Comprehensive two-dimensional gas chromatography coupled to high resolution time-of-flight mass spectrometry for screening of organohalogenated compounds in cat hair

Martin Brits [a,b,c], Peter Gorst-Allman [d], Egmont R. Rohwer [c], Jayne De Vos [a], Jacob de Boer [b], Jana M. Weiss [ef]

[a] National Metrology Institute of South Africa (NMISA), CSIR Campus, Meiring Naude Road, Pretoria 0040, South Africa

[b] VU University, Department Environment and Health, De Boelelaan 1087, 1081 HV Amsterdam, The Netherlands

[c] Laboratory for Separation Science, Department of Chemistry, Faculty of Natural and Agricultural Sciences, University of Pretoria, Lynnwood Road, Pretoria 0002, South Africa

[d] LECO Africa, Kempton Park, South Africa

[e] Department of Environmental Science and Analytical Chemistry, Arrhenius Laboratory, Stockholm University, SE-10691 Stockholm

[f] Department of Aquatic Sciences and Assessment, Swedish University of Agricultural Sciences, SE-750 07 UPPSALA

Highlights:

- Analysis of organohalogenated compounds by GC×GC coupled to HR-TOFMS
- First results for non-target analysis of pet cat hair samples
- Mass spectral database searches and elemental formula prediction for compound identification
- Classical and novel environmental contaminants found in cat hair samples
- Detection and identification of emerging flame retardants in the South African indoor environment

Abstract

The coupling of comprehensive two-dimensional gas chromatography with high-resolution time-of-flight mass spectrometry offers the best separation efficiency combined with accurate mass measurements over a wide mass range. The tremendous power of this screening tool is illustrated by trace qualitative

screening analysis of organohalogenated compounds (OHCs) in pet cat hair. Tentative identification was supported by mass spectral database searches and elemental formula prediction from the experimentally determined accurate mass data. This screening approach resulted in the first tentative identification of pentabromoethylbenzene, decabromodiphenyl ethane, hexabromocyclododecane, trisbromoneopentyl alcohol, tris(2-chloroethyl) phosphate and tris(2-chloroisopropyl)phosphate in the South African indoor environment. A total of seventy-two OHCs were identified in the samples and include known flame retardants, such as polybrominated diphenyl ethers, and legacy contaminants such as polychlorinated biphenyls and organochlorine, organophosphorous and pyrethroid pesticides. The results obtained from cat hair indicate that these pets are exposed to complex mixtures of OHCs and the detection of these compounds suggests that non-invasive cat hair samples can be used to model indoor exposure with reference to external deposition of OHCs present in the air and dust surrounding people. Toddlers share the same environment as pet cats and therefore also the same health risks.

Keywords: Two-dimensional gas chromatography; High-resolution time-of-flight mass spectrometry; Pet cat hair; Organohalogenated compounds; Indoor exposure to pollutants

Corresponding author: Martin Brits (mbrits@nmisa.org/ m.brits@vu.nl)

1. Introduction

Organohalogenated compounds (OHCs) constitute one of the largest and most diverse groups of chemicals characterised by the presence of one or more halogens. Among this group of chemicals polychlorinated biphenyls (PCBs), organohalogen pesticides and brominated flame retardants (BFRs) have been widely used in industry and society. The pesticides were intentionally introduced into the environment while the PCBs and BFRs unintentionally leached from electronic and electric equipment, textiles and other materials. Recently, a review on dust related contaminants reported that 485 compounds have been identified in literature [1]. Many of these OHCs are toxic, persistent, and resistant to environmental degradation and are included or listed for inclusion in the Stockholm Convention on persistent organic pollutants (POPs) (http://chm.pops.int/). In addition to these priority pollutants, several potentially persistent and bio-accumulative chemicals currently in use are regularly detected in

a variety of environmental matrices [2]. Because of their ubiquitous prevalence and use in household items and consumer products, indoor contamination may be a significant source of human exposure to OHCs, especially for toddlers.

Many OHCs are known to have adverse neurotoxic effects, such as the development of the brain [3]. Studies also suggest that postnatal exposure to polybrominated diphenyl ethers (PBDEs) is associated with a higher risk of certain Attention Deficit Hyperactivity Disorder (ADHD) symptoms and poor social competence of children at the age of 4 years [4]. Household dust was shown to be a major source of human exposure to OHCs [5]. The exposure to BFRs in indoor environments can overshadow that of the outdoor environment due to strong indoor sources, poor ventilation, deposition and organic film build-up on indoor surfaces, resuspension of indoor dust caused by human activities and slower chemical degradation [6]. Pets, especially cats, share similar environments with toddlers and have been presented as a potential bio-sentinel for indoor pollution exposure [7]. Apart from inhalation, their meticulous grooming make cats particularly susceptible to exposure to house dust and in turn, to the chemicals accumulated on dust particles. OHCs have been reported in cat blood [7,8] and detected in hair samples taken from pet cats and dogs from Pakistan [8]. Hair, as a non-destructive monitoring system, has been used as a bio-indicator for human exposure to organic pollutants [9]. Being a non-invasive matrix, hair samples allow for sample stability, information on short to long term exposure (depending on the length of the hair) and the high lipid content allows for the analysis of a wide variety of lipophilic OHCs. Hair is also directly exposed to the environment allowing for continuous accumulation of environmental contaminants from air or dust particles.

Several OHCs are complex mixtures, consisting of several theoretically possible congeners [10]. Mass spectrometry (MS) is the detection technique most extensively used for non-targeted analysis of OHCs. Recent screening studies employed liquid chromatography (LC) and comprehensive two-dimensional liquid chromatography (LC×LC), hyphenated to an Orbitrap analyzer and high resolution time-of-flight mass spectrometer (HR-TOFMS) [11,12]. Gas chromatography was predominately used as separation technique for OHC screening analysis coupled to different MS systems. These include low resolution quadrupole MS systems, HR-TOFMS and ultra-high resolution Fourier transform type mass spectrometers using electron impact ionization (EI) and electron capture negative ionization (ECNI) techniques [13–17]. New approaches used direct probe and GC as sample introduction systems to HR-TOFMS with atmospheric pressure chemical ionization (APCI) [18]. The large number of possible

compounds that can be detected, along with their degradation products present an analytical challenge for a reliable identification and interpretation of an unprecedented quantity of data generated by modern mass spectrometers. Since the advent of comprehensive two-dimensional gas chromatography (GC×GC) [19], this unique separation technique has been frequently applied for the analysis of complex samples. Numerous detailed overviews on the principle, development and application of multidimensional chromatography have been published [20–23].

The distribution of the analytes over a two-dimensional retention plane created by two independent columns, allows GC×GC to provide improved separation of complex compound mixtures, resulting in higher peak capacity. The retention structure of different compound classes provides additional information to assist with the identification of structurally related compounds. These advantages allow GC×GC coupled with time-of-flight mass spectrometry (GC×GC-TOFMS) in EI mode and GC×GC coupled to HR-TOFMS in APCI and ECNI modes to be successfully used in environmental forensic investigations and in targeted and non-targeted analysis of OHCs [16,18,19,24].

Advances in commercially available HR-TOFMS allows for reproducible collection of HR-EI mass spectra at unmatched scan speeds to resolve more discrete chemical compounds [25]. By combining GC×GC with HR-TOFMS, the peak capacity of the chromatographic separation process is complemented with the advantage of recording HR-EI mass spectra over a large mass range [16,26,27]. As opposed to Fourier transform type mass spectrometers where resolution and mass accuracy are negatively correlated with the mass spectral acquisition frequency, the HR-TOFMS does not suffer from this phenomenon and mass resolving power increases with *m/z* [25]. With appropriate mass spectral information and accurate mass measurements, elemental composition of compounds can be calculated, which allows rapid identification of molecular ions (and fragments) belonging to a homologous series [17].

Although screening using GC×GC-HR-TOFMS has not previously been applied to the analysis of cat hair samples, this technique was successfully applied to the identification of OHCs in dust [26], flame retardants and plasticisers in electronic waste and car interiors [18], organic pollutants in water [28], and chlorinated and brominated polycyclic aromatic hydrocarbons in soil [27]. In the present study, hair samples taken from six longhair Persian cats were analysed using GC×GC-HR-TOFMS. These cats are typically closely associated with indoor environments, thus sharing a common environment with toddlers. Cat hair was specifically selected as sample matrix since the lipid content allows for the

analysis of a wide variety of OHCs. Since indoor cats shed hair all year round, the exposure time frame includes both short and long term exposure; the samples reflect a real-time snapshot of the current exposure to their surroundings. Due to difficulties in distinguishing between external and internal exposure as previously reported by Kucharska *et al.* [29], unwashed cat hair was extracted; the extracts fractionated and screening analysis was performed to identify BFRs and other OHCs using GC×GC-HR-TOFMS.

2. Experimental

2.1. Chemicals and reagents

High purity grade acetone, hexane, dichloromethane (DCM) and toluene were purchased from Burdick and Jackson (Honeywell International Inc., USA). Florisil®, concentrated sulphuric acid (H_2SO_4) and sodium sulphate (Na_2SO_4) were from Sigma–Aldrich (Chemie GmbH, Germany). Silica gel 60 to 200 Mesh was obtained from Merck (Darmstadt, Germany). Cleaned Florisil® and silica gel was heated for 48 hours in an oven at 160 °C. The PBDE mixture (BFR-PAR) containing 41 PBDE congeners, pentabromoethylbenzene (PBEB), hexabromobenzene (HBB), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) and decabromodiphenyl ethane (DBDPE) was purchased from Wellington Laboratories Inc. (Guelph, ON, Canada). Individual BDE209 was purchased from Sigma-Aldrich (Johannesburg, South Africa). Aldrin, cis and trans-Chlordane, 4,4'-DDT, 2,4-DDT, 4,4'-DDE, 4,4'-DDD, Dieldrin, Endosulfan I and II, Endosulfan sulphate, Endrin, Heptachlor, Heptachlor epoxide and Hexachlorocyclohexane (alpha, beta, delta and gamma isomers) were purchased from Restek, Bellefonte, USA. All GC capillary columns were purchased from Restek, Bellefonte, USA

2.2. Sample preparation

Cat hair samples were collected from a local pet grooming service in Pretoria, South Africa, during September 2016. The cats originated from six family homes in the Pretoria area. The hair samples were placed in resealable plastic bags and stored in the dark at room temperature until chemical analysis. Compound losses because of the storage conditions and absorption to labware were not taken into account. To avoid possible compound losses due to hair swelling, as previously reported for forensic hair analysis, samples were not frozen [30].

During the development of the extraction method, the identification of OHCs from internal incorporation or absorption through the outer layer of the hair shafts was considered. After extraction (as discussed

below), the hair was subjected to digestion using a weak acid as previously described for human hair [31]. The results (not discussed in this paper) were ambiguous and no OHCs could be identified. The procedure for the extraction and clean-up was subsequently modified from previously described methods for the analysis of brominated and organophosphate flame retardants in dust and human hair [31–33]. Two grams of unwashed/ untreated hair was cut into small pieces (<5 mm) using pre-cleaned stainless steel scissors, added to clean amber glass vials, 30 mL of hexane/acetone (3:1, *v/v*) added, extracted by sonication in an ultrasonic bath (Brandson 8800, USA) for 10 min at 25 °C, followed by vortexing and centrifugation at 3500 rpm for 5 min. The solvent fraction was transferred to a clean glass test tube. This step was repeated twice and the combined solvent extracts were evaporated to near dryness at 35 °C under a gentle steam of nitrogen and reconstituted in 1 mL of hexane. The extracts were fractionated on Florisil® prior to clean-up on acidified silica. Pre-cleaned empty glass columns fitted with ceramic frits were filled from the bottom with 4 g of Florisil® and 0.5 g anhydrous Na_2SO_4 and conditioned with 10 mL DCM followed by 20 mL hexane. The extracts were quantitatively transferred to the column and the first fraction (F1) eluted with 10 mL hexane, the second fraction (F2) with 20 ml DCM/hexane (1:4, *v/v*) and the third fraction (F3) with 10 mL DCM. All fractions were evaporated to near dryness at 35 °C under a gentle steam of nitrogen. Fractions 1 and 3 were reconstituted in 25 µL toluene for instrumental analysis, and the DCM/hexane fraction was reconstituted in 1 mL of hexane for clean-up on acidified silica. Glass columns were filled from the bottom with 0.5 g Na_2SO_4, 4 g acidified silica gel (44:56, *w/w*) and 0.5 g Na_2SO_4. The column was conditioned with 20 mL hexane and the F2 extract quantitatively transferred and eluted with 20 mL hexane, evaporated to near dryness at 35 °C under a gentle steam of nitrogen and reconstituted in 25 µL toluene. No OHC contamination was detected in either the method blanks subjected to the same analytical procedure as used on the actual samples, or solvent blanks included in the analysis sequence. A schematic representation of the sample extraction procedure is shown in Figure 1.

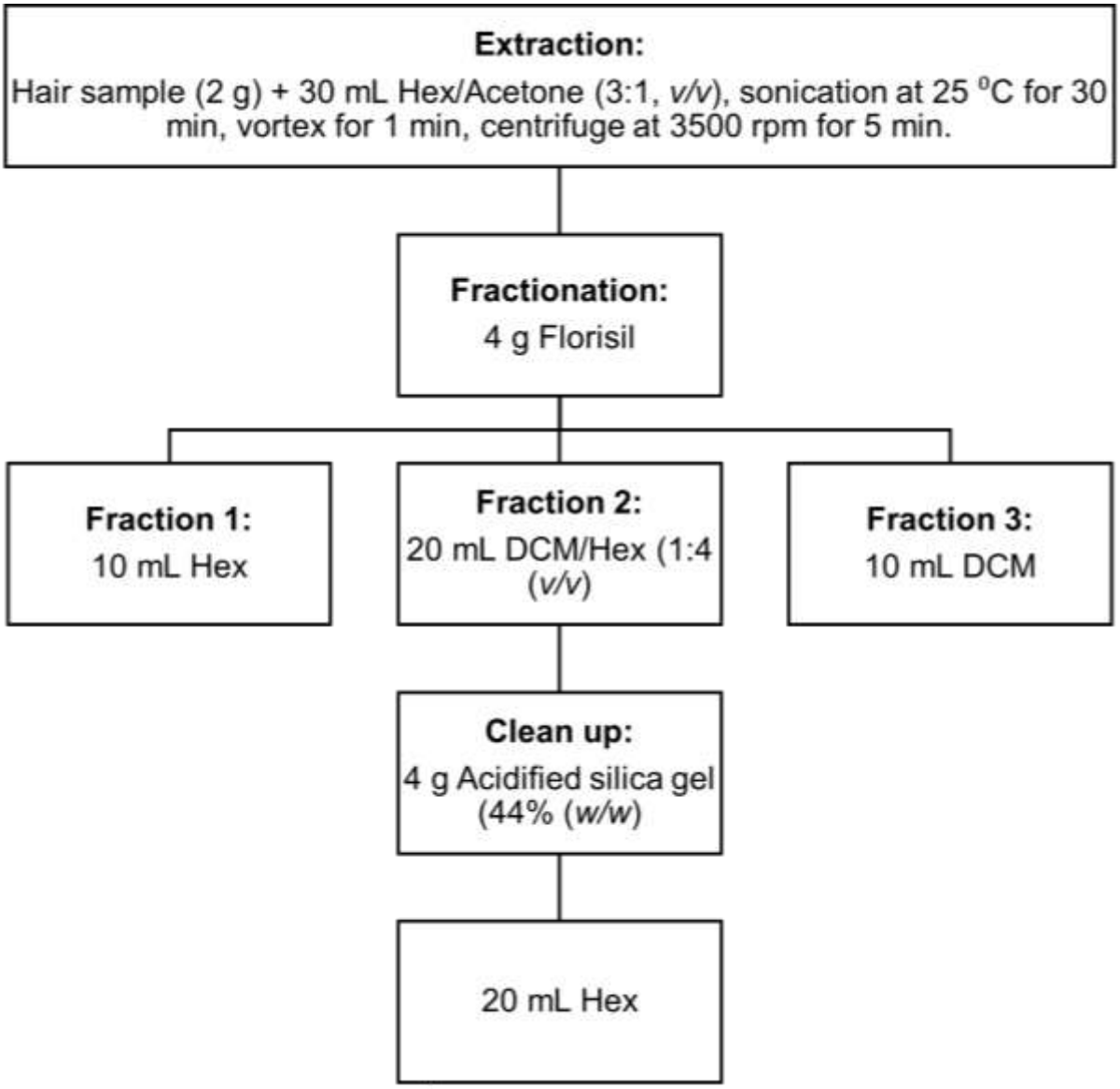

Fig. 1. Schematic representation of the sample extraction procedure.

2.3. Instrumental conditions and data analysis

The GC×GC–HR-TOFMS system used was a Pegasus® GC-HRT equipped with an electron ionisation source operated in high resolution mode (>25,000 FWHM at *m/z* 218.98) (LECO Corporation, St Joseph, MI, USA). The GC×GC system comprised both primary and secondary column ovens and fitted with a non-moving quadjet dual stage thermal modulator. A 15 m Rxi-5HT (0.25 mm I.D. × 0.1 µm df) was used as the first dimension (^{1}D) column and a 1 m Rxi-PAH (0.25 mm I.D. × 0.1 µm df) as the second dimension (^{2}D) column. Detailed instrument parameters are provided in the Supporting Information. A distinguishing feature of this instrument is the multi-reflecting TOF mass analyser based on the Folded Flight Path® concept providing a long ion path, thereby achieving HR measurements without significant loss in sensitivity [34].

2.4. GC×GC–HR-TOFMS mass calibration

To collect accurate mass data, correct mass calibration is an important instrumental process to be performed. The mass calibration generates coefficients that allow for the conversion of time-of-flight data to mass-to-charge (*m/z*) data, by fitting a set of user definable exact masses to the TOF data that is collected. Perfluorotributylamine (PFTBA) was used as mass calibration compound. Eight masses were used for the pre-analysis calibration corresponding to CF_3 (*m/z* 68.9947), C_2F_4 (*m/z* 99.9931), C_3F_5 (*m/z* 130.9915) C_4F_9 (*m/z* 218.9851), $C_5F_{10}N$ (*m/z* 263.9866), $C_8F_{16}N$ (*m/z* 413.9770), $C_9F_{18}N$ (*m/z* 463.9738) and $C_9F_{20}N$ (*m/z* 501.9706). The mass accuracy root mean square (RMS) was better than 0.3 ppm. Data was acquired with constant infusion of the reference compound PFTBA during the entire analysis. The mass of the electron (0.000549 Da) was taken into account for the calculation of the ionic masses.

2.5. Data processing and compound identification.

The GC×GC–HR-TOFMS data processing was performed using the LECO ChromaTOF-HRT® software (version 1.90.). Data processing for screening analysis included automatic peak finding using mass spectral deconvolution (embedded within software). Peak identification was performed through spectral searching against three low (nominal) resolution mass spectral libraries, NIST 2014 (NIST/EPA/NIH Mass Spectral Library, NIST 2014) and two user libraries previously created at NMISA using authentic standards and built to assist in the correct identification of POPs and pesticides. Elemental composition was obtained by comparing the experimentally determined accurate mass of a molecular and/ or fragment isotope ion with the software calculated exact mass. The formula calculator parameters were set to limit the elements used for formula prediction to the formula derived from the library search result. Identification through these database queries must therefore be regarded as tentative and not as conclusive identification. Retention times for PBDEs and organochlorine pesticides (OCPs) were compared to authentic standards.

3. Results and discussion

3.1. Analyte elucidation - Chromatographic considerations and peak detection

The sample extraction and clean-up processes are crucial considerations when compounds with different physical and chemical properties are targeted. Although the hexane/acetone (3:1, *v/v*) solvent mixture has shown to sufficiently extract OHCs from the surface of the hair samples, it is not possible

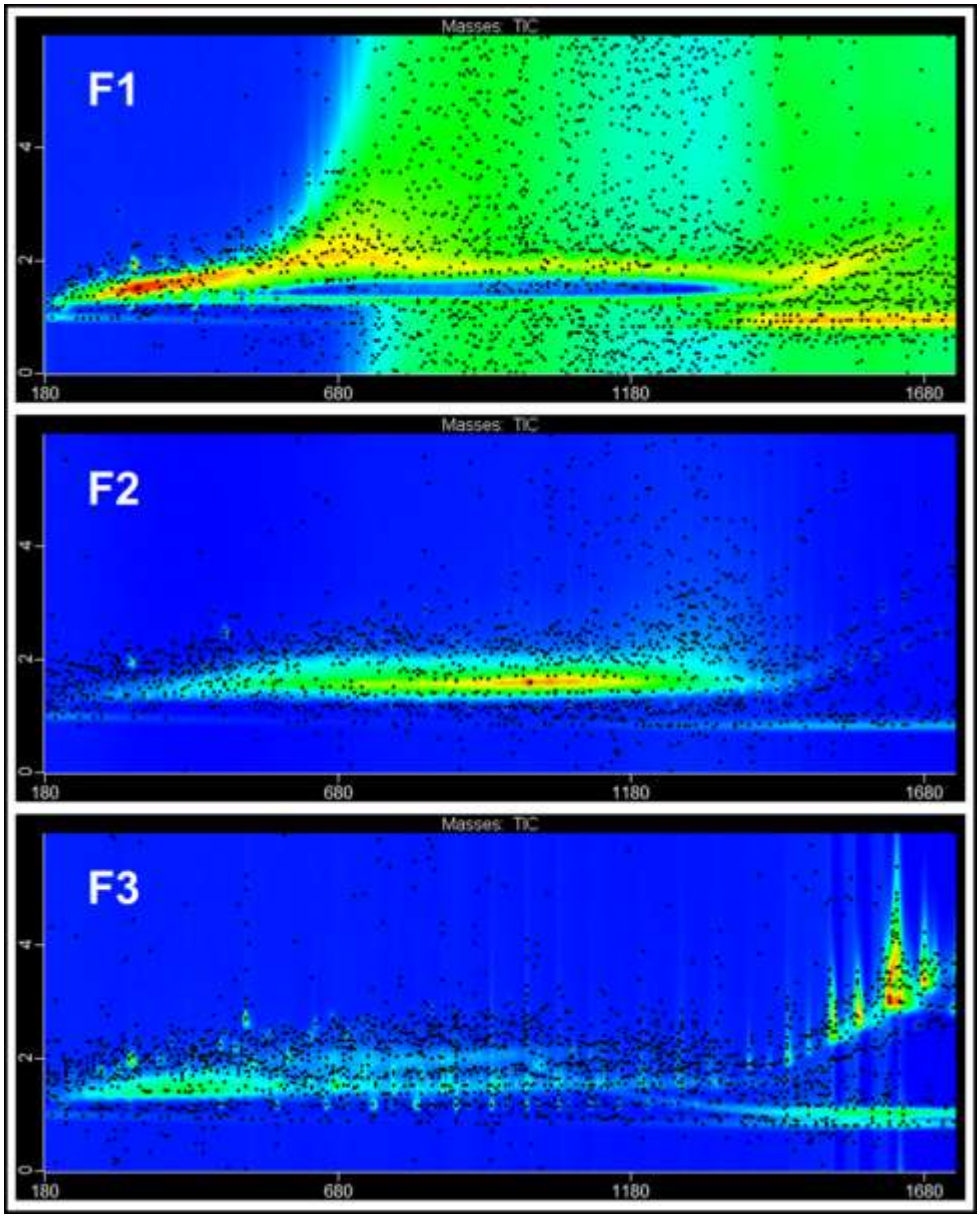

Fig. 2. Two-dimensional total ion chromatogram (TIC) of the cat hair extract fractions eluted with hexane (F1), DCM/hexane (1:4, *v/v*) (F2) and DCM (F3).

to assess how much was extracted from the inner cortex and medulla of the hair. One of the major challenges in the screening analysis of the cat hair samples, was the lipid rich matrix and the large number of detected compounds over a wide concentration range. To remove most of the matrix interference while extracting as wide a selection of OHCs as possible, partial fractionation using Florisil® was performed to elute most of the PBDEs and alt-BFRs in a single fraction. Although column chromatography using alumina, and gel permeation chromatography has frequently been used for lipid separation [35], these options were not explored. Figure 2 shows the ^{2}D total ion chromatogram (TIC) plots of the three hair extract fractions. The fractionation improved the performance of the acid silica

step on F2 by reducing the number of polar compounds thereby limiting the conversion of higher molecular mass compounds to lower molecular mass interferences. The extraction method allowed for OHCs with different polarities to be extracted. The fractionation steps reduced the sample complexity and the PBDEs and alternative BFRs (alt-BFRs) could be separated into a single fraction to be subjected to additional acid silica clean-up.

The GC×GC separation was optimised using a PBDE mixture, to limit the well-known degradation of higher molecular weight PBDEs [35], and to obtain good separation between the target compounds and matrix components. An individual BDE209 standard was injected to evaluate the possible formation of breakdown products in the system and no thermal degradation was observed. A short thin film low-polarity phase column was used in the ^{1}D in combination with a 1 m mid-polarity column in the ^{2}D. The ^{1}D column provided good chromatographic separation with good response for BDE209 and DBDPE. The ^{2}D column with the same column diameter and film thickness was used to separate components by polarity, moving the analytes further away from the matrix interferences. The two columns successfully separated the components due to different physical properties, providing more comprehensive separation than could be achieved by using a single column. Different oven temperature programs and modulation times were evaluated to limit the target analytes wrapping around into the region of the interference. Lower temperature ramp rates resulted in more modulation slices because of the broadening of ^{1}D peak widths. This resulted in more ^{2}D peak slices with low intensities, which had a negative impact on the mass spectrum deconvolution process. A modulation time of 6 s was selected to provide one large and two smaller symmetrical peak slices to maximise detection sensitivity for BDE209, and reduce wrap-around. The disadvantage in using long modulation times to increase sensitivity for PBDEs is that ^{1}D separations can be compromised resulting in co-elution of the closely eluting congeners in the same homologue group. This method allowed sufficient ^{2}D separation of the analytes, although the chromatographic space was not fully utilised.

As part of the screening approach, a series of steps were taken to attempt identification of the various OHCs. The contour plot layout is very useful to locate compound classes diagonally on the two-dimensional plane. In addition to the chromatographic structure, the full scan accurate mass spectra acquired over a large mass range (*m/z* 60, to 980) allows for comparison with mass spectral libraries. The predicted identity from the library search results with reverse match factors of more than 650 were used as a guide and mass spectra from isolated chromatographic peaks were examined for the

presence of characteristic identifiable fragment ions (often halogenated isotopic clusters). The accurate mass measurement of ions recorded was then used to generate a list of recommended elemental formulae and provides values for the *m/z* error between the measured *m/z* and predicted theoretical *m/z*. The OHCs were then tentatively identified when the difference for molecular ions was lower than 2 ppm. In cases where the reverse match factors were less than 650 and/ or in the absence of molecular ions, the mass error had to remain below 2 ppm for the postulated fragment ions. Retention times for PBDEs and OCPs were compared to authentic standards to support the identification, as many of these compounds produce similar mass spectra. Due to the peak slicing, the largest GC×GC modulation slice was used to determine the reported retention times.

The matrix contained a broad range of low *m/z* masses, which could saturate the dual microchannel plate detector, and suppress the detection of analytes present at low concentrations. This can be observed by monitoring an accurate mass of the constantly infused reference compound, which should ideally result in constant intensity. When detector saturation occurs, a decrease in the abundance of the reference mass is typically observed, indicating that the signal for other ions may also be reduced. It has also been suggested that shielding of the electron beam might occur at high matrix concentrations resulting in more electron-matrix collisions and fewer electron-reference gas collisions. As shown in Figure 3, the high abundance of the matrix compounds does have an effect on the intensity of the reference mass. The intensity of the reference compound *m/z* 68.9947 (± 0.0005), as shown in the extracted ion chromatogram (XIC), follows an inverse chromatographic pattern to the total ion chromatogram (TIC) extracted for the samples. This decrease in abundance of reference masses shows possible signal suppression of *m/z* ions of the unknown compounds. This can be seen in cases where poor library match factors were obtained from mass spectra lacking low intensity peaks (Supplementary Information). All results obtained from the samples were therefore manually inspected. In some cases, where peaks were miss-assigned or not found, the peaks were manually added, which is permitted by the data processing software. This peak assignment was done by using two background subtraction regions (each the width of the peak) at the start and end of the peak and selecting the average scans over the entire peak.

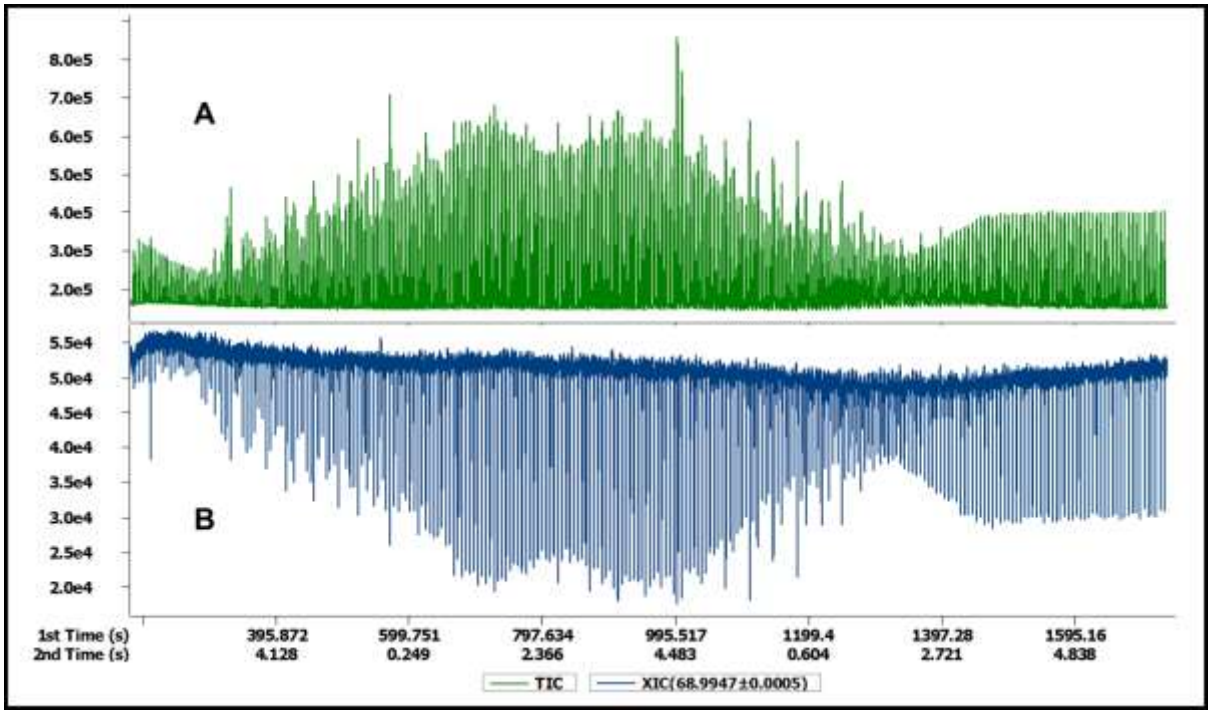

Fig. 3. (A) The total ion chromatogram (TIC) constructed from *m/z* 60 to 980 for the cat hair extract (F2). (B) The extracted ion chromatogram (XIC) of the reference compound *m/z* 68.9947 (± 0.0005).

3.2. Identification of OHCs

The structured chromatographic separation, full scan mass spectra and the exact mass measurement generated by the GC×GC-HR-TOFMS, in combination with the elemental formula prediction, can yield tentative identification of the compounds and compound classes. An overview of OHCs found on the six cat hair samples is presented in Table 1. As observed from the accurate mass measurement results, all ions gave good mass accuracy; less than 2 ppm mass error using PFTBA as internal mass calibration compound. Commercial (low resolution) mass spectral libraries were used to identify the compounds (mass spectra are provided in the Supplementary Information). The OHCs tentatively identified in this study were limited to compounds listed in libraries and it must be noted that ultimately, comparison of retention times with authentic analytical standards is still necessary to confirm identity.

This screening analysis also resulted in the identification of chloro-phosphorous flame retardants. Tris(2-chloroethyl) phosphate (TCEP) and two tris(2-chloroisopropyl)phosphate (TCIPP) isomers have been reported to be mainly used as flame retardants in polyurethane products [36]. As shown in Table 1, these chlorinated organophosphate esters were detected in all samples. No molecular ion was observed in the mass spectra. The elemental composition could be proposed based on the accurate

Table 1.
Non-target screening results for organohalogenated chemicals tentatively identified in the cat hair samples

Compound name	^{1}D RT [a] (s)	^{2}D RT [b] (s)	Elemental composition	Commercial (low res) library search result		Isotope molecular/ fragment ions					
				S match factor [c]	R match factor [d]	Elemental composition	Measured *m/z*	Theoretical *m/z*	Mass error (ppm)	Detection frequency	Fraction
Trichloroaniline	341.904	2.196	$C_6H_4Cl_3N$	685	790	C_6H4Cl_3N	194.9403	194.9404	-0.65	6/6	F3
						C_6H_3ClN	123.9947	123.9949	-1.13		
Trisbromoneopentyl alcohol (TBNPA)	365.89	2.366	$C_5H_9Br_3O$	861	870	$C_4H_6Br_2$	211.8834	211.8831	1.37	4/6	F3>F2
						C_4H_6Br	132.9648	132.9647	0.78		
Alpha-hexachlorocyclohexane	431.851	2.298	$C_6H_6Cl_6$	714	714	$C_6H_5Cl_4$	216.9137	216.9140	-1.18	4/6	F2
						$C_6H_4Cl_3$	180.9375	180.9373	0.94		
Hexachlorobenzene (HCB)	443.844	2.077	C_6Cl_6	703	783	C_6Cl_6	281.8126	281.8131	-1.73	1/6	F2
						C_6Cl_5	246.8439	246.8443	-1.65		
Beta-hexachlorocyclohexane	467.829	2.842	$C_6H_6Cl_6$	890	893	$C_6H_5Cl_4$	216.9141	216.9140	0.34	6/6	F2
						$C_6H_4Cl_3$	180.9375	180.9373	1.03		
Gamma-hexachlorocyclohexane	473.826	2.366	$C_6H_6Cl_6$	926	927	$C_6H_5Cl_4$	216.9140	216.9140	0.10	6/6	F2
						$C_6H_4Cl_3$	180.9375	180.9373	1.25		
Dichlorobiphenyl (Di-CB)	479.822	2.136	$C_{12}H_8Cl_2$	959	959	$C_{12}H_8Cl_2$	221.9999	221.9998	0.74	6/6	F2>F1
						$C_{12}H_8$	152.0622	152.0621	1.27		
Tri(2-chloroethyl) phosphate (TCEP)	479.822	2.459	$C_6H_{12}Cl_3O_4P$	511	564	$C_6H_{12}Cl_2O_4P$	248.9855	248.9850	1.91	2/6	F3
						$C_4H_8Cl_2O_3P$	204.9585	204.9588	-1.69		
Tris(2-chloroisopropyl)phosphate (TClPP)	503.808	1.976	$C_9H_{18}Cl_3O_4P$	662	772	$C_9H_{18}Cl_2O_4P$	291.0316	291.0314	0.23	3/6	F3>F2
						$C_8H_{16}Cl_2O_4P$	277.0156	277.0158	-0.59		
Delta-hexachlorocyclohexane	503.808	2.776	$C_6H_6Cl_6$	865	865	$C_6H_5Cl_4$	216.9137	216.9140	-1.25	4/6	F2
						$C_6H_4Cl_3$	180.9375	180.9373	1.05		
Tris(2-chloroisopropyl)phosphate (TClPP)	509.805	2.169	$C_9H_{18}Cl_3O_4P$	744	775	$C_9H_{18}Cl_2O_4P$	291.0315	291.0314	0.22	3/6	F3>F2
						$C_9H_{16}Cl_3O_3$	277.0161	277.0160	0.39		
Diazinone	509.805	1.873	$C_{12}H_{21}N_2O_3PS$	792	792	$C_{12}H_{21}N_2O_3PS$	304.1002	304.1005	-0.93	1/6	F3
						$C_{11}H_{18}N_2O_3PS$	289.0766	289.0770	-1.57		
Trichlorobiphenyls (Tri-CB)	539.787	2.192	$C_{12}H_7Cl_3$	797	844	$C_{12}H_7Cl_3$	255.9612	255.9608	1.58	6/6	F2
						$C_{12}H_7Cl$	186.0233	186.0231	1.03		
Dichloroanthracene	605.748	2.550	$C_{14}H_9Cl$	486	760	$C_{14}H_9Cl$	212.0390	212.0393	-1.10	6/6	F2
						$C_{14}H_6$	174.0468	174.0470	-0.63		
Chlorpyrifos	611.744	2.086	$C_9H_{11}Cl_3NO_3PS$	687	688	$C_9H_{11}Cl_2NO_3PS$	313.9568	313.9569	-0.37	6/6	F3
						$C_5H_2Cl_3NO$	196.9200	196.9196	1.57		
Tetrachlorobiphenyls (Tetra-CB)	647.723	2.210	$C_{12}H_6Cl$[4]	713	843	$C_{12}H_6Cl_4$	289.9214	289.9218	-1.26	6/6	F2
						$C_{12}H_6Cl_2$	221.9811	221.9812	-0.22		
trans-Chlordane	665.712	2.310	$C_{10}H_6Cl_8$	809	822	$C_{10}H_6Cl_8$	405.7976	405.7972	0.91	6/6	F2
						$C_{10}H_6Cl_7$	370.8286	370.8284	0.71		
cis-Chlordane	677.705	2.257	$C_{10}H_6Cl_8$	838	854	$C_{10}H_6Cl_8$	405.7970	405.7972	-0.60	6/6	F2
						$C_{10}H_6Cl_7$	370.8280	370.8284	-0.88		
Endosulfan I	683.702	2.214	$C_9H_6Cl_6O_3S$	806	821	$C_9H_4Cl_5O_3S$	370.8258	370.8265	-1.92	3/6	F2
						$C_9H_6Cl_5O_3$	336.8763	336.8760	0.94		
trans-Nonachlor	689.698	1.980	$C_{10}H_5Cl_9$	700	711	$C_{10}H_5Cl_9$	441.7555	441.7553	0.56	6/6	F2
						$C_{10}H_5Cl_8$	404.7890	404.7894	-0.93		
2,3,3',4,4',5,5'-Heptachloro-1'-methyl-1,2'-bipyrrole	695.695	1.973	$C_9H_3Cl_7N_2$	674	865	$C_9H_3Cl_7N_2$	383.8115	383.8116	-0.34	4/6	F2
						$C_9H_3Cl_6N_2$	348.8421	348.8422	-0.27		
Dichlorophenylaniline	695.695	2.645	$C_{12}H_9Cl_2N$	625	805	$C_{12}H_9Cl_2N$	237.0110	237.0107	1.46	4/6	F3
						$C_{12}H_8ClN$	201.0341	201.0340	0.68		
4,4'-DDE	707.687	2.201	$C_{14}H_8Cl_4$	852	895	$C_{14}H_8Cl_4$	315.9374	315.9375	-0.30	6/6	F2
						$C_{14}H_8Cl_2$	245.9998	245.9998	0.05		
Dieldrin	707.687	2.287	$C_{12}H_8Cl_6O$	657	657	$C_{12}H_8Cl_6O$	377.8700	377.8706	-1.79	1/6	F2

						$C_7H_2Cl_5$	260.8598	260.8599	-0.33		
Endrin	725.677	2.448	$C_{12}H_8Cl_6O$	765	766	$C_{12}H_8Cl_5O$	342.9020	342.9018	0.65	1/6	F2
						$C_7H_2Cl_5$	260.8598	260.8599	-0.35		
Endosulfan II	737.67	2.627	$C_9H_6Cl_6O_3S$	854	855	$C_9H_6Cl_5O_3$	338.8735	338.8730	1.40	3/6	F2
						$C_9H_6Cl_5O$	306.8826	306.8832	-1.95		
Pentachlorobiphenyls (Penta-CB)	743.666	2.281	$C_{12}H_5Cl_5$	749	820	$C_{12}H_5Cl_5$	325.8799	325.8799	0.09	6/6	F2
						$C_{12}H_5Cl_3$	255.9423	255.9422	0.29		
cis-Nonachlor	755.659	2.262	$C_{10}H_5Cl_9$	667	674	$C_{10}H_5Cl_8$	404.7891	404.7894	-0.72	2/6	F2
						C_5Cl_6	269.8127	269.8126	0.55		
4,4'-DDD/ 2,4'-DDT	755.659	2.359	$C_{14}H_{10}Cl_4$	777	833	$C_{14}H_9Cl_4$	318.9421	318.9423	-0.85	6/6	F2
						$C_{13}H_9Cl_2$	235.0075	235.0076	-0.34		
Pentabromoethylbenzene (PBEB)	773.648	2.525	$C_8H_5Br_5$	591	616	$C_8H_5Br_5$	497.6276	497.6282	-1.22	2/6	F2
						$C_7H_2Br_5$	482.6039	482.6047	-1.81		
Endosulfan sulfate	779.645	2.785	$C_9H_6Cl_6O_4S$	849	856	$C_9H_6Cl_6O_4S$	419.8112	419.8112	-0.09	6/6	F2
						C_5Cl_6	271.8098	271.8096	0.79		
4,4'-DDT	791.638	2.375	$C_{14}H_9Cl_5$	790	795	$C_{14}H_9Cl_5$	351.9140	351.9141	-0.30	6/6	F2
						$C_{13}H_9Cl_2$	235.0076	235.0076	-0.04		
Hexachlorobiphenyls (Hexa-CB)	797.634	2.251	$C_{12}H_4Cl_6$	681	784	$C_{12}H_4Cl_6$	357.8435	357.8439	-1.04	6/6	F2
						$C_{12}H_4Cl_4$	287.9060	287.9062	-0.39		
Endrin ketone	827.616	2.908	$C_{12}H_8Cl_6O$	819	819	$C_{12}H_8Cl_5O$	342.9017	342.9018	-0.29	6/6	F2
						$C_{11}H_8Cl_5$	316.9035	316.9039	-1.26		
Heptachlorobiphenyls (Hepta-CB)	869.591	2.119	$C_{12}H_3Cl_7$	495	528	$C_{12}H_3Cl_7$	391.8051	391.8049	0.49	3/6	F2
						$C_{12}H_3Cl_5$	321.8673	321.8672	0.45		
Tetrabromodiphenyl ether (Tetra-BDE)	869.591	2.557	$C_{12}H_6Br_4O$	689	733	$C_{12}H_6Br_4O$	481.7145	481.7147	-0.32	6/6	F2
						$C_{12}H_6Br_2O$	325.8760	325.8759	0.04		
Biphenthrin	881.584	1.712	$C_{23}H_{22}ClF_3O_2$	846	856	$C_{23}H_{22}ClF_3O_2$	422.1254	422.1255	-0.16	5/6	F3
						$C_{14}H_{13}$	181.1010	181.1012	-1.16		
Pentabromodiphenyl ether (Penta-BDE)	983.524	2.597	$C_{12}H_5Br_5O$	651	713	$C_{12}H_5Br_5O$	559.6260	559.6252	1.54	5/6	F2
						$C_{12}H_5Br_3O$	401.7879	401.7885	-1.58		
Permethrin	1013.51	2.021	$C_{21}H_{20}Cl_2O_3$	883	891	$C_{21}H_{20}Cl_2O_3$	390.0786	390.0784	0.41	6/6	F3
						$C_{13}H_{11}O$	183.0802	183.0804	-1.23		
Cypermethrin	1013.51	2.218	$C_{22}H_{19}Cl_2NO_3$	788	790	$C_{14}H_{10}NO$	208.0755	208.0757	-0.71	6/6	F3
						$C_7H_9Cl_2$	163.0074	163.0076	-1.41		
Hexabromodiphenyl ether (Hexa-BDE)	1085.46	2.643	$C_{12}H_4Br_6O$	749	749	$C_{12}H_4Br_6O$	643.5292	643.5295	-0.50	2/6	F2
						$C_{12}H_4Br_4O$	483.6945	483.6949	-0.83		
Hexabromocyclododecane isomers (HBCD)	1109.45	2.903	$C_{12}H_{18}Br_6$	656	674	$C_{12}H_{15}Br_2$	316.9539	316.9540	-0.37	1/6	F2
						$C_{12}H_{14}Br$	237.0274	237.0279	-1.87		
Heptabromodiphenyl ether (Hepta-BDE)	1181.41	2.848	$C_{12}H_3Br_7O$	509	523	$C_{12}H_3Br_7O$	719.4424	719.4427	-0.39	6/6	F2
						$C_{12}H3Br_5O$	563.6044	563.6039	0.86		
Octabromodiphenyl ether (Octa-BDE)	1289.34	3.101	$C_{12}H_2Br_8O$	493	516	$C_{12}H_2Br_8O$	799.3504	799.3511	-0.91	6/6	F2
						$C_{12}H_2Br_6O$	641.5143	641.5144	-0.17		
Nonabromodiphenyl ether (Nona-BDE)	1409.27	3.383	$C_{12}HBr_9O$	645	652	$C_{12}HBr_9O$	879.2590	879.2596	-0.70	6/6	F2
						$C_{12}HBr_7O$	719.4241	719.4250	-1.15		
Decabromodiphenyl ether (Deca-BDE)	1541.19	5.131	$C_{12}Br_{10}O$	646	685	$C_{12}Br_{10}O$	959.1674	959.1681	-0.64	6/6	F2
						$C_{12}Br_8O$	799.3328	799.3334	-0.76		
Decabromodiphenyl ethane (DBDPE)	1637.14	1.004	$C_{14}H_4Br_{10}$	676	676	$C_{14}H_4Br_{10}$	971.2061	971.2044	1.69	6/6	F2
						$C_7H_2Br_5$	484.6032	484.6027	1.10		

[a] First dimension retention time
[b] Second dimension retention time
[c] Software similarity match factor
[d] Software reverse match factor

mass of the fragment resulting from a loss of chlorine ([M-Cl]) and supported by the full scan mass spectra. As shown in Figure 4, the elution order for these esters using a 5% phenyl-methylpolysiloxane stationary phase column was similar to previous studies [37,38].

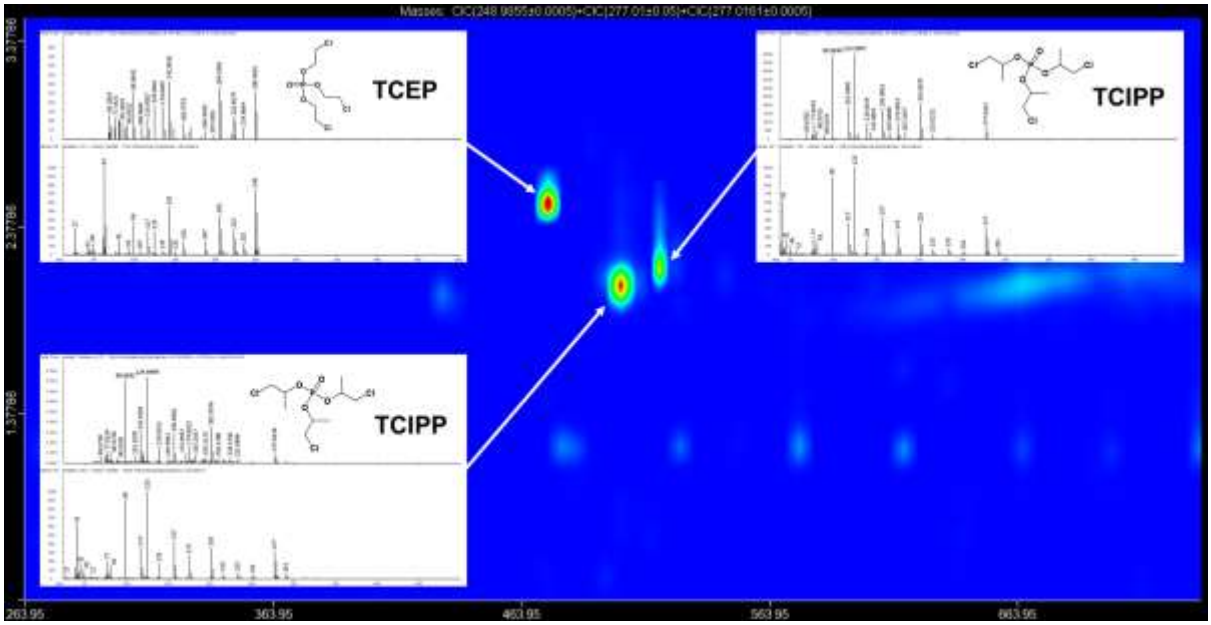

Fig. 4. The extracted mass two-dimensional contour plot and mass spectra tentatively identified as tris(2-chloroethyl) phosphate (TCEP) and the two tris(2-chloroisopropyl)phosphate (TCIPP) isomers in a cat hair extract.

Seven PBDE homologue groups and four alt-BFRs were also identified in the samples (Fig. 5). To support the identification of these compounds, retention times were compared to the standard mixture (BFR-PAR). Based on the full scan mass spectra and the retention time comparison, BDE-47 was identified as the only tetrabromodiphenyl ether (tetra-BDE), BDE99 and 100 as the pentabromodiphenyl ethers (penta-BDE) and BDEs 153 and 154 as the hexabromodiphenyl ethers (hexa-BDE). Three nonabromodiphenyl ethers (nona-BDE) were identified as BDE206, 207 and 208. Although library matching results for heptabromodiphenyl ether (hepta-BDE) and octabromodiphenyl ether (octa-BDE) were low, the retention time comparison showed that the hepta-BDE could be identified as BDE183. Due to a co-elution on this specific column set, the octa-BDEs were tentatively identified as either BDE204 or 197 and BDE196. The tetra, penta-, octa-, nona and decabromodiphenyl ethers were present in all six hair samples and hexa- and hepta-BDE congeners only in two of the samples. Of the four alt-BFRs suggested, the retention times for PBEB and DBDPE could be confirmed through the standard mixture. Based on the mass spectral match factor and the accurate mass measured for specific fragments, hexabromocyclododecane (HBCD) and trisbromoneopentyl alcohol (TBNPA) could

be identified. In addition to PBDEs, the occurrence of HBCD has been reported in indoor environments (dust) and on children's handwipes [39]. This compound consists of three diastereomers, primarily analysed using liquid chromatography coupled to mass spectrometry (LC-MS); and GC methods are not able to separate the diastereomers resulting in a broader peak compared to the PBDEs [40]. The peak identified as HBCD elutes in the region where the hexa-BDEs elute, similar to the elution order previously reported by Korytár *et al.*, (2002) [10]. Tribromoneopentyl alcohol is a reactive BFR used in the synthesis of high molecular-weight flame retardants and as an additive in the manufacturing of polymers [41].

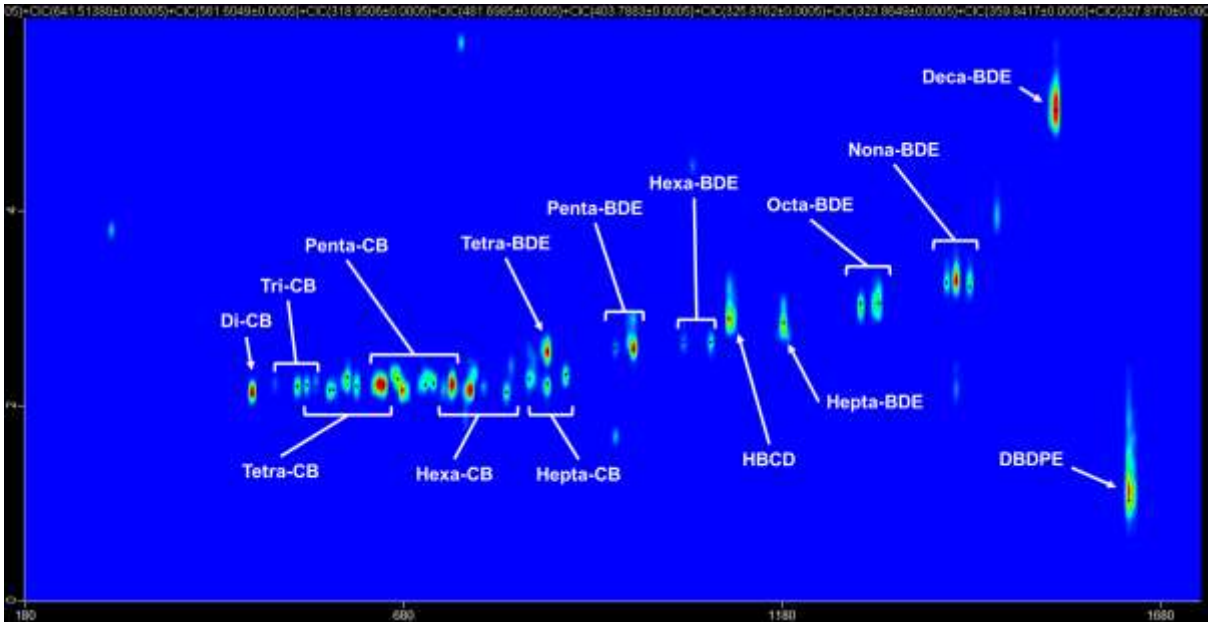

Fig. 5. Extracted mass two-dimensional contour plot of brominated flame retardants and di- to hepta chlorinated biphenyl congeners tentatively identified in a cat hair extract.

As shown in Table 1, PCBs were detected in all six cat hair samples. The prevalence of tri- through hepta-CB congeners in indoor dust has been reported with regular detection of the low and high molecular weight congeners [42]. In a recent study from South Africa, three PCB congeners representing the tri-, hexa- and hepta-CB groups were analysed in indoor dust samples [43]. The higher molecular mass congeners were found at higher intensities. As shown in Figure 5, di- through hepta-CB congeners could be detected in the cat hair samples. The di- through hexa-CBs were present in all six samples and the hepta-CB congeners were only detected in three of the samples. Interestingly, a single di-CB congener was present in all samples at very high intensities. Recent publications reported on the detection of the dichloro congener 3,3′dichlorobiphenyl (PCB 11) in air, water, biota, and

sediment [44]. This compound is produced during the production of diarylide yellow pigments used in printing and other applications. As no authentic PCB standards were used in this study, the congeners could not be verified.

The screening approach employed also resulted in the detection and identification of numerous organochlorine pesticides (OCPs), organophosphorous pestides (OPPs) and pyrethroids (Fig.6). Because many of the OCPs produce similar mass spectra, retention time comparison with authentic standards aided the identification. As one of the major importers of pesticides on the African continent, South-Africa has a highly organised agricultural sector with vast rural areas. A wide range of toxic chemicals are used for crop protection; DDT and other chemicals are also used to control the vector mosquitoes [45]. Of the POPS listed in the Stockholm Convention, the four hexachlorocyclohexane (HCH) isomers (alpha, beta, gamma and delta-HCH), hexachlorobenzene, chlordanes (cis and trans), dieldrin, endrin, DDT, DDD, DDE could be identified. Although OCPs were not previously reported for South African indoor dust, their occurrence is well documented for ambient air in industrial and residential areas [46]. It must be emphasised that the sampling site is more than 400 km from the nearest known site where DDT is legally used for indoor spraying.

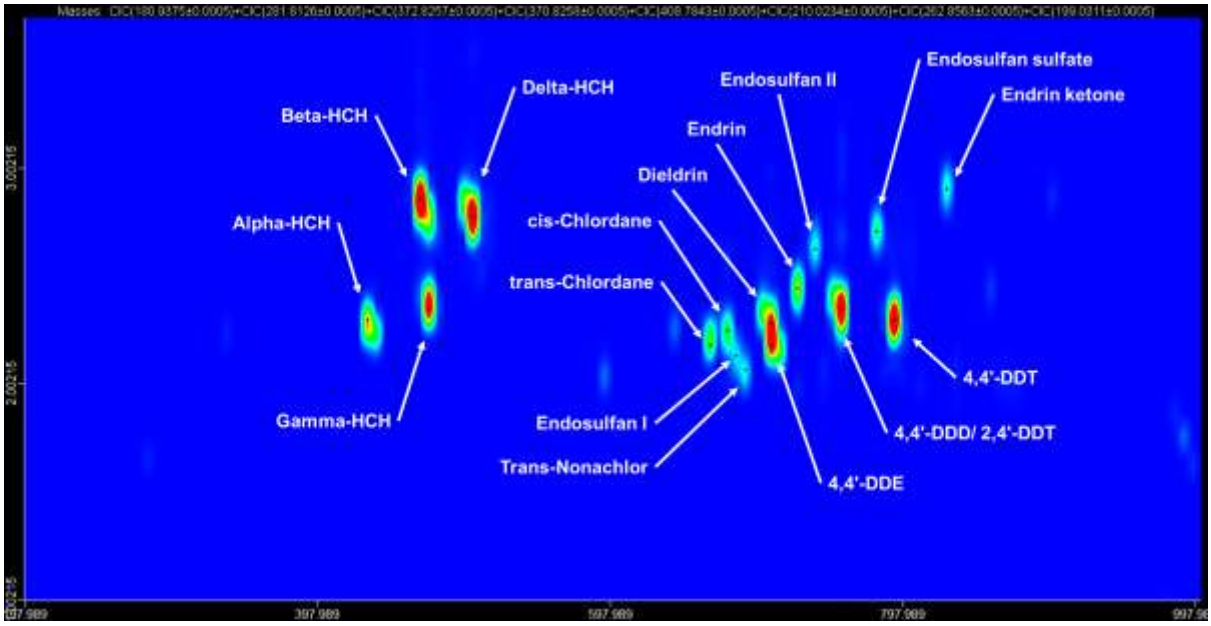

Fig. 6. Extracted mass two-dimensional contour plot of pesticides tentatively identified in a cat hair extract

This approach also enables detection and tentatively identification of 2,3,3',4,4',5,5'-Heptachloro-1'-methyl-1,2'-bipyrrole (MBP-Cl_7); a compound with similar physical properties to PBDEs [47]. Vettery [48] was the first to identify this compound as a natural heptachloro compound associated with the marine environment and found in fish, seabirds and marine mammals [49]. Fujii *et al*. [50] reported on MBP-Cl_7 levels in Japanese breast milk and suggested that the possible source may be through biota or the food chain. As this compound was detected in four of the six samples, the only plausible source might be from cat food containing fish products, but this would have to be confirmed by analysing the food.

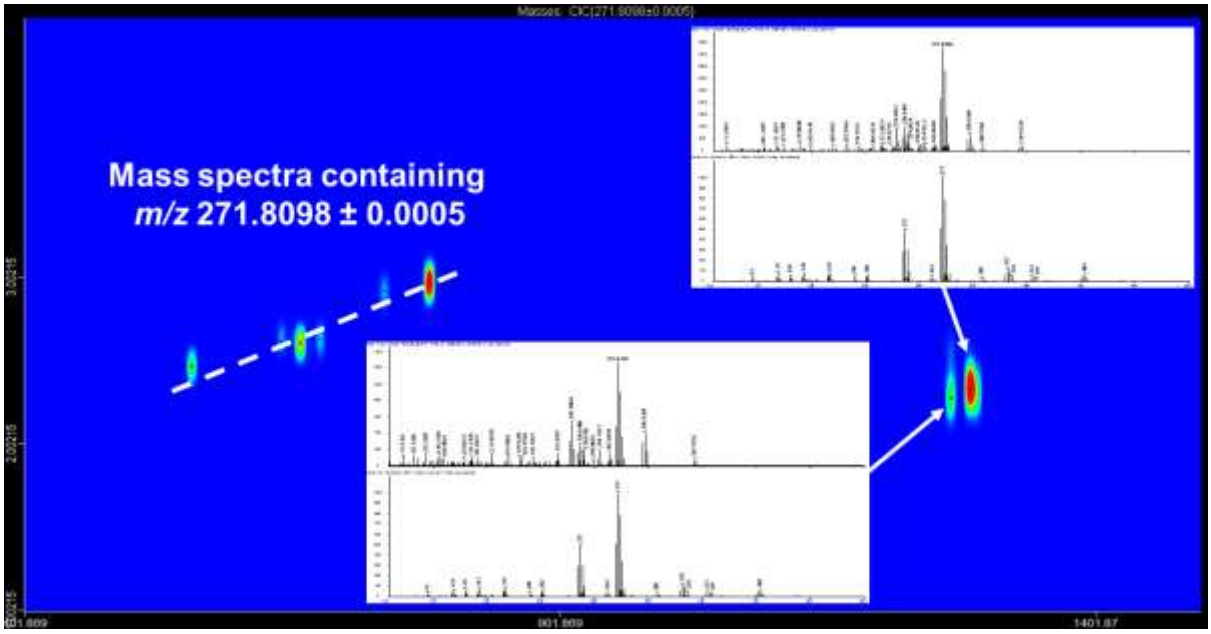

Fig. 7. Contour plot of a cat hair extract showing the elution of compounds containing *m/z* 271.8098 (± 0.0005 Da) in their mass spectra and the accurate full scan mass spectrum extracted for the two compounds identified by the library search as Mirex.

This screening analysis using GC×GC-HR-TOFMS in electron impact (EI) ionisation mode also presents some limitations. As shown in Figure 7, two compounds eluting at 1265.36 s (^{1}D Rt), 2.287 s (^{2}D Rt) and 1283.35 s (^{1}D Rt), 2.341 s (^{2}D Rt) were identified by the library as Mirex. Mirex, an OCP, is also used as the flame retardant Dechlorane [51]. Analogues of Dechlorane have been studied in environmental samples under EI conditions. Due to the extreme fragmentation and the low intensity of the molecular ion as a result of the retro Diels-Alder fragmentation, the most intense fragment isotope ion produced is $C_5Cl_6^+$ with theoretical *m/z* of 271.8096 [52]. The retention time of these two compounds was comparable to those from previous studies where BFRs and Dechlorane Plus (DP) were analysed

on a similar low-polarity phase column. It is thus proposed that these compounds might be syn-DP and anti-DP [53]. As seen in Figure 7, the characteristic ion is also present in the mass spectra of other early eluting OHCs and the information is therefore not sufficient to positively identify DP.

4. Conclusion

This paper presents a first report using hair from South African pet cats to investigate the occurrence of OHCs in the domestic environment. The screening method utilises GC×GC coupled to a HR-TOFMS system to detect as many GC-amenable compounds as possible. This technique can successfully screen samples as it provides structured separation of compound classes and library searchable full scan EI mass spectra with accurate mass measurements (mass accuracy of better than 2 ppm) to predict chemical formulae for molecular and corresponding fragment ions. The matrix effects in quantitative TOFMS analysis was confirmed, but posed no limitation to the screening procedure proposed. The method allows for the detection and tentative identification of various OHC classes including pesticides (OCPs, OPPs, pyrethroids), PCBs and halogenated flame retardants. Although OHCs were previously reported in the South African environment, the majority of the studies applied a targeted analysis approach. While the solvent mixture allows for the adequate extraction of OHCs from the hair samples, further studies will be conducted to distinguish between external deposition and internal incorporation. The PBDEs and PCBs detected in cat hair samples were comparable to those found in house dust, demonstrating that cat hair might be a possible indicator for environmental exposure with reference to external deposition of OHCs present in the air and dust surrounding people. This study is also the first to report detection of DBDPE, TBNPA, HBCD, PBEB, TCEP and TCIPP in the South African indoor environment and confirms the ubiquitous occurrence of halogenated flame retardants in the indoor environment.

The results obtained from the hair samples indicates that cats are exposed to complex mixtures of industrial chemicals and the detection of these compounds suggests the use of cat hair as a non-invasive sample for modelling indoor exposure. Toddlers share the same environment as cats and exposure would result in similar health risks. The presence of these persistent chemicals in cat hair may sound a cautionary warning for the immediate and long term health of children.

Acknowledgement

This work was based on the research supported in part by the National Research Foundation of South Africa (VU University Amsterdam - NRF Desmond Tutu doctoral scholarship) (Grant number: 94075) and by the Swedish research council FORMAS (Project MiSSE number: 210-2012-131). The authors acknowledge that opinions, findings and conclusions or recommendations expressed in this publication which is generated by the NRF supported research are that of the authors, and the NRF accepts no liability whatsoever in this regard. The authors wish to thank Jack Cochran for insightful discussions and valuable analytical information; and Le York, a pet grooming service in Pretoria (South Africa) for kindly providing the hair samples.

References

[1] J. Zhang, J.H. Kamstra, M. Ghorbanzadeh, J.M. Weiss, T. Hamers, P.L. Andersson, In Silico Approach To Identify Potential Thyroid Hormone Disruptors among Currently Known Dust Contaminants and Their Metabolites, Environ. Sci. Technol. 49 (2015) 10099–10107. doi:10.1021/acs.est.5b01742.

[2] P.H. Howard, D.C.G. Muir, Identifying new persistent and bioaccumulative organics among chemicals in commerce, Environ. Sci. Technol. 44 (2010) 2277–2285. doi:10.1021/es201196x.

[3] P.R.S. Kodavanti, M.C. Curras-Collazo, Neuroendocrine actions of organohalogens: Thyroid hormones, arginine vasopressin, and neuroplasticity, Front. Neuroendocrinol. 31 (2010) 479–496. doi:10.1016/j.yfrne.2010.06.005.

[4] M. Gascon, M. Vrijheid, D. Martínez, J. Forns, J.O. Grimalt, M. Torrent, J. Sunyer, Effects of pre and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age, Environ. Int. 37 (2011) 605–611. doi:10.1016/j.envint.2010.12.005.

[5] D. Lankova, A. Svarcova, K. Kalachova, O. Lacina, J. Pulkrabova, J. Hajslova, Multi-analyte method for the analysis of various organohalogen compounds in house dust., Anal. Chim. Acta. 854 (2015) 61–9. doi:10.1016/j.aca.2014.11.007.

[6] I. Liagkouridis, I.T. Cousins, A.P. Cousins, Emissions and fate of brominated flame retardants in the indoor environment: A critical review of modelling approaches, Sci. Total Environ. 491–492 (2014) 87–99. doi:10.1016/j.scitotenv.2014.02.005.

[7] A.C. Dirtu, S.J.M. Niessen, P.G. Jorens, A. Covaci, Organohalogenated contaminants in domestic cats' plasma in relation to spontaneous acromegaly and type 2 diabetes mellitus: a clue for endocrine disruption in humans?, Environ. Int. 57–58 (2013) 60–7. doi:10.1016/j.envint.2013.04.004.

[8] N. Ali, R.N. Malik, T. Mehdi, S.A.M.A.S. Eqani, A. Javeed, H. Neels, A. Covaci, Organohalogenated contaminants (OHCs) in the serum and hair of pet cats and dogs: Biosentinels of indoor pollution, Sci. Total Environ. 449 (2013) 29–36. doi:10.1016/j.scitotenv.2013.01.037.

[9] B.M.R. Appenzeller, A.M. Tsatsakis, Hair analysis for biomonitoring of environmental and occupational exposure to organic pollutants: State of the art, critical review and future needs, Toxicol. Lett. 210 (2012) 119–140. doi:10.1016/j.toxlet.2011.10.021.

[10] P. Korytár, P. Haglund, J. De Boer, U.A.T. Brinkman, Comprehensive two-dimensional gas chromatography for the analysis of organohalogenated micro-contaminants, TrAC Trends Anal. Chem. 25 (2006) 373–396. doi:10.1016/j.trac.2005.12.003.

[11] R. Cariou, E. Omer, A. Léon, G. Dervilly-Pinel, B. Le Bizec, Screening halogenated environmental contaminants in biota based on isotopic pattern and mass defect provided by high resolution mass spectrometry profiling, Anal. Chim. Acta. 936 (2016) 130–138. doi:10.1016/j.aca.2016.06.053.

[12] X. Ouyang, J.M. Weiss, J. de Boer, M.H. Lamoree, P.E.G. Leonards, Non-target analysis of household dust and laundry dryer lint using comprehensive two-dimensional liquid chromatography coupled with time-of-flight mass spectrometry, Chemosphere. 166 (2017) 431–437. doi:10.1016/j.chemosphere.2016.09.107.

[13] N. Rosenfelder, N.J. Van Zee, J.F. Mueller, C. Gaus, W. Vetter, Gas chromatography/electron ionization-mass spectrometry-selected ion monitoring screening method for a thorough investigation of polyhalogenated compounds in passive sampler extracts with quadrupole systems, Anal. Chem. 82 (2010) 9835–9842. doi:10.1021/ac102134x.

[14] C. Hauler, W. Vetter, A non-targeted gas chromatography/electron capture negative ionization mass spectrometry selected ion monitoring screening method for polyhalogenated compounds in environmental samples, Rapid Commun. Mass Spectrom. 29 (2015) 619–628. doi:10.1002/rcm.7143.

[15] J.D. Byer, G. Pacepavicius, M. Lebeuf, R.S. Brown, S. Backus, P. V. Hodson, M. Alaee, Qualitative analysis of halogenated organic contaminants in American eel by gas chromatography/time-of-flight mass spectrometry, Chemosphere. 116 (2014) 98–103. doi:10.1016/j.chemosphere.2014.02.032.

[16] S. Fernando, K.J. Jobst, V.Y. Taguchi, P.A. Helm, E.J. Reiner, B.E. McCarry, Identification of the halogenated compounds resulting from the 1997 Plastimet Inc. fire in Hamilton, Ontario, using comprehensive two-dimensional gas chromatography and (ultra)high resolution mass spectrometry, Environ. Sci. Technol. 48 (2014) 10656–10663. doi:10.1021/es503428j.

[17] K.J. Jobst, L. Shen, E.J. Reiner, V.Y. Taguchi, P.A. Helm, R. McCrindle, S. Backus, The use of mass defect plots for the identification of (novel) halogenated contaminants in the environment, Anal. Bioanal. Chem. 405 (2013) 3289–3297. doi:10.1007/s00216-013-6735-2.

[18] A. Ballesteros-Gómez, J. De Boer, P.E.G. Leonards, Novel analytical methods for flame retardants and plasticizers based on gas chromatography, comprehensive two-dimensional gas chromatography, and direct probe coupled to atmospheric pressure chemical ionization-high resolution time-of-flight-mass spectrom, Anal. Chem. 85 (2013) 9572–9580. doi:10.1021/ac4017314.

[19] Z. Liu, J.B. Phillips, Comprehensive two-dimensional gas chromatography using an on-column thermal modulator interface, J. Chromatogr. Sci. 29 (1991) 227–231. doi:10.1093/chromsci/29.6.227.

[20] J. Dallüge, J. Beens, U.A.T. Brinkman, Comprehensive two-dimensional gas chromatography: a powerful and versatile analytical tool, J. Chromatogr. A. 1000 (2003) 69–108. doi:10.1016/S0021-9673(03)00242-5.

[21] M. Adahchour, J. Beens, R.J.J. Vreuls, U. a T. Brinkman, Recent developments in comprehensive two-dimensional gas chromatography (GC×GC) I. Introduction and instrumental set-up, TrAC - Trends Anal. Chem. 25 (2006) 438–454. doi:10.1016/j.trac.2006.03.002.

[22] P.J. Marriott, S.T. Chin, B. Maikhunthod, H.G. Schmarr, S. Bieri, Multidimensional gas chromatography, TrAC - Trends Anal. Chem. 34 (2012) 1–20. doi:10.1016/j.trac.2011.10.013.

[23] C. Meinert, U.J. Meierhenrich, A new dimension in separation science: Comprehensive two-dimensional gas chromatography, Angew. Chemie - Int. Ed. 51 (2012) 10460–10470. doi:10.1002/anie.201200842.

[24] D. Megson, E.J. Reiner, K.J. Jobst, F.L. Dorman, M. Robson, J.-F. Focant, A review of the determination of persistent organic pollutants for environmental forensics investigations, Anal. Chim. Acta. 941 (2016) 10–25. doi:10.1016/j.aca.2016.08.027.

[25] C.F. Klitzke, Y.E. Corilo, K. Siek, J. Binkley, J. Patrick, M.N. Eberlin, Petroleomics by ultrahigh-resolution time-of-flight mass spectrometry, Energy and Fuels. 26 (2012) 5787–5794. doi:10.1021/ef300961c.

[26] M. Ubukata, K.J. Jobst, E.J. Reiner, S.E. Reichenbach, Q. Tao, J. Hang, Z. Wu, A.J. Dane, R.B. Cody, Non-targeted analysis of electronics waste by comprehensive two-dimensional gas chromatography combined with high-resolution mass spectrometry: Using accurate mass information and mass defect analysis to explore the data, J. Chromatogr. A. 1395 (2015) 152–159. doi:10.1016/j.chroma.2015.03.050.

[27] T. Ieda, N. Ochiai, T. Miyawaki, T. Ohura, Y. Horii, Environmental analysis of chlorinated and brominated polycyclic aromatic hydrocarbons by comprehensive two-dimensional gas chromatography coupled to high-resolution time-of-flight mass spectrometry, J. Chromatogr. A. 1218 (2011) 3224–3232. doi:10.1016/j.chroma.2011.01.013.

[28] F. Hernández, T. Portolés, E. Pitarch, F.J. López, Target and nontarget screening of organic micropollutants in water by solid-phase microextraction combined with gas chromatography/high-resolution time-of-flight mass spectrometry, Anal. Chem. 79 (2007) 9494–9504. doi:10.1021/ac071551b.

[29] A. Kucharska, A. Covaci, G. Vanermen, S. Voorspoels, Non-invasive biomonitoring for PFRs and PBDEs: New insights in analysis of human hair externally exposed to selected flame retardants, Sci. Total Environ. 505 (2015) 1062–1071. doi:10.1016/j.scitotenv.2014.10.043.

[30] G.A.A. Cooper, R. Kronstrand, P. Kintz, Society of Hair Testing guidelines for drug testing in hair, Forensic Sci. Int. 218 (2012) 20–24. doi:10.1016/j.forsciint.2011.10.024.

[31] A. Kucharska, E. Cequier, C. Thomsen, G. Becher, A. Covaci, S. Voorspoels, Assessment of human hair as an indicator of exposure to organophosphate flame retardants. Case study on a Norwegian mother–child cohort, Environ. Int. 83 (2015) 50–57. doi:10.1016/j.envint.2015.05.015.

[32] N. Van Den Eede, A.C. Dirtu, N. Ali, H. Neels, A. Covaci, Multi-residue method for the determination of brominated and organophosphate flame retardants in indoor dust, Talanta. 89 (2012) 292–300. doi:10.1016/j.talanta.2011.12.031.

[33] N. Ali, S. Harrad, D. Muenhor, H. Neels, A. Covaci, Analytical characteristics and determination of major novel brominated flame retardants (NBFRs) in indoor dust, Anal. Bioanal. Chem. 400 (2011) 3073–3083. doi:10.1007/s00216-011-4966-7.

[34] A.N. Verentchikov, M.I. Yavor, Y.I. Hasin, M.A. Gavrik, Multireflection planar time-of-flight mass analyzer. II: The high-resolution mode, Tech. Phys. 50 (2005) 82–86.

[35] J. de Boer, C. Allchin, R. Law, B. Zegers, J.P. Boon, Method for the analysis of polybrominated diphenylethers in sediments and biota, Trends Anal. Chem. 20 (2001) 591–599. doi:10.1016/S0165-9936(01)00097-8.

[36] T. Salthammer, F. Fuhrmann, E. Uhde, Flame retardants in the indoor environment - Part II: release of VOCs (triethylphosphate and halogenated degradation products) from polyurethane, Indoor Air. 13 (2003) 49–52. doi:10.1034/j.1600-0668.2003.01150.x.

[37] P. Haglund, Traffic as a source of organophosphorus flame retardants and plasticizers in snow, Environ. Sci. Technol. 39 (2005) 3555–3562.

[38] A. Möller, R. Sturm, Z. Xie, M. Cai, J. He, R. Ebinghaus, Organophosphorus flame retardants and plasticizers in airborne particles over the Northern Pacific and Indian Ocean toward the Polar Regions: Evidence for global occurrence, Environ. Sci. Technol. 46 (2012) 3127–3134. doi:10.1021/es204272v.

[39] H.M. Stapleton, J. Misenheimer, K. Hoffman, T.F. Webster, Flame retardant associations between children's handwipes and house dust, Chemosphere. 116 (2014) 54–60. doi:10.1016/j.chemosphere.2013.12.100.

[40] J. de Boer, R.J. Law, Developments in the use of chromatographic techniques in marine laboratories for the determination of halogenated contaminants and polycyclic aromatic hydrocarbons, J. Chromatogr. A. 1000 (2003) 223–251.

[41] O. Segev, W. Meusel, M. Friedenberger, A. Brenner, A. Kushmaro, Aerobic biodegradation of the brominated flame retardants, dibromoneopentyl glycol and tribromoneopentyl alcohol, Biodegradation. 20 (2009) 621–627. doi:10.1007/s10532-009-9249-z.

[42] S. Harrad, C. Ibarra, M. Robson, L. Melymuk, X. Zhang, M. Diamond, J. Douwes, Polychlorinated biphenyls in domestic dust from Canada, New Zealand, United Kingdom and United States: Implications for human exposure, Chemosphere. 76 (2009) 232–238. doi:10.1016/j.chemosphere.2009.03.020.

[43] O.A. Abafe, B.S. Martincigh, Polybrominated diphenyl ethers and polychlorinated biphenyls in indoor dust in Durban, South Africa, Indoor Air. 25 (2015) 547–556. doi:10.1111/ina.12168.

[44] L.A. Rodenburg, J. Guo, S. Du, G.J. Cavallo, Evidence for unique and ubiquitous environmental sources of 3,3'-dichlorobiphenyl (PCB 11), Environ. Sci. Technol. 44 (2010) 2816–2821. doi:10.1021/es901155h.

[45] L.P. Quinn, J. De Vos, C. Roos, H. Bouwman, H. Kylin, R. Pieters, J. Van Den Berg, in: M. Stoytcheva (Ed.), Pesticide Use in South Africa : One of the Largest Importers of Pesticides in Africa. Pesticides in the Modern World – Pesticides Use and Management, InTech, Rijeka, Croatia, 2011: pp. 49–96. doi:10.5772/16995.

[46] S.A. Batterman, S.M. Chernyak, Y. Gounden, M. Matooane, R.N. Naidoo, Organochlorine pesticides in ambient air in Durban, South Africa, Sci. Total Environ. 397 (2008) 119–130. doi:10.1016/j.scitotenv.2008.02.033.

[47] S.A. Tittlemier, E. Braekevelt, T. Halldorson, C.M. Reddy, R.J. Norstrom, Vapour pressures, aqueous solubilities, Henry's Law constants, and octanol/water partition coefficients of a series of

mixed halogenated dimethyl bipyrroles, Chemosphere. 57 (2004) 1373–1381. doi:10.1016/j.chemosphere.2004.08.061.

[48] W. Vetter, Environmental occurrence of Q1, a C9H3Cl7N2 compound, that has been identified as a natural bioaccumulative organochlorine, Chemosphere. 46 (2002) 1477–1483. doi:10.1016/S0045-6535(01)00245-4.

[49] W. Vetter, P. Haase-Aschoff, N. Rosenfelder, T. Komarova, J.F. Mueller, Determination of halogenated natural products in passive samplers deployed along the Great Barrier Reef, Queensland/Australia, Environ. Sci. Technol. 43 (2009) 6131–6137. doi:10.1021/es900928m.

[50] Y. Fujii, Y. Ito, K.H. Harada, T. Hitomi, A. Koizumi, K. Haraguchi, Regional variation and possible sources of brominated contaminants in breast milk from Japan, Environ. Pollut. 162 (2012) 269–274. doi:10.1016/j.envpol.2011.11.022.

[51] N. Gandhi, R.W.K. Tang, S.P. Bhavsar, E.J. Reiner, D. Morse, G.B. Arhonditsis, K. Drouillard, T. Chen, Is mirex still a contaminant of concern for the North American Great Lakes?, J. Great Lakes Res. 41 (2015) 1114–1122. doi:10.1016/j.jglr.2015.09.015.

[52] E. Sverko, G.T. Tomy, E.J. Reiner, Y.F. Li, B.E. McCarry, J.A. Arnot, R.J. Law, R.A. Hites, Dechlorane plus and related compounds in the environment: A review, Environ. Sci. Technol. 45 (2011) 5088–5098. doi:10.1021/es2003028.

[53] X. Zhang, X. Luo, H. Liu, S. Chen, Bioaccumulation of Several Brominated Flame Retardants (BFRs) and Dechlorane Plus (DP) in Waterbirds from an E-waste Recycling Region in South China : Associated with Trophic Level and Diet Sources, 45 (2011) 400–405.