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Assessment of organohalogenated pollutants in breast milk from the Czech Republic

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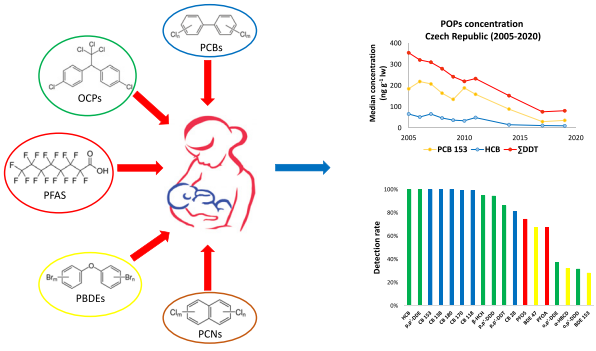
HIGHLIGHTS

- 94 organohalogenated compounds were monitored in breast milk of Czech mothers.
- An overall decrease in the body burden of chlorinated pollutants was observed.
- Only a few brominated contaminants were determined.
- Concentrations of perfluoroalkyl substances in breast milk were low.

GRAPHICAL ABSTRACT



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ABSTRACT

This biomonitoring survey brings new information on the occurrence of a total of 94 organohalogenated pollutants in 231 human breast milk samples collected in 2019 and 2021 from women living in two regions of the Czech Republic (Karvina and Ceske Budejovice). This study aimed to evaluate the concentrations of 6 indicator polychlorinated biphenyls (PCBs), 10 organochlorine pesticides (OCPs), 34 halogenated flame retardants (HFRs), 29 perfluoroalkyl and polyfluoroalkyl substances (PFAS) and 15 polychlorinated naphthalenes (PCNs). PCBs, OCPs, most of HFRs and PCNs were identified/quantified by gas chromatography coupled to (tandem) mass spectrometry (GC–MS(/MS)), while PFAS, hexabromocyclododecane isomers (HBCD), brominated phenols, and tetrabromobisphenol A (TBBPA) by ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC–MS/MS). The mean value of the sum of the 6 indicator PCBs was 123.12 nanogram per gram of lipid weight (ng g^{-1} lw). Hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH) and *p,p'*-dichlorodiphenyl-dichloroethylene (*p,p'*-DDE) were the most abundant OCPs, detected in 100 % (mean 11.8 ng g^{-1} lw), 94.8 % (mean 6.1 ng g^{-1} lw) and 100 % (mean 101.5 ng g^{-1} lw) of samples, respectively. PCN congeners 20, 52 and 66 were detected in <1 % of the samples. The HFRs concentrations were relatively low compared to the levels of OCP; The detection rate of polybrominated diphenyl ethers (PBDEs, # 47, 99 and 153) ranged 21–68 % with a mean concentrations of 0.34 ng g^{-1} lw - 0.42 ng g^{-1} lw. PFAS concentrations were also low, with perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) dominant in this group (means of 22 pg ml^{-1} and 21 pg ml^{-1}, respectively). Our results confirmed the long-term trend of declining levels of banned POPs in Czech mothers. The amounts of PCBs and OCPs were higher in older breastfeeding primiparous women.

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1. Introduction

Human breast milk is a commonly used matrix in human biomonitoring studies as the measurement of this matrix provides information on the exposure levels of both the mother and her child. Due to its relatively high fat content, milk is usually employed in the monitoring of lipophilic chemicals, such as persistent organic pollutants (POPs) (Esteban and Castano, 2009). POPs are a broad group of compounds comprising polychlorinated biphenyls (PCBs), polychlorinated naphthalenes (PCNs), organochlorine pesticides (OCPs), halogenated flame retardants (HFRs) including novel brominated and chlorinated flame retardants. and perfluoroalkyl substances (PFASs) (Muller et al., 2019; Awad et al., 2020; Li et al., 2021). Due to their persistence, potential toxic properties to human and environmental health, bioaccumulation, and long-range atmospheric transport ability, some of these compounds are listed in the Stockholm Convention ("Listing of POPs in the Stockholm Convention", 2022). Although some POPs have been prohibited or limited in use and production, they are still frequently detected in the human body (Bruce-Vanderpuije et al., 2019). Unlike PCBs and OCPs, PFAS do not tend to accumulate in lipids, but rather form a strong bond to protein fractions in the blood (Sochorova et al., 2017). People are exposed to POPs mainly through contaminated food, water, and air. Human exposure to these compounds, even at low levels, especially for a long time, can negatively affect human health, resulting in an increased risk of cancer, reproductive disorders, changes in the immune system, neurotoxicity, endocrine disruption, diabetes, genotoxicity, and birth defects (Guo et al., 2019; Fry and Power, 2017; Vafeiadi et al., 2017).

PCBs and OCPs, representatives of the classic POPs, have been for a long time (since 1994) monitored in the Czech Republic by the National Institute of Public Health (Cerna et al., 2017). In the past, PCBs were part of a technical mixture called Delor, which was produced in the territory of Czechoslovakia until 1984. In addition to other OCPs, HCB and DDT were produced by the Spolana Neratovice chemical plant (Mikes et al., 2012; Polachova et al., 2021). Previous biomonitoring studies have suggested that the exposure of the Czech general population to OCPs and PCBs is still ongoing, even after their use and production has been banned (Mikes et al., 2012; Banyiova et al., 2017). PCN mixtures have been produced since the beginning of the last century mainly as various chemical technical mixtures, also known as, Halowax (USA), Seekay wax (UK), Nibren Germany), Clonacire wax (France). The limitation of their production began in the 70s of the last century, when they were replaced by the supposedly less toxic PCBs. PCNs have also been unintentionally produced as by-products in the manufacture of PCBs (Lega et al., 2017; Falandysz and Fernandes, 2020). PCNs were added to the Stockholm Convention list in 2017. HFR are a group of compounds used in a wide range of polymeric materials to delay or prevent their ignition. This includes, their use in plastics, textiles, furniture and electronics. Polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCD) constitute an important group of HFRs. They were introduced in the 1970s and have been widely used worldwide since then, until their legislative restrictions in Europe and the USA in 2004 (Meng et al., 2021; Zuiderveen et al., 2020). Since 2009, tetra- to octa-BDEs have been listed in Annex of the Sockholm Convention list, in 2017 deca-BDEs were also added to the list. HBCD was listed in Annex A of the Stockholm Convention in 2013. Another important group of HFRs are chlorinated flame retardants, which include dechlorans and its related compounds. Dechlorane plus (DP) and its related substances (dechloran # 602, 603 and 604) have been produced in the USA since the 1960s. They were produced as a replacement for dechloran, also known as mirex, which served as a flame retardant and insecticide. However, it was banned in 1978 due to its toxicity, persistence and bioaccumulation (Ghelli et al., 2021). Dechloran plus is currently on the candidate list of the Stockholm Convention. Although the production of PFAS dates back to the 1940s, concerns about their occurrence have only arisen in recent decades, mainly due to their widespread use, bioaccumulation potential, persistence in the environment and biomagnification in the food chain (Macheka-Tendenguwo et al., 2018). There are three representatives of PFAS on the list of the Stockholm Convention. These are PFOS and its salts, added to the list in 2009 (Appendix B) and PFOA, its salts and derivatives were added in 2020 (Appendix A) (UNEP, 2019a, 2019b). Perfluorohexane sulfonic acid (PFHxS), its salts was listed in 2022 (Apendix A) (UNEP, 2022). Currently, two studies on the occurrence of PFAS in human breast milk in the Czech Republic have already been published. Studies have shown a significant decrease of monitored PFASs since 2006. The most frequently detected PFASs were PFOS, PFOA and PFNA (Cerna et al., 2020; Lankova et al., 2013). The long-term monitoring of all POPs groups in human milk is a useful tool for understanding the time trend of exposure to POPs. Knowledge of population exposure is necessary for health risk assessment and regulation of adverse pollutants in the environment. In this study carried out within the project "Healthy Aging in the Industrial Environment" (HAIE), the concentrations of 94 organohalogenated pollutants in samples of breast milk of Czech mothers are presented. These monitored organohalogenated compounds include groups of long-term monitored POPs listed in the Stockholm Convention, such as indicator PCBs, PCNs, PBDEs, HBCD, PFOS and PFOA ("Listing of POPs in the Stockholm Convention", 2022). The targeted chemicals also involve compounds with Stockholm Convention candidate status such as Dechloran plus, PFHxS and long-chain perfluorocarboxylic acids. Furthermore, other compounds with similar properties.

2. Materials and methods

2.1. Sample collection

A total of 231 human breast milk samples were provided within the HAIE research program (2018–2022), which evaluates the impact of selected environmental and lifestyle risk factors on the health and aging of the population in industrial areas ('https://www.4haie.cz/en/haie-2/'). The samples were collected from September 2019 to January 2021 from nursing mothers (age: 18–42, median 30) living in two cities in the Czech Republic (Karvina and Ceske Budejovice). The samples were collected 3–5 days after the delivery. Approximately 40 ml of breast milk was collected into 50 ml pre-washed glass containers. The breast milk sample was then stored in a freezer until analysis. Karvina is a city on the Czech-Polish border with 51,000 inhabitants. Due to its history of coal mining and heavy industry, it is one of the most polluted areas in the Czech Republic. Ceske Budejovice is a city in the south of the Czech Republic with 94,000 inhabitants. In contrast to Karvina, this town is without any significant industrial burden. Data about exposure in these districts to air pollutants in the period 1997–2019 are summarized by (Michalik et al., 2022). All nursing mothers included in the study have resided in the area for at least 5 years prior to giving birth. Mothers signed an informed consent form approved by the Ethics Committees of University of Ostrava (OU-87633/90–2018, November 30, 2018), Hospital of Ceske Budejovice, a.s. (101/19, January 4, 2019), Hospital Karvina-Raj (16,827, October 25, 2018). All participants filled in a detailed questionnaire describing the parameters of exposure and lifestyle. The main characteristics of women participating in the study are summarized in Table 1.

2.2. Standards, chemicals, and other material

Methanol, cyclohexane, and isooctane (HPLC grade) were supplied by Merck (Germany). Ethyl acetate, acetonitrile (HPLC grade) and formic acid (98 %) were obtained from Honeywell (USA). Acetonitrile (HPLC grade) and anhydrous magnesium sulphate (98 %) were obtained from Sigma-Aldrich (USA); acetone, sulphuric acid (98 %) and sodium chloride (99.9 %) from Penta (Czech Republic). Microfilters (nylon, pore size 0.2 μm) were obtained from Costar (USA). The bulk bondesil C18 sorbent (40 μm) was obtained from Agilent Technologies (USA).

The characteristics of all target analytes (full name of the compound, abbreviation, concentration of analytical standard, CAS number, and other information) are presented in Supplementary Tables S1 and S2. The preparation of calibration standards and working standards solutions is

Table 1
Characteristics of nursing women and milk samples. Differences in the recorded parameters were statistically insignificant.

Sampling region	Karvina	Ceske Budejovice
Number of samples	161	70
Age (years) Mean (min-max)	29 (18–41)	31 (18–42)
Weight (kg) Mean (min-max)	69 (43–133)	68 (39–98)
Height (cm) Mean (min-max)	166 (148–180)	168 (152–181)
Pre-pregnancy BMI (kg/m^2) Mean (min-max)	25 (17–42)	24 (16–37.5)
Infant birthweight (kg) Mean (min-max)	3.37 (2.34–4.29)	3.38 (2.55–4.1)
Parity		
1	48 %	36 %
2	36 %	37 %
3	13 %	20 %
>3	3 %	7 %
Maternal Education Level		
Primary	4 %	3 %
Secondary	58 %	43 %
University	38 %	54 %
Gestation –weeks Mean (min-max)	39.3 (36–41)	39.3 (37–41)
Milk lipid content (%) Mean (min-max)	2.8 (0.4–6.2)	1.9 (0.5–5.8)

described in the Supplementary material (Additional information S1). The individual standards of 29 PFAS (# 13 PFCA, 10 PFSA, 3 FOSA, 3 novel PFAS) were obtained from Wellington Laboratories (Guelph, Ontario, Canada). HFR standards, including 16 congeners of PBDE (# 28, 47, 49, 66, 85, 99, 100, 153, 154, 183, 196, 197, 203, 206, 207, 209) and other HFRs (PBT, PBEB, HBB, BTBPE, OBIND and DBDPE), TBBPA and HBCD isomers (α-, β- and γ-) were supplied by Wellington Laboratories. The brominated phenols (DBP, TBP, PBP) and seven novel FRs (*syn*-DP, anti-DP, DPTE, EH-TBB, HCDBCO, TBCO and DBE-DBCH) were obtained from AccuStandard (New Haven, CT, USA). Individual PCB standards (# 65, 166 and 118), a standard mixture of PCBs consisting of six PCB congeners (# 28, 52, 101, 138, 153 and 180) and ten OCP individual standards (*α*-HCH, *β*-HCH, *γ*-HCH, HCB, *o,p'*-DDE, *p,p'*-DDE, *o,p'*-DDD *p,p'*-DDD, *o,p'*-DDT, *p,p'*-DDT) were supplied by Dr. Ehrenstorfer (Augsburg, Germany). The PCN standard mixture represented by 15 PCNs (# 1, 2, 4, 9, 18, 20, 41, 42, 52, 56, 66, 70, 73, 74, 75) was supplied by Wellington laboratories (Guelph, Ontario, Canada). The internal standards of the HFRs (*α*-$^{13}C_{12}$-HBCD, *β*-$^{13}C_{12}$-HBCD, *γ*-$^{13}C_{12}$-HBCD, $^{13}C_{12}$-TBBPA) and 11 isotopically labelled internal standards of PFAS were purchased from Wellington Laboratories. The purity of all standards was at least 97 %.

2.3. Sample-preparation procedure

The sample preparation procedures used for milk analysis were based on previously published studies that were originally designed for the determination of PAHs (Pulkrabova et al., 2016) and PFAS (Lankova et al., 2013) in milk.

For the extraction of PCBs, OCPs, PCNs and GC-amenable HFRs, 10 ml of breast milk were transferred into a 50 ml polypropylene cuvette. Subsequently, internal standards (PBDE 37, PBDE 77, ^{13}C-PBDE 209, PCB 65, PCB 166) and 10 ml of ethyl acetate were added. After 1 min of vigorous shaking, 2 g of NaCl and 4 g of $MgSO_4$ were added to the cuvette and the contents of the cuvette were shaken again for 1 min. Finally, the cuvette was centrifuged for 5 min at 10000 rpm. An aliquot of 5 ml was removed from the upper organic layer. Extracts were carefully evaporated using a vacuum rotary evaporator and the solvent residue was removed using a gentle stream of nitrogen. The lipid content of the sample was determined gravimetrically. The obtained extract was cleaned using a gel permeation chromatography column packed with the Biobeads S-X3 stationary phase and eluted using a mixture of cyclohexane:ethyl acetate (1:1, *v/v*) as the mobile phase. A fraction of 17–36 ml of the purified extract was collected, evaporated in a vacuum evaporator, blown to dryness under a gentle stream of nitrogen, and finally dissolved in 0.25 ml of isooctane.

For PFAS, HBCDs and TBBPA analysis, 5 ml of breast milk were transferred into a 50 ml polypropylene cuvette, internal standards (^{13}C-PFAS mixture, ^{13}C-TBBPA and ^{13}C-HBCD isomers), 360 μL of formic acid, and 5 ml of acetonitrile were added. After 1 min of vigorous shaking, 0.5 g of NaCl and 2 g of $MgSO_4$ were added to the cuvette and the contents of the cuvette were shaken again for 1 min. The samples were then purified by dispersive solid phase extraction (d-SPE) using 180 mg of sorbent C18 and 0.6 g of $MgSO_4$. The purified extract was evaporated to near dryness and the residues were dissolved in 0.5 ml of MeOH, filtered through Costar microfilters (nylon, pore size 0.2 μm), transferred to a vial and prepared for LC-MS/MS analysis.

2.4. Instrumental analysis

Analysis of PCBs, OCPs, PCNs and HFRs (PBDEs, HBB, BTBPE, OBIND, PBEB, PBT, and DBDPE) was performed using an Agilent 7890A GC gas chromatograph (Agilent Technologies, USA), coupled to an Agilent 7000C MS triple quadrupole mass spectrometer (Agilent Technologies, USA), operated in the electron ionisation (EI) mode for OCPs, PCBs, and PCNs, and negative chemical ionisation (NCI) mode for HFRs. For the separation of OCPs, PCBs and PCNs, a HP-5MS capillary column (30 m × 0.25 mm id. × 0.25 μm film thickness; Agilent Technologies, USA) was used. In the case of HFRs analysis, a DB-XLB capillary column (15 m × 0.25 mm i.d. × 0.1 μm film thickness; Agilent Technologies) was employed. For more information about the parameters of GC–MS analysis, see the studies published by (Kalachova et al., 2013), (Polachova et al., 2021) and Tables S4-S7 in the Supplementary material. The GC conditions are listed in Supplementary materials (Additional information S2).

The ultra-high performance liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS/MS) analysis of PFASs, HBCDs and TBBPA was carried out on an Agilent 1290 Infinity II LC system interfaced by a mass spectrometer Agilent Triple Quadrupole G6495A (Agilent Technologies, USA), operated in the multiple reaction monitoring mode (MRM) using electrospray ionisation in a negative mode (ESI). The target analytes were separated on an Acquity UPLC BEH C18 analytical column (100 mm × 2.1 mm i.d., 1.7 μm particle size, Waters, USA). The mobile phase consisted of A) 5 mM ammonium acetate in water:MeCN (80:20, *v/v*) and B) MeOH:MeCN (80:20, *v/v*). The measurement conditions are described in detail in the study by (Lankova et al., 2013) and in Table S3 in the Supplementary material. The LC conditions are listed in the Supplementary material (Additional information S2).

2.5. Quality control and quality assurance

To control background contamination, a procedural blank (deionised water was used instead of milk) was prepared with each batch of 20 samples. All analyzed compounds were below the limit of detection in all procedure blanks. LOQs were estimated as the lowest calibration standard with the signal-to-noise ratio (S/N) > 10 for the quantitative transition (ion), and S/*N* > 3 for at least one confirmation transition (ion). Isotopically labelled surrogates (^{13}C-PFAS, ^{13}C-TBBPA and ^{13}C-HBCDs) were applied to correct for possible matrix effects in the ion source of the LC-MS system and the extraction efficiency (recoveries of analytes). To compensate for unexpected matrix effects (mainly in the GC injector), PCB (#65 and 166) and HFRs (BDE 37, 77 and ^{13}C-BDE 209) standards were used.

The validation of the analytical method for the analysis of 94 organohalogenated contaminants has been performed by analysing six replicates of artificially contaminated human milk samples at two concentration levels (high and low level). The spike concentrations were 1 and 10 ng g^{-1} lw for OCPs, PCBs and PCNs, 3 and 15 ng g^{-1} lw for HFRs; 0.3 and 1.5 ng ml^{-1} for TBBPA, HBCDs, 0. 03 and 0.15 ng ml^{-1} for PFASs. Detailed characteristics of the analytical method validation method are described in the Supplementary Material (Additional Information S3). Artificially

contaminated blank cow's milk (spiked concentration same as mentioned above for the validation experiments) and one duplicate sample were analyzed for all target analytes with each batch of 20 samples for quality control.

2.6. Statistical analyses

Statistical analyses were performed in Metaboanalyst (metboanalyst.ca). *t*-test was used to evaluate differences in the levels of contaminants between sites. One and two way analyses of variance (ANOVA) were used to evaluate differences between age groups, parity and weight gain factor. For analytes the concentrations of which significantly (p-value <0.05) differed between investigated classes (such as sites and age groups), ratios were calculated using the median concentrations of the group. Additionally, the principal component analysis (PCA) was performed to reveal trends in the data and the Spearman rank correlation coefficient was calculated. Logarithmic transformation was used prior to any univariate statistical test to normalize data distributions; prior to building the PCA model, autoscaling and mean centering were also performed.

3. Results and discussion

Results of 94 organohalogenated compounds concentrations (mean, median, 5–95 % percentile and the number of positive samples) measured in the human breast milk from both sampling areas are summarized in Table 2. Indicator PCBs, OCPs, PBDEs and PFAS were the most frequently detected componds. Individual groups of investigated chemicals are discussed below. As the concentrations of a vast majority of the analyzed compounds did not significantly differ between sites, the concentrations discussed below will describe the combined dataset from both sites.

3.1. PCBs and OCPs

Previous biomonitoring studies performed in the Czech Republic show above-average PCB concentrations compared to other European studies (Mikes et al., 2012; Polachova et al., 2021). In this study, the sum of six indicator PCBs ranged from 3.1 to 1607.3. ng g^{-1} lw (median 80.7 ng g^{-1} lw). The most abundant PCB congeners in milk samples were PCB 138 (median 19.1 ng g^{-1} lw), PCB 180 (median 26.9 ng g^{-1} lw) and PCB 153 (median 33.8 ng g^{-1} lw). The levels of indicator PCBs 138, 153 and 180 were generally high compared to studies from other countries (Asamoah et al., 2018; Klincic et al., 2016). PCB 28 was detected in 80 % of samples, their concentrations were, however, low (medians 0.5 ng g^{-1} lw). As shown in Table 3, the median values of 6 indicator PCBs in the presented study are similar to those reported from France (Antignac et al., 2016). Compared to other European studies, the median values of selected PCBs are approximately 2–10 times higher than studies from Croatia (Klincic et al., 2016) and the Netherlands (Cechova et al., 2017). On the contrary, the median values of selected PCBs in our study are approximately 2 times lower than those in recently published eastern European studies (Cechova et al., 2017; Mamontova et al., 2017). Compared to recent studies outside Europe, the results of the presented study are several times higher than, for example, those from Canada, Ghana or Turkey (Asamoah et al., 2018; Rawn et al., 2017; Agus et al., 2022).

Of the 10 OCPs monitored in the presented study, 10 were identified in at least one sample. The amounts of the most abundant OCPs are compared to those reported in recently published studies in Table 4. The most commonly detected substances included HCB, *p,p´-DDE, p,p´-DDD, p,p´-DDT* and *β*-HCH, with a detection rate >80 %. The total ΣDDTs (*p,p´*-DDE; *o,p´*-DDE; *p,p´*-DDD; *o,p´*-DDD; *p,p´*-DDT and *o,p´*-DDT) content in breast milk varied between 4.4 and 1347.1 ng g^{-1} lw (median 77 ng g^{-1} lw). Among the HCH isomers, *β*-HCH was the most abundant (median 4.4 ng g^{-1} lw). HCB concentrations ranged between 0.4 and 183.2 ng g^{-1} lw (median 9.6 ng g^{-1} lw). Similarly to the indicator PCBs, the OCP median values are comparable to the French study (Antignac et al., 2016). Nevertheless, median concentrations of *p,p'*-DDE published in Turkey (Agus et al., 2022), Croatia (Klincic et al., 2016), Poland (Witczak et al., 2021) are 2–10 times lower compared to the Czech Republic. On the other hand, median values for p,p'-DDE in breast milk from Tanzania were approx. Twice

Table 2
Concentrations of selected PCBs, OCPs, HFRs, and PFAS in human breast milk samples[a,b,c].

	Ceske Budejovice (n = 70)					Karvina (n = 161)				
	Analyte	Samples > LOQ	Mean	Median	5–95 % percentile	Samples > LOQ	Mean	Median	5–95 % percentile	LOQ
ng g^{-1} lw	PCB 28	83 %	1.32	0.48	0.05–1.64	81 %	0.79	0.49	0.05–2.43	0.1
	PCB 101	10 %	0.10	NC	0.05–0.16	30 %	0.21	NC	0.05–1.08	0.1
	PCB 138	100 %	28.85	19.49	7.43–63.80	100 %	31.57	18.52	5.38–99.92	0.1
	PCB 153	100 %	53.16	35.34	12.67–105.69	100 %	48.98	30.45	7.73–147.01	0.1
	PCB 180	100 %	46.04	31.08	9.22–80.12	100 %	38.52	22.66	6.31–119.91	0.1
	o,p'-DDE	0 %	ND	ND	ND	53 %	0.21	0.12	0.05–0.69	0.1
	p,p'-DDE	100 %	126.72	93.08	36.8–328.88	100 %	90.21	64.74	21.27–210.46	0.1
	o,p'-DDD	25 %	0.11	NC	0.05–0.46	34 %	0.13	NC	0.05–0.50	0.1
	p,p'-DDD	10 %	1.4	NC	0.05–3.52	96 %	1.10	0.79	0.15–3.19	0.1
	o,p'-DDT	22 %	0.43	NC	0.25–1.48	43 %	0.71	NC	0.25–2.24	0.5
	p,p'-DDT	88 %	8.03	5.97	0.25–22.29	85 %	4.70	3.70	0.25–13.97	0.5
	HCB	100 %	10.92	10.68	4.07–20.26	100 %	12.06	9.15	4.06–25.36	0.1
	β-HCH	99 %	6.88	4.97	1.19–16.71	93 %	5.77	4.14	0.05–13.03	0.1
	γ-HCH	10 %	0.36	NC	0.05–0.47	30 %	0.49	NC	0.05–1.05	0.1
	BDE 47	83 %	0.28	0.19	0.05–0.69	61 %	0.42	0.15	0.05–0.99	0.1
	BDE 99	9 %	0.18	NC	0.15–0.34	27 %	0.54	NC	0.15–1.31	0.3
	BDE 153	51 %	0.35	0.32	0.15–0.79	18 %	0.34	NC	0.15–0.74	0.3
ng ml^{-}	α-HBCD	33 %	6.14	NC	0.25–11.82	31 %	3.3	NC	0.25–17.12	0.15
	PFOS	68 %	0.014	0.008	0.002–0.04	77 %	0.025	0.01	0.002–0.07	0.003
	PFOA	77 %	0.034	0.022	0.004–0.011	55 %	0.017	0.01	0.004–0.08	0.006

NOTES: - NC not calculated; ND - not detected

[a] Median values were calculated when the analyte was positively detected in a concentration above LOQ in >50 % of samples.

[b] For results below LOQ, 50 % of the LOQ value was used for mean, median and percentile calculations.

[c] PCBs: PCB 52 was quantified in 0 and 2 % of samples from the respective sites. [c]OCPs: α-HCH was quantified in 4 and 11 % of samples from the respective sites. [c]PCNs: PCN 20, 52, 66 were quantified in <1 %; PCN 1,2, 4, 9, 18, 20, 41, 42, 56, 70, 73, 74, 75 were not detected in any sample. [c]HFRs: anti DP was quantified in 20 % of samples, α- TBECH and β – TBECH were quantified in 10 and 27 %, respectively; BDE 209 was quantified in 12 % of samples; BDE 100, BDE 154, BDE 183, BDE 196, BDE 197, BDE 203, BDE 207, DBDPE, syn DP, EH-TBB, were detected in <3 % of samples; BDE 28, BDE 49, BDE 66, BDE 85, BDE 206, BTBE, *β*-HBCD, *γ*-HBCD, TBBPA, PBP, DPTE, HBBz, HCDBCO, OBIND, PBEB, PBT, TBCO, 2 were not detected in any sample. [c]PFAS: PFNA was quantified in 19 % of samples, PFBS, PFHxS, PFBA, PFHxA, PFDA, PFHpA, PFUdA were quantified in <7 % and < 9 %, respectively. FOSA, N-MeFOSA, N-EtFOSA, PFDS, PFPeA, PFHxA, PFHxDA, PFODA, PFPrS, PFNS, PFDoS, HFPO-DA, NaDONA, 11Cl-PF3OudS, PFTeDA, PFPeS, 9Cl-PF3ONS were not detected in any sample.

Table 3
Overview of current studies (2016–2021) – PCB median concentrations (ng g^{-1} lw) in human breast milk samples.

Year of sampling	Country	Number of samples	PCB 28	PCB 52	PCB 101	PCB 138	PCB 153	PCB 180	Sum of 6 PCB[a]	Reference
1997–2009	Russia	38	3.5	0.88	1.9	53	47	13	157.28	(Mamontova, 2017)
2008–2011	Canada	298	1	0.13	0.17	5.1	7.9	4	18.3	(Rawn et al., 2017)
2010–2012	Slovakia	37	1.11	0.13	0.22	10.68	15.96	44.32	72.42	(Cechova et al., 2017)
2011–2014	France	96	1.29	0.24	0.39	38.2	20.28	24.06	84.46	(Antignac et al., 2016)
2011–2014	Netherlands	120	0.79	0.17	0.19	10.68	15.95	10.72	38.5	(Cechova et al., 2017)
2011	Croatia	79	1	3.7	0.2	3.5	6.4	2.8	17.6	(Klincic et al., 2016)
2013	Turkey	48	11.44[b]	22.99[b]	12.22[b]	ND	1.7[b]	0.58[b]	48.93	(Agus et al., 2022)
2014–2016	Ghana	47	0.87	0.10	0.43	0.68	0.09	0.39	2.56	(Asamoah et al., 2018)
2019–2021	Czech Republic	231	0.49	0.05	0.24	19.11	33.85	26.95	80.69	The presented study

NOTES: - Not mentioned; ND not detected
[a] Sum of medians of 6 indicator PCB (28, 52, 101, 138, 153, 180).
[b] Mean

as high as in our study (Muller et al., 2019) and up to four times higher in samples from Russia (Mamontova, 2017) and China (Lu et al., 2015). The highest recently published values of HCB and HCH isomers are also from China (Lu et al., 2015). Our study is in agreement with the aforementioned studies, finding β-HCH to be the most abundant isomer compared to α-HCH and γ-HCH. However, an opposite trend was observed in a Polish study (Witczak et al., 2021), where concentrations of all selected HCH isomers were similar.

The biomonitoring study in human breast milk organized by the Czech National Institute of Public Health between 1994 and 2009 showed a declining trend in the levels of selected PCBs represented by PCB 153 and OCPs represented by DDTs and HCB (Mikes et al., 2012). Between the years 2005 and 2009 a decreasing trend of indicator PCBs was observed in the median PCB 153 concentration in breast milk of mothers in the Czech Republic from 183 ng g^{-1} lw to 135 ng g^{-1} lw (Mikes et al., 2012). A similar long-term trend was documented between 2005 and 2009 for OCPs, HCB concentration in breast milk of Czech mothers decreased from 97 ng g^{-1} lw to 35 ng g^{-1} lw (Mikes et al., 2012). Comparing the results of a 15-year biomonitoring study from the Czech Republic (Mikes et al., 2012) with results presented by us, we found tthe concentration of PCB 153 in breast milk decreased from 135 ng g^{-1} lw to 33.8 ng g^{-1} between the years 2009 and 2021. An significant drop in HCB concentration in breast milk (from 35 ng g^{-1} lw to 9.6 ng g^{-1} lw) was document between 2009 and 2021 for. This deecrease can be observed in recent decades, indicating that there is no new source of monitored PCBs and OCPs. This trend is probably influenced by established legislative measures, which is also documented by biomonitoring data from the last decades.

3.2. PFAS

Of the 29 target PFAS, 19 were not detected in any of the analyzed samples; only 10 compounds (PFBS, PFHxS, PFBA, PFHxA, PFDA, PFHpA, PFUdA, PFOS, PFOA, PFNA) were found at concentrations above the LOQ in at least one sample and only 2 PFASs (PFOS, PFOA) were detected in >30 % of the samples. PFOA (median 13 pg ml^{-1}) was the compound with the highest median concentration in this group, followed by PFOS (median 9 pg ml^{-1}).

Table 5 shows a comparison of the median concentrations detected in the presented study with those reported in similar biomonitoring studies. Very similar data on the occurrence of PFAS as in our study were published in Germany, where their mean value were 17 pg ml^{-1} (PFOS) and 22 ng ml^{-1} (PFOA) (Fromme et al., 2022). In general, the concentrations of PFOS, PFOA and PFNA in the Czech Republic are the lowest compared to the other countries in Europe. The highest concentrations of PFOS (median: 69 pg ml^{-1}), PFOA (median 138 pg ml^{-1}) and PFNA (median 7 pg ml^{-1}) were reported in breast milk in Spain (Beser et al., 2019). Concentrations of these three PFAS in breast milk from the Czech Republic are approximately half of those reported in the USA (Zheng et al., 2021) and China (Jin et al., 2020). Median values for PFOS and PFOA measured in this study are lower than the worldwide published median values reported by (Fiedler and Sadia, 2021), where pooled breast milk samples from primiparae from 42 countries, including Czech Republic, were analyzed. Based on previously published biomonitoring studies from the Czech Republic, we can say that the PFOS and PFOA concentrations in breast milk keep decreasing, with median PFOS/PFOA concentrations being 47/44 pg ml^{-1} in 2010, 29/35 pg ml^{-1} in 2014, 20/23 pg ml^{-1} in 2017, and: 9/12 pg ml^{-1} in 2019–2021) (Cerna et al., 2020; Lankova et al., 2013).

3.3. HFRs

Out of the 34 monitored HFRs, 20 compounds were detected in >1 % of the samples. BDE 47 (median 0.16 ng g^{-1} lw) and BDE 153 (median 0.15 ng g^{-1} lw) were the most commonly detected HFRs; they were present in 68 % and 51 % of breast milk samples, respectively. Among PBDEs, BDE 99 and 209 were detected in >10 % of samples. A comparison of the median concentrations from this study with those reported elsewhere is shown in Table 6. In general, the concentrations of PBDE found in Czech milk samples are relatively low compared to other European studies (Darnerud et al., 2015; Aerts et al., 2019; Wemken et al., 2020). The highest PBDE concentrations (discussing only recent results) were reported from the USA,

Table 4
Overview of current studies (2015–2021) – published OCP median concentrations (ng g^{-1} lw) in human breast milk samples.

Year of sampling	Country	Number of samples	HCB	pp´-DDE	pp´-DDD	pp´-DDT	α-HCH	β-HCH	γ-HCH	Reference
2002–2007	China	142	49.8	292	3.1	4.1	0.97	20.5	10.2	(Lu et al., 2015)
1997–2009	Russia	38	42	324	0.71	22	2.1	2.6	0.26	(Mamontova, 2017)
2011	Croatia	79	0.5	8.1	0.3	0.6	0.1	0.4	1	(Klincic et al., 2016)
2012	Africa Tanzania	47	1.41	135	0.48	3.59	–	–	–	(Muller et al., 2019)
2011–2014	France	42	10.28	60.07	–	2.16	–	15.05	–	(Antignac et al., 2016)
2013–2016	Taiwan	68	–	9.24	0.23	0.41	0.13	0.12	0.1	(Kao et al., 2019)
2013	Turkey	48	0.016[a]	0.86[a]	–	3.33[a]	0.24[a]	0.16[a]	–	(Agus et al., 2022)
2014	Belgium	206	5.5	36.95	ND	2.8	ND	2.4	ND	(Aerts et al., 2019)
2013–2015	Poland	96	–	0.015	0.118	0.13	3.15	3.19	3.13	(Witczak et al., 2021)
2019–2021	Czech Republic	231	9.62	70.20	0.85	4.13	0.05	4.42	0.05	The presented study

NOTES: - Not mentioned; ND not detected
[a] Mean

Table 5
Overview of current studies (2013 – 2021) dealing with median PFAS concentrations (pg ml^{-1}) in human breast milk samples collected worldwide.

Year of sampling	Country	Number of samples	PFOS	PFOA	PFNA	Reference
2010	Czech Republic	50	47	44	–	(Lankova et al., 2013)
2011	Korea	293	48	40	17	(Lee et al., 2018)
–	Ireland	16	20	100	14	(Abdallah et al., 2020)
2014	Czech Republic	164	29	35	ND	(Cerna et al., 2020)
2015	Spain	20	69	138	70	(Beser et al., 2019)
2017	Czech Republic	232	20	23	7[b]	(Cerna et al., 2020)
2019	USA	50	30	14	6	(Zheng et al., 2021)
2020	China	174	25[a]	29[a]	70[a]	(Jin et al., 2020)
2020	Sweden	10	39[a]	42[a]	10[a]	(Awad et al., 2020)
2019–2021	Czech Republic	231	9	13	2	The presented study

NOTES: - Not mentioned; ND not detected
[a] Mean.

where the BDE 99 and 153 were the most common congeners, with median concentrations of 3.45 and 4.86 ng g^{-1} l, respectively, which is approx. 10 times higher than in our study. Given the high production of PBDEs in the United States at the end of the last century, this increased burden in this area is foreseeable. Still, these concentrations have been declining over the last decade even in the USA (Guo et al., 2016; Johnson-Restrepo and Kannan, 2009). From the group of the monitored novel HFR, TBECH was the most commonly detected one, present in 22 % of breast milk samples (mean: 0.85 ng g^{-1} lw). Anti-Dechlorane Plus (anti- DP) was also detected in 13 % of samples (mean: 0.14 ng g^{-1} lw). The reports on anti-DP in human breast milk samples are limited. Comparing the current results with the findings in Canadian and Chinese cities, anti-DP concentrations in the Czech Republic are 5 times lower than in Canada (Siddique et al., 2012) and up to 200 times lower than in China, where the high concentrations may be caused by the widespread presence of e-waste recycling plants in China (Ben et al., 2013).

Other detected HFR compounds include α-HBCD (median: 0.25 ng ml^{-1}), with a detection rate higher than 30 %. β-HBCD and γ-HBCD were not detected in any of the tested samples. The α-HBCD median concentration in the Czech Republic is 6 times lower than in an Irish study by (Wemken et al., 2020), and up to 20 times lower in comparison with a Chinese study (Chen et al., 2019). This may be caused by the fact that HBCD is still used in China as a flame retardant for various electronic products (Lu et al., 2018).

3.4. PCNs

Of the 15 analyzed PCN congeners, none were detected in >1 % of the measured samples. PCN congeners 20, 52 and 66 were present in at least one sample each. Individual concentrations of these congeners ranged between 250 and 832 pg g^{-1} lw. The findings of PCN congeners in the breast milk of Czech mothers are probably caused by accidental contamination from the environment, as there is no obvious source of these compounds in the Czech Republic. PCN levels are assumed to be affected by emissions from sources related to the historical use of technical mixtures and waste incineration. In the last century, PCNs were manufactured mainly in Western Europe (Germany, UK) and the USA (Odabasi et al., 2012) but not in the Czech Republic; their major occurrence in the Czech Republic, therefore, was not expected. It should be mentioned that not many publications have focused on PCN biomonitoring in European countries (Pratt et al., 2013; Lunden and Noren, 1998). When comparing the results of the presented study with foreign studies, congeners 52 and 66 are commonly found in biotic samples. For further comparison, studies dealing with the incidence of PCNs are listed below. In Ireland, total concentrations of 12 PCN congeners in breast milk (n = 109) ranged from 59 to 168 pg g^{-1} lw in 2010 (Pratt et al., 2013). Between 2017 and 2019, breast milk was sampled in 19 provinces of China. Total PCN concentrations were several times higher than in the Irish study, ranging from 211 to 2497 pg g^{-1} lw, depending on the region in which the collection was performed (Li et al., 2021).

3.5. Differences between sampling sites (Karvina and Ceske Budejovice)

By comparing the two data groups from each region using different statistical tools (Student t-test, PCA), slight differences in the concentrations of the individual analytes were found. The result of the comparison based on Student's t-test can be seen in Table 7. Concentrations of 6 out of 94 monitored compounds were significantly differed between sites. At least two-fold difference between sites was observed only for four analytes (*o, p'*-DDE, *p,p'*-DDT, BDE 153 and PFOA). In general, however, no significant difference between localities was observed, despite the hypothesis that the Karvina area should be more heavily burdened due to the industrial nature of the area. It should be mentioned that the sites were primarily chosen to investigate exposure to polycyclic aromatic hydrocarbons (Pulkrabova et al., 2016), not to halogenated POPs. As dietary intake likely represents the main source of exposure to the target POPs and dietary intake is not expected to significantly change between sites, this lack of difference is not surprising (Pavlikova et al., 2022).

3.6. Differences between age groups

6 of the 94 analyzed organohalogenated compounds, specifically 3 PCBs (PCB 138, PCB 153 and PCB 180) and 3 OCPs (β-HCH, HCB and *p, p'*-DDE), met the criterium of ANOVA (p-value <0.05) followed by Fisher LSD test, that confirmed significantly different concentrations of the

Table 6
Overview of current studies (2016–2021) published median HFR concentrations (ng g^{-1} lw) in human breast milk samples.

Year of sampling	Country	Number of samples	BDE 47	BDE 99	BDE 153	BDE 209	α –HBCD[a]	Reference
2010	Sweden	30	0.46	0.07	0,45	–	–	(Darnerud et al., 2015)
2012	Tanzania	47	1.44	8.23	1.44	–	–	(Muller et al., 2019)
2009–2012	USA	67	16.7	3.5	4.9	–	–	(Guo et al., 2016)
2011–2014	France	96	0.43	0.1	0.54	0.21	0.56	(Antignac et al., 2016)
2014	Belgium	206	0.13	ND	0.16	–	–	(Aerts et al., 2019)
2016	China	20	0.3	0.05	0.41	5.39	4.87	(Chen et al., 2019)
2016–2018	Ireland	92	0.5	ND	0.71	1.4	1.7	(Wemken et al., 2020)
2019–2021	Czech Republic	231	0.17	0.15	0.15	0.75	0.5	The presented study

NOTES: - Not mentioned; ND not detected.
[a] Concentration in ng ml^{-1}

Table 7
Ratios of median concentration of significantly differing (based on *t*-test, *p*-value <0.05) contaminants between localities.

Group of POPs	Analyte	Ratio of median concentrations (Karvina:Ceske Budejovice)	t-test (P-value)
OCPs	*p,p'*-DDT	0.613	2.373e-3
	o,p'-DDE	2.293	3.42e-13
	p,p'-DDE	0.691	1.444e-4
	γ-HCH	0.83	3.104e-2
HFRs	BDE 153	0.468	3.508e-4
PFAS	PFOA	0.444	1.879e-4

targeted POPs between maternal age groups (17–24; 25–30; 30–35 and 35–42 years of age) and parity. Selected contaminants, showed a correlation with increasing age for group of primiparous women. Spearman rank correlation coefficient was also calculated for confirmation and summarized in Table 8. Box-plots of breast milk concentrations of the investigated analytes in Karvina for individual age groups of primiparous women are shown in the Supplementary Material (Fig. S1). Application of the same statistical criteria as for primiparous mothers to mothers with two or more children did not confirm significant differences between age groups. The effects of BMI and weight gain of breastfeeding mothers on organohalogenated compounds levels in milk was further investigated. However, no statistically significant relationships between these examined factors and breast milk concentrations were discovered.

4. Conclusions

These data document the current body burden of breastfeeding mothers (and thus effectively, exposure of newborns) in the Czech Republic to 94 organohalogenated compounds. In the case of PCBs and OCPs, concentrations in the Czech Republic are still higher compared to most European countries. Despite the significantly higher exposure of the Czech population in the past, this study confirmed the decreasing trend in PCBs and OCPs exposure. The concentrations of PFAS and HFRs are low, and only some representatives of these groups were quantified in breast milk samples. In the last decade, a decrease in PFAS concentrations in breast milk has been documented in the Czech Republic. In this study the first data on the occurrence of PCNs in breast milk are presented, confirming the low exposure of the Czech population. Statistical analysis showed that concentrations of selected halogenated contaminants differed signifficantly between age groups of primiparous women. In contrast, there was no trend between sampling sites and organohalogened compounds concentrations in breast milk. The presented results on the occurrence of POPs in human monitoring are unique and complement the knowledge about their occurrence in Europe.

CRediT authorship contribution statement

Ondrej Parizek: Formal analysis, Investigation, Validation, Visualization, Writing – original draft. **Tomas Gramblicka:** Data curation, Investigation, Validation. **Andrea Polachova**: Validation. **Kamila Bechynska:** Statistical data analysis. **Darina Dvorakova:** Methodology, Review and editing, Validation. **Michal Stupak:** Methodology, Review and editing **Jiri Dusek:** Sampling **Jitka Pavlikova:** Sampling **Jan Topinka:** Project administration, Review and editing, Resources **Radim J. Sram:** Project administration, Resources Review and editing **Jana Pulkrabova:** Conceptualization, Review and editing, Funding acquisition, Project administration, Supervision.

Table 8
The correlation between a selected statisticaly significant POPs (ANOVA, *p*-value <0.05 followed by Fisher LSD test and Spearman correlation) between various age groups of primiparous women.

Group of POPs	Analyte	ANOVA p-value	Fisher's LSD	Pattern hunter Spearman correlation
	PCB 138	7.47e-10	2–1; 3–1; 4–1; 5–1; 5–2	0.47666
	PCB 153	2.20e-6	2–1; 3–1; 4–1; 5–1; 5–2	0.52869
	PCB 180	1.99e-6	2–1; 3–1; 4–1; 5–1; 3–2; 5–2; 5–3; 5–4	0.53491
	p,p'-DDE	2.23e-3	3–1; 4–1; 5–1; 3–2; 5–2	0.4602
OCPs	β-HCH	4.71e-3	2–1; 3–1; 4–1; 5–1	0.35165
	HCB	4.56e-4	2–1; 3–1; 4–1; 5–1; 4–2	0.44881

Data availability

The data that has been used is confidential.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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