-1}$  for total PAEs, DiNP ( $984 \mu\text{g kg}^{-1}$ ) then DEHP ( $599 \mu\text{g kg}^{-1}$ ) being the prevailing compound;  $1.7 \text{ ng g}^{-1}$  for total PCBs, CB153 ( $0.50 \mu\text{g kg}^{-1}$ ) then CB52 ( $0.42 \mu\text{g kg}^{-1}$ ) prevailing; and  $0.088 \text{ ng g}^{-1}$  for total PBDEs, BDE47 ( $0.048 \mu\text{g kg}^{-1}$ ) then BDE153/154 ( $0.030 \mu\text{g kg}^{-1}$ ), underlining strong discrepancies of contamination levels among the three EDC families (Fig. 1).

On the whole, the cat food contamination was similar to that reported in other countries. In Italy, DEHP detected in cat food samples ranged from 2500 to  $8700 \mu\text{g kg}^{-1}$  (Ežerskis et al. 2007).

For PCBs, similar concentrations of total PCBs were found in cat food, with a mean concentration of  $4.1 \mu\text{g kg}^{-1}$  in Japan (Kunisue et al. 2005) and of  $2.69 \mu\text{g kg}^{-1}$  in Spain (Ruiz-Suarez et al. 2015) and the PCB indicators at a frequency of



**Fig. 1** Distribution of PAEs, PCBs, and PBDEs in food, indoor air (gas + particle), and cat serum

100 %. In both studies, the low molecular weight congeners were prevailing.

On the other hand, for total PBDEs, in the USA, a high mean concentration of 2.6 µg kg<sup>-1</sup> was found in cat food (Dye et al. 2007) that might be explained by the use of penta-BDE commercial mixtures in that country.

**Cat serum contamination**

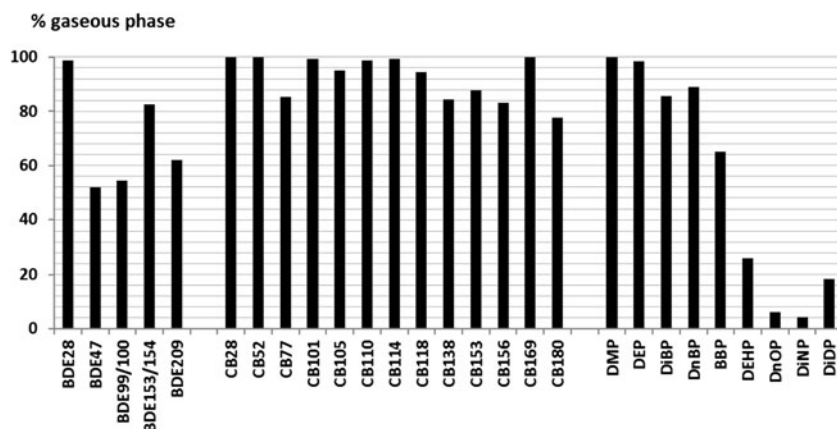
*PAEs*

In cat serum, DnBP was the main compound, followed by DiBP and DiNP (Table 1, Fig. 3), whereas in terms of production and usage, DEHP remained the most important PAE,

followed by DiNP, DiDP, and DiBP (German Federal Environment Agency 2011). No concentration differences were found between young and adult cats, and important discrepancies were observed between individuals, ranging from 81,000 to 451,000 ng L<sup>-1</sup> as Σ9PAEs (Table 1). Mean DEHP concentration in cat serum (32,800 ng L<sup>-1</sup>) was in the same range, remaining above human levels (from 11,600 to 18,500 ng L<sup>-1</sup>) (Inoue et al. 2005).

Up to now, no data for PAEs in cat serum were available in the literature. PAEs found in a number of products of everyday life were involved in estrogenic effects (Akingbemi et al. 2004), and their potential to affect thyroid signaling was demonstrated in animal experiments (Meeker 2010). As a consequence, pets as well as humans might be exposed through

**Fig. 2** Distribution of compounds in the gaseous phase of indoor air



**Table 1** Concentrations of PAEs, PCBs, and PBDEs in cat blood serum (ng L<sup>-1</sup>)

ng L <sup>-1</sup>	1 (y)	2 (y)	3 (a)	4 (a)	5 (a)	6 (a)	7 (a)	8 (a)	Mean	SD
DMP	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	400	3000	600	600	1300
DEP	1200	25,500	6700	23,100	5400	<LOQ	1900	21,200	12,700	14,100
DiBP	21,400	57,200	22,500	168,500	12,400	14,400	63,300	66,200	53,200	51,600
DnBP	42,800	10,600	<LOQ	134,500	<LOQ	<LOQ	87,900	123,800	79,900	52,700
DEHP	14,200	33,900	26,400	<LOQ	64,400	23,100	35,800	31,700	32,830	15,700
BBP	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ		
DnOP	<LOQ	<LOQ	1100	<LOQ	<LOQ	<LOQ	1100	<LOQ	1100	
DiNP	<LOQ	<LOQ	130,000	105,000	44,000	<LOQ	70,000	<LOQ	43,800	52,900
DiDP	<LOQ	<LOQ	<LOQ	19,500	7500	<LOQ	<LOQ	<LOQ	4600	6400
∑9PAEs	81,000	128,000	190,000	451,000	134,000	40,000	267,000	262,000	107,000	98,000
CB28	<LOQ	90	179	80	244	112	116	118	134	58
CB52	88	307	1091	334	795	626	719	117	509	355
CB77	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	
CB81	3	21	<LOQ	20	13	18	<LOQ	<LOQ	15	7
CB101	<LOQ	234	734	357	289	273	486	117	355	201
CB105	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	58	50	18	42	21
CB110	<LOQ	64	525	399	91	184	319	<LOQ	264	182
CB114	<LOQ	19	<LOQ	27	<LOQ	<LOQ	<LOQ	<LOQ	23	
CB118	<LOQ	45	149	99	342	276	81	<LOQ	165	118
CB123	78	63	32	26	<LOQ	46	33	83	45	28
CB126	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ		
CB138	56	171	185	7	44	99	120	29	89	66
CB153	1088	1496	1239	1229	1449	1174	1223	1128	1378	450
CB156	<LOQ	<LOQ	8	10	43	23	14	<LOQ	19	15
CB157	18	15	30	<LOQ	57	39	26	<LOQ	31	15
CB167	7	41	<LOQ	<LOQ	53	33	40	<LOQ	35	17
CB169	<LOQ	<LOQ	25	<LOQ	48	32	17	18	28	13
CB180	68	143	23	<LOQ	<LOQ	14	20	<LOQ	54	54
CB189	<LOQ	<LOQ	58	<LOQ	12	14	<LOQ	<LOQ	28	26
∑PCBi	1299	2487	3601	2105	3162	2574	2766	1509	2438	782
∑PCB-DL	107	204	302	182	568	540	260	120	285	178
∑19PCBs	1406	2710	4279	2586	3479	3022	3264	1628	2797	947
BDE 28	1.2	<LOQ	<LOQ	<LOQ	<LOQ	2.2	3.7	<LOQ	2.4	1.2
BDE 47	3.7	4.6	11.7	16.4	10.9	11.9	15.4	<LOQ	10.7	4.9
BDE 99/100	16.6	7.3	4.6	8.9	9.5	5.5	7.6	6.8	8.4	3.7
BDE153/154	59.8	32.9	24.8	26.1	38.4	33	31.2	31.7	34.7	11
BDE 181/183	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ		
BDE 209	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ		
∑9BDEs	81.3	44.8	41.1	51.4	58.8	52.6	57.9	38.4	56.1	20.8

<LOQ below the limit of quantification, (y) young, (a) adult

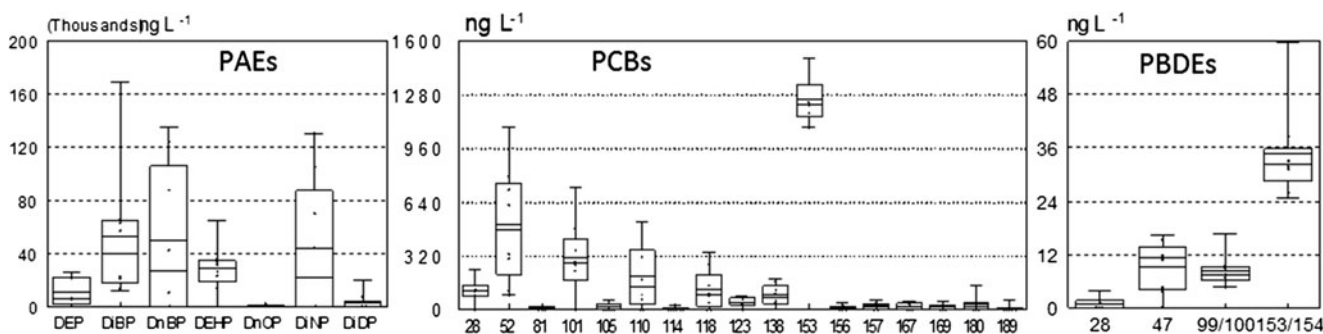
digestive or respiratory routes to a wide variety of chemicals occurring in food, air, water, and dust, mostly at low doses, the dermal pathway remaining of minor importance (Fournier et al. 2014).

### PCBs

PCBs, well known to be highly resistant to biodegradation, were found at concentrations ranging from 1406 to

4279 ng L<sup>-1</sup> as ∑18PCBs in cat serum (Table 1, Fig. 3). Nevertheless, CB138 was close to the LOQ and some dioxin-like congeners (CB77, CB123, CB114, CB115) failed to be found (Table 1). Few data were available about the characterization of PCB congeners in pet serum, particularly PCB-DL. In the USA, PCB concentrations in canine serum ranged from 1 to 3 μg L<sup>-1</sup> (Schilling et al. 1988).

In our study, ∑PCBi concentrations ranged from 1299 to 3601 ng L<sup>-1</sup> and ∑PCB-DL concentrations ranged from 107



**Fig. 3** Concentrations of PAEs, PCBs, and PBDEs in cat serum ( $n = 8$ ), as mean, median, and 5th and 95th percentile

to 568 ng L<sup>-1</sup> (Table 1). Our concentrations were higher than those of house cats in California (Guo et al. 2012): for CB101, 355 against 33 ng L<sup>-1</sup>; for CB105, 42 against 6 ng L<sup>-1</sup>; for CB118, 165 against 35 ng L<sup>-1</sup>; for CB153, 1378 against 96 ng L<sup>-1</sup>; and for CB180, 54 against 47 ng L<sup>-1</sup>. However, literature data indicated strong discrepancies among PCB and PBDE concentrations in animals according to the location worldwide (Ali et al. 2013).

We observed a high variability of concentrations among congeners in serum, with a clear prevalence of CB153 (Fig. 3). Among the PCB<sub>i</sub>, the rank order was CB153 > CB52 > CB101 > CB110 > CB118 > CB138 > CB180. This observation was consistent with the tendency of some highly chlorinated PCBs to bioaccumulate in tissues of animals as compared to slightly chlorinated ones (Beyer and Biziuk 2009). In Pakistan, significantly higher PCB levels in cat serum as compared to dogs and inversely for HO-PCBs were reported, suggesting lower metabolic abilities in cats than in dogs (Ali et al. 2013). Similarly, in Spain, plasma levels of PCBs were significantly higher in cats than in dogs, although dietary intake of dogs was over twice higher than for cats (Ruiz-Suarez et al. 2015). Moreover, in Italy, in adipose tissue of cats, higher PCB levels than in dogs were observed. The main congeners were CB153, then CB138 and CB180, with an occurrence frequency of 100 %, while it was only 3.8 % for CB52 (Storelli et al. 2009).

**PBDEs**

PBDE concentrations in cat serum ranged from 2.4 to 34.7 ng L<sup>-1</sup> (Table 1 and Fig. 3). The rank order was BDE153/154 > BDE47 > BDE99/100 > BDE28. For BDE181/183 and BDE209, concentrations were below the LOQ. However, the LOQ for BDE209 was 8- to 70-fold higher than for the other PBDEs due to a lower sensitiveness of the MS/MS detector for this particular compound.

In Pakistan, similar range concentrations from 3.5 to 69 ng L<sup>-1</sup> as ΣPBDEs were reported (Ali et al. 2013). In the USA, a spectrum of PBDEs in all the studied cats, with the sequence BDE47 < BDE99 < BDE207 < BDE209, was

reported (Dye et al. 2007). Total PBDE concentrations in US cat serum, ranging from 4.3 to 12.7 ng mL<sup>-1</sup>, were 20- to 100-fold higher than median concentrations found in US adult humans. Particularly high BDE concentrations of 1230 to 44,000 ng L<sup>-1</sup> were found in California house cats (USA) which was approximately 50-fold higher than the levels of human residents in the same region (Guo et al. 2012).

However, these investigations were performed in countries with a regulation for PBDEs that is different from the European one: PBDE uses in California were prohibited since 2006 only (California Environmental Protection Agency 2006). In the beginning, PBDEs were composed of three major commercial formulations: penta-BDEs, octa-BDEs, and deca-BDEs (de Wit et al. 2010). Since 2003, penta- and octa-BDEs were banned for use in all applications for the European Union market (Directive 2003/11/EC). Deca-BDE was registered under the “Registration, Evaluation, Authorisation and Restriction of Chemicals” (REACH) in 2010 and, thus, its uses were restricted to applications such as automotive equipment, textiles, and construction and suppressed for electric and electronic equipment (Deca-BDE Factsheet 2012). The phasing out of deca-BDE in the USA started in the end of 2013. BDE47 was the most volatile BDE detected (vapor pressure 3.3 × 10<sup>-4</sup> Pa) and the most abundant. In spite of its ban in the European Economic Community since July 2008, this compound might originate from several sources, including emissions from the components of electronic equipment such as computers (desktops and notebooks), printers (laser, ink-jet, and all-in-one machines), and photocopy machines (Destailats et al. 2008).

The high PBDE concentrations reported in cat serum, as compared to human one, might be related to cat licking behavior and also to the poor PBDE elimination in cats, the degradation of PBDEs to OH-PBDEs being a minor metabolic pathway. A possible alternative for PBDE elimination could be the cleavage of the diphenyl ether bond, leading to production of one ring brominated phenols. Indeed, bromophenols were detected in higher quantities than OH-PBDEs in cat serum (Norrgran et al. 2012).



## Relationships between cat serum and air/food contaminations

Intake estimations via indoor air inhaled or food ingested by cats are reported in Table 2. The ratio between the two contamination intake routes highlights the prevalence of food ingestion as compared to indoor air breathing.

The PAE pattern of cat serum was similar to that of food and of indoor air, and the two isomers DnBP and DiBP represented together 60 % of the whole PAE amount (Fig. 1). The major PAE intakes reported for humans in France were DEHP and DnBP (Blanchard et al. 2013). Even though PAE patterns in cat serum are not quite similar to those observed in humans, this study emphasizes the fact that, like humans, pet cats are contaminated by the same groups of air pollutants (De Nardo 2002). In that way, pets, being exposed to the same “pollutant mixtures” as humans, might contribute to improve knowledge of environmental health issues.

For PCBs, the global trend in the three matrices showed a predominance of PCB<sub>i</sub> as compared to coplanar and mono-ortho substituted congeners (Fig. 1). The pattern of PCBs in cat serum was correlated with that of food ( $r=0.932$ ,  $p<0.001$ ) with a predominance of CB153 then CB52, which is consistent with the prevalence of a dietary source of exposure and the high potency of PCBs to bioaccumulate (Fig. 2). A relationship between human thyroid disruption and PCBs occurrence was suggested (Meeker 2010). Indeed, PCBs that were banned in insulating fluids and transformers since the 1980s are still created as by-products of some combustion processes such as incineration (Beyer and Biziuk 2009) or as by-products of diarylide yellow or other pigment production (Rodenburg et al. 2010) and must be taken into account. In Sweden, concentrations of CB138, CB153, and CB180 characterized in serum of cats under non-hyperthyroid, hyperthyroid, and hyperthyroid medication were similar to those found in the human population, indicating similar routes of uptake, most likely via food (Kupryianchyk et al. 2009). Similarly to humans, dietary intake of PCBs is a major exposure route for pet contamination, but indoor dust ingestion by cats can represent another exposure pathway (Dirtu et al. 2013). In Spain, cat plasma levels around  $90.9\pm 45.7$  ng g<sup>-1</sup> lipid weight were

reported as the consequence of dietary intakes from industrial food of  $41.4\pm 32.1$  ng kg<sup>-1</sup> body weight per day (Ruiz-Suarez et al. 2015).

For PBDEs, no relationship was found between patterns of cat serum and those of food or air (Fig. 1). The main compounds were BDE153/154 in serum whereas BDE47 was predominant in food and BDE209 in air (Fig. 1). This result is in line with literature data (Guo et al. 2012) and might be explained by an enhanced biodegradation of PBDEs, as compared to the minor metabolism of PCBs. Lupton et al. (2009) showed that human liver microsomes metabolized BDE47 and BDE99 but not BDE153, which could provide a hypothesis for the high bioaccumulation rate of BDE153 in humans and in cats. Guo et al. (2012) reported a lower proportion of BDE209 in cat serum than in house dust linked to metabolic debromination by biologic system in cats. Cats may swallow PBDEs in food and by licking house dust due to their meticulous grooming habits. The potential link between PBDEs and hyperthyroidism is still discussed, but literature data suggest that cats (monitored by serum concentration tracking) might be sentinels of exposure for family members, particularly for crawling toddlers (finger to mouth reflexes) and also possible sentinels of health chronic effects (Betts 2007) as their PBDE load happens to be much higher than that of humans. Dust ingestion by cats is 7-fold higher than by adult humans. In 2008, the Environmental Working Group (non-governmental association) analyzing pet serum showed that it was contaminated by 48 among the 70 chemicals tracked and that cats may display levels of PBDEs more than 20-fold higher than humans ( $5.2$  ng mL<sup>-1</sup> vs.  $0.1$  to  $0.2$  ng mL<sup>-1</sup>) (EWG 2008). A line of research for the future could be the investigation of PBDE metabolites (OH-PBDEs and polybromophenols) since their quantifications were validated as well in cat sera as in humans (Dahlberg et al. 2014).

## Conclusion

The investigation of three EDC groups simultaneously, PAEs, PCBs, and PBDEs, were developed for the first time in cat blood serum in France. Together, cat food and indoor air were explored.

**Table 2** Intakes of PAEs, PCBs, and PBDEs through the digestive tract (food intake) and the respiratory tract (indoor air intake) (ng day<sup>-1</sup>)

	Indoor air intake (ng day <sup>-1</sup> )	Food intake (ng day <sup>-1</sup> )	Indoor air/food intakes
DEHP	42	3300	$0.1 \times 10^{-2}$
∑9PAEs	1100	7400	$1.5 \times 10^{-2}$
∑PCBi	1.8	72	$2.5 \times 10^{-2}$
∑PCB-DL	0.06	22	$0.3 \times 10^{-2}$
∑19PCBs	1.9	96	$2.0 \times 10^{-2}$
BDE47	0.055	2	$2.7 \times 10^{-2}$
∑9PBDEs	0.08	4.8	$1.7 \times 10^{-2}$

These simultaneous quantifications might be of interest given the potent toxic interactions suspected between pollutants.

The contamination levels of indoor air and of cat food were in line with the literature from other countries of Europe likely related to the common European regulations.

New considerations brought about relationships between systemic contamination and ingested food or breathed air. It appears that all the three pollutant levels as well as their distribution patterns encountered in cat serum seem to result from a combined influence of contaminated diet and indoor air breathing. However, the prevailing contamination pathway was clearly through the digestive tract, which is consistent with previous data. These findings raise the question of the pertinence of using house cats as sentinels for assessing chronic exposure to contaminants via indoor life.

From our findings, it would be of interest to develop in the future cohort studies using non-invasive markers both strong and easy such as cat hair EDC contents.

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