Egypt. J. Chem. **Vol. 64,** No. 2 pp. 573 - 579 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

A two years study of dioxin-like polychlorinated biphenyls (dl-PCBs) in mother's milk in Qalyubia governorate, Egypt.

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Abstract

The high cost of dl-PCBs analysis using a high-resolution gas chromatography/mass spectrometry (HR-GC/MS) generally minimizes it is regular analysis studies, especially in human tissue. In this study, a survey was carried out for analysis of dl-PCBs in thirty human milk samples collected from Qalyubia governorate, Egypt (2016-2018). Significant correlations were observed between Σdl-PCBs (TEQ), age, and numbers of deliveries. All dl-PCBs congeners were detected in all collected samples. Besides, the non-ortho PCB congener (PCB 126) was found at elevated concentrations. The mean TEQ concentrations of non-ortho and mono-ortho PCBs in the breast milk of the primiparous mothers were 7.30 and 0.20 pgTEQg^{-1} lipid, respectively. On the other hand, multiparous mothers have a mean TEQ concentration for these dl-PCBs (non-ortho and mono-ortho PCBs) of 6.1 and 0.3 pg TEQ g^{-1} lipid, respectively. The most found dl-PCBs were PCB-118 and PCB-156, both account 64.9% from ΣPCBs concentrations without TEF. Estimation of infant daily intakes (EIDI) showed that they are at high risk of adverse effects caused by PCBs.

Keywords: Dioxins like compounds, High-Resolution Gas Chromatography/Mass Spectrometry, Breast milk, Egypt, TEF, EIDI.

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1. Introduction

Polychlorinated biphenyls (PCBs) are organic chlorine compounds that were manufactured previously for its use as insulating fluids (coolants) [1, 2]. As these compounds are of high chemical stability, high dielectric constant, and low flammability [3, 4]. However, some of these PCBs are structurally and toxicologically similar to the well-known carcinogenic dioxin compounds, called dioxin-like PCBs (dl-PCBs) [5]. There are twelve dl-PCBs congeners have wide range toxicity to human. The most toxic PCBs congeners is the PCB-126 congener, which has same tumour effects consistent with those seen for dioxin according to US National Toxicology Program (NTP) [6]. In addition, PCBs were classified as persistent organic pollutants (POPs), according to Stockholm Convention, causing long-term environmental contamination and damaging effects on health. It was previously reported that [7], the risk of mortality due to breast cancer may be increased with increased levels of PCBs. It was also reported that [8], low chlorinated-PCBs have anti-androgenic and estrogenic effects by inhibition of AhR signaling and moderate CAR/PXR-mediated activities. A toxicity of dioxin-like PCBs to endocrine was also reported [9, 10]. Therefore, the production of PCBs was completely prohibited in the 1970s. Even though, residues of PCBs and dl-PCBs are still present in the soil, air, and food, especially animal origin food. Furthermore, the lipophilicity of these compounds makes them present also in human fatty tissues. Such residues were mainly produced as unwanted by-products in the flue gas of various waste incinerators. In addition, residues of dl-PCBs were frequently found in oils of old transformers [3].

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Receive Date: 01 September 2020, Revise Date: 15 September 2020, Accept Date: 06 October 2020
DOI: 10.21608/EJCHEM.2020.41413.2838

It is well known that human milk contains the necessary nutrients and basic required biologically active components that required for the early development of infant [11]. However, infants are the most subjected group for exposure to dl-PCBs [12]. Since, these lipophilic toxic compounds were transferred to mothers through several years and tend to be accumulated in mothers. In addition, pregnant women tend to consume more animal origin food that may contain high levels of dl-PCBs. This situation is twofold in the developing countries, that have uncontrolled environmental practices especially during the work of the present incinerators [13]. Transplacental route and breastfeeding resemble the main two roots for transferring dl-PCBs from mother to her child. Therefore, monitoring dl-PCBs in breast milk is not only required to protect the health of new infant, but also introduce useful information about the degree of contamination by dl-PCBs during long time.

Analysis of dl-PCBs at very low concentrations (ng/kg) in a complex sample like breast milk (containing high levels of fat and proteins) is a challenging situation, especially in the developing countries. Where such low detection limits require advanced mass spectrometry techniques of high cost. In addition, such specific residue analyses require experienced researchers not only for their work on the advanced mass spectrometry instruments, but also for carrying out proper sample preparation and extraction [14]. The commonly used instrument for the residue analysis of dl-PCBs at very low traces levels is the High Resolution Gas Chromatography Mass Spectrometry, HR-GC/MS [15]. Recently; there some studies have been carried out for the residue analysis of dl-PCBs in breast milk using Gas Chromatography Tandem Mass Spectrometry (GC-MS/MS). However, HR-GC/MS can detect dl-PCBs at much lower levels than GC-MS/MS. Few studies reported the proper application of GC-MS/MS with a soft ionization Atmospheric Chemical Ionization (APCI) for the detection of dl-PCBs even at low concentrations [16]. However, APCI is not commonly used as the well-known Electron Ionization (EI) in most analytical laboratories. Finally, not all lactating mothers are welcome to participate in such survey programs that add more difficulties on such studies.

In the current study, breast milk samples were collected from 30 lactating women living in Qalyubia governorate, Egypt, during 2016-2018. These mothers were multipara (18) and primipara (12). Each detected dl-PCBs congener was expressed by toxic equivalencies (TEQ) according to the toxic equivalent factor which has recommended by world health organization 2005 (TEF-WHO_{2005}) [17]. The correlations between age and the total TEQ concentrations of dl-PCBs in the collected breast milk samples were also calculated and discussed. Finally, a risk assessment of dl-PCBs was evaluated for infants. The present study aimed to present a model for human contamination by dioxin-like PCBs and the transportation of this risk to infants in Egypt

2. Materials and Methods

2.1.Chemicals and reagents

Toluene, n-hexane, tetradecane, nonane, and celite 545 were purchased from Merck Chemicals. Sulphuric acid (purity ≥98%), dichloromethane, acetone, ethanol, diethyl ether were obtained from Sigma–Aldrich. A Millipore water purification system (Milli-Q) was used to prepare deionized water (DIW) of 18.2 Ω cm. Silica gel 60 (0.063-0.2mm mesh) was purchased from Fluka. Anhydrous sodium sulfate and carbopack (80/100 mesh) were supplied from SUPPELCO. Basic alumina was purchased from ICN biomedical company. Readymade labeled and native dl-PCBs stock standard solutions of catalogue numbers; 68C-LCS (1000 ng/ml), 68C-PAR (2000 ng/ml), respectively, were purchased from WELLINGTON Laboratories Inc. Labeled internal/injection standard of catalogue number 68C-IS was also purchased from WELLINGTON Laboratories Inc. Working standard solutions of labeled, and native dl-PCBs were prepared in nonane at 20 and 40 ng/ml, respectively. A working labeled internal/injection standard was prepared in nonane at 200 ng/ml. The stock standard solutions and working standard solutions were kept at -20 and 4ºC, respectively.

2.2.Sample preparation

A total of 30 breast milk samples were collected at the period from 2016 to 2018 from Qalyubia governorate, Egypt. All the participants participated in a questionnaire concerning some available information like; mother age, baby age and the number of deliveries. Breast milk samples were collected in glass sample bottles and transferred to the laboratory in a refrigerator car to then store at -20°C until its analysis in the laboratory.

2.3.Sample Extraction and clean up

Extraction of dl-PCBs in the studied breast milk samples and the subsequent clean up steps were carried out using a standard dl-PCBs method, US-EPA Method 1668 standard [18]. While, breast milk fat was extracted using a liquid-liquid extraction method (LLE), after addition 100 µL of isotopically Labeled analogs working standard solution of 12 of the substituted dl-PCBs (a mixture of 13C12 dl-PCBs) as an internal standard followed by saturated sodium oxalate solution to prevent coagulation,

ethanol was added in order to precipitate proteins. Fat was extracted by a mixture of diethyl ether: n-Hexane, after extraction, 50 µL (Tetradecane) was added as a keeper for analytes during its evaporation. Thereafter, the extract was rotary evaporated and concentrated to near dryness, the remaining solvent is completely removed by using a stream of nitrogen. Finally, milk fat content was gravimetrically calculated using the following equation (eq. 1) before its clean-up.

$$Lipid\ (\%) = \frac{Weight\ of\ lipid,g}{\text{weight of sample,g}}\ x\ 100 \qquad \text{Eq. 1}$$

The clean-up and fractionation of the analyzed dl-PCBs were carried out on the extracted breast milk fat using different clean-up steps, firstly extracted lipids were dissolved in n-hexane and mixed with acidified silica gel at overnight. The mixture was filtered over anhydrous sodium sulfate and the filtrate was concentrated as mentioned above, then the concentrated extract from the previous process was applied on multi-layer silica gel column using n-hexane, then the concentrated extract was applied to basic alumina column, finally, the extract resulting from the previous column was applied to carbopack column. Nonane (10µl) was added to the eluting solution. Injection labeled working standard solution (10 µl) was added to the sample extract immediately before injection.

2.4.High resolution gas chromatography mass spectrometry

The studied dl-PCBs were detected using high-resolution gas chromatography–high-resolution mass spectrometry (HRGC– HRMS), at the QCAP Egypt laboratory (The Central Laboratory for analysis of pesticide residues and heavy metals in food). The MS was operated in positive electron ionization (EI+) mode at 35 eV and with a resolution of 10.000 (±5% valley). Mass parameters and chromatographic conditions were used as in the standard dl-PCBs method, US-EPA Method 1668. The injection volume was about 1 µL of each sample. Oven GC program was set for dl-PCBs run time (40min); at 90°C (1min), 15°C min^{-1} to 220°C (15 min) followed by 8°C min^{-1} to 290°C (7 min) for dl-PCBs, respectively. Helium at a constant flow rate of 1ml min^{-1} was used as a carrier gas. The injector and interface GC temperatures were 280°C and 260°C, respectively. The statistical analysis was conducted using GraphPad Prism 7. Statistical significance was assumed at the 5% level.

2.5.Statistical analysis

The statistical analysis was conducted using GraphPad Prism 7 program. Statistical significance was assumed at the 5% level.

3.Results and Discussion

3.1.Concentrations of dioxin-like compounds (dl-PCBs) in breast milk

The average age of participating women was 26.6 years old and ranged between (20 to 33 years). The mean lipid content of thirty breast milk samples was 3.11g ranged from (1.2 to 7.8g). All the 12 congeners of dl-PCBs were detected in all samples even the most toxic congener PCB 126 with TEF (0.1), the same trend was found in other studies. Without TEF, the four non-ortho dl-PCB congeners accounted for about 1.15% from the total PCBs concentration; while the eight mono-ortho dl-PCB congeners accounted for 98.85% from the total PCBs, as shown in Figs. 1b and 2a, due to confirm the most abundant homologs (mono-ortho dl-PCB) and congener (PCB 118).

PCB 118 was the predominant congener in all samples with a mean percentage of 42.7 % with a concentration ranging from 998.2 to 17893.8 pg/g lipid weight of the total PCBs as shown in Fig. 2a. This results in agreement with previous results in Turkey [19] and China [20]. While, PCB 153 and 138 were the predominant congeners in the breast milk, Northern Russia [21]. The concentrations of the twelve congeners of dl-PCBs (pg/g lipid) and (pgTEQ/g lipid) in breast milk samples were summarized in Table 1. The mean concentration was 10238.3 pg/g lipid, ranged from 2387.6 to 43359.8 pg/g lipid.

Expressed TEQ concentrations, PCB 126 was the most contributed congener in all samples as shown in Fig.2b with a mean percentage contribution of 88.3 % (6.04 pg TEQ/g lipid), with concentration ranging from 1.77 to 9.41 pg TEQ/g lipid weight of the total TEQ dl-PCBs (±1.72), in which refer to its highly toxic equivalent factor (0.1).

In our investigated results, it revealed that the four non-ortho dl-PCB congeners represented for about 95.6% from the total TEQ dl-PCBs, while the eight mono-ortho dl-PCB congeners accounted for 4.4% from the total TEQ dl-PCBs, as shown in Fig. 1a. On the other hand, the concentrations (TEQ) of the twelve congeners (pgTEQ/g lipid) were summarized in Table 1, in which showed that the total TEQ of dl-PCBs was ranged from (2.5 to 10.34) pg WHO2005-TEQ/g lipid with a mean concentration of 6.8 pg WHO2005- TEQ/g lipid (±1.72).

3.2.Effects of maternal age and delivery on the levels of dioxin like compounds

The collected breast milk samples were grouped in order to analyze the effect of age on contamination levels. Donors were divided into groups considering age (age groups lower than 25, from 25 to 30 and higher than 30 years).

Age was significantly related to dl-PCBs concentrations and older mothers had a higher level of dl-PCBs in their milk than younger mothers 7.85, 6.15, and 5.43 pg TEQ/g lipid, respectively. This point of age was in agreement with previous studies reporting a positive correlation between age of the mother and dl-PCBs levels in breast milk [19, 20].

Also, according to the number of deliveries, it was founded that the mean concentration (TEQ) of dl-PCBs in breast milk samples of primiparous and multiparous mothers were 7.41 and 6.22 pg TEQ/g lipid, respectively. Indicating that the concentration (TEQ) of dl-PCBs in breast milk samples of multiparous mothers were lower than those of primiparous mothers. This means that the levels of dl-PCBs in breast milk samples tended to decrease with the increase of the number of deliveries our investigated results were in agreement with other recent studies [21, 22].

3.3.Risk assessment for infants

In this study, it assumed that the average breast milk consumption of a 5 kg infant to be 700 g/day.

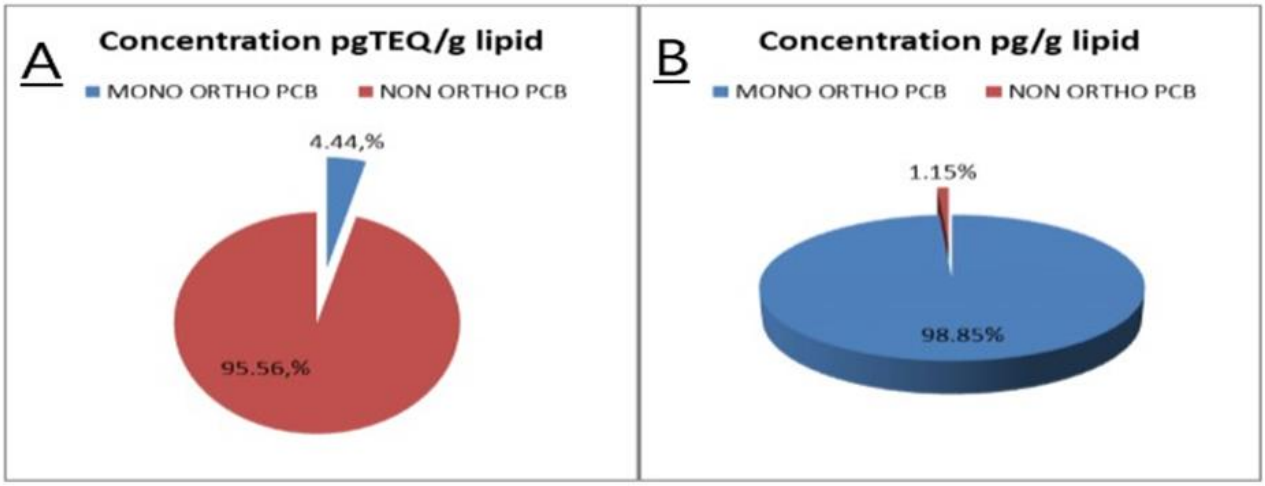

Fig. 1. The contribution percentage of mono-ortho and non-ortho to the total TEQ dl-PCBs in pgTEQg lipid (A) and to the total dl-PCBs in pg/g lipid (B).

The average daily intake (ADI) of dl- PCBs for each infant via breastfeeding was expressed as (pg TEQ/kg/day), was calculated based on the following equation (eq. 2):

$$ADI = V \times F \times C \times 0.95 \qquad \text{Eq. 2}$$

Where's, V = Volume of the daily breast milk intake adjusted to body weight (g/kg bw)

F = Breast milk fat content (g/100g milk)

C= Concentrations of dl-PCBs (pg TEQ/g fat)

0.95 = Absorption efficiency of dl-PCBs in the gastrointestinal tract.

The estimated daily intake (EDI) of dl-PCBs for breast-fed infants was 49.06 pg TEQ kg^{-1} bw day^{-1} ranged from 21.03 to 112 pg TEQ kg^{-1}bw day^{-1}. Our results were similarly and matched with other countries such as; Turkey [26], France [27] and Greek [28].

Conclusion

Levels of the twelve dioxin-like polychlorinated biphenyls in the breast milk of 30 women in Qalyubia (Egypt) were analyzed using a high-resolution gas chromatography-mass spectrometry. PCB 118 was the predominant congener to the total dl-PCBs, while PCB 126 was the most contributed congener to TEQ Concentration of dl-PCBs. concentrations of each congener of non-ortho PCBs, and mono-ortho PCBs in the primiparous were notably higher than multiparous mothers. Concentrations of non-ortho PCBs, and mono-ortho PCBs were significantly related to maternal age. Our results elucidated also that the body burdens of dl-PCBs in mother's milk were higher than the tolerable daily intake. The result of this survey study aimed not only to protect both the mothers and infants from the dangers of cancer but also to explore the long term of the environmental

contamination by dl-PCBs in Egypt. It is aimed that the results of this study help the Egyptian authorities to improve both the legislations and increase the capacity of current laboratories that can carry out such important analysis.

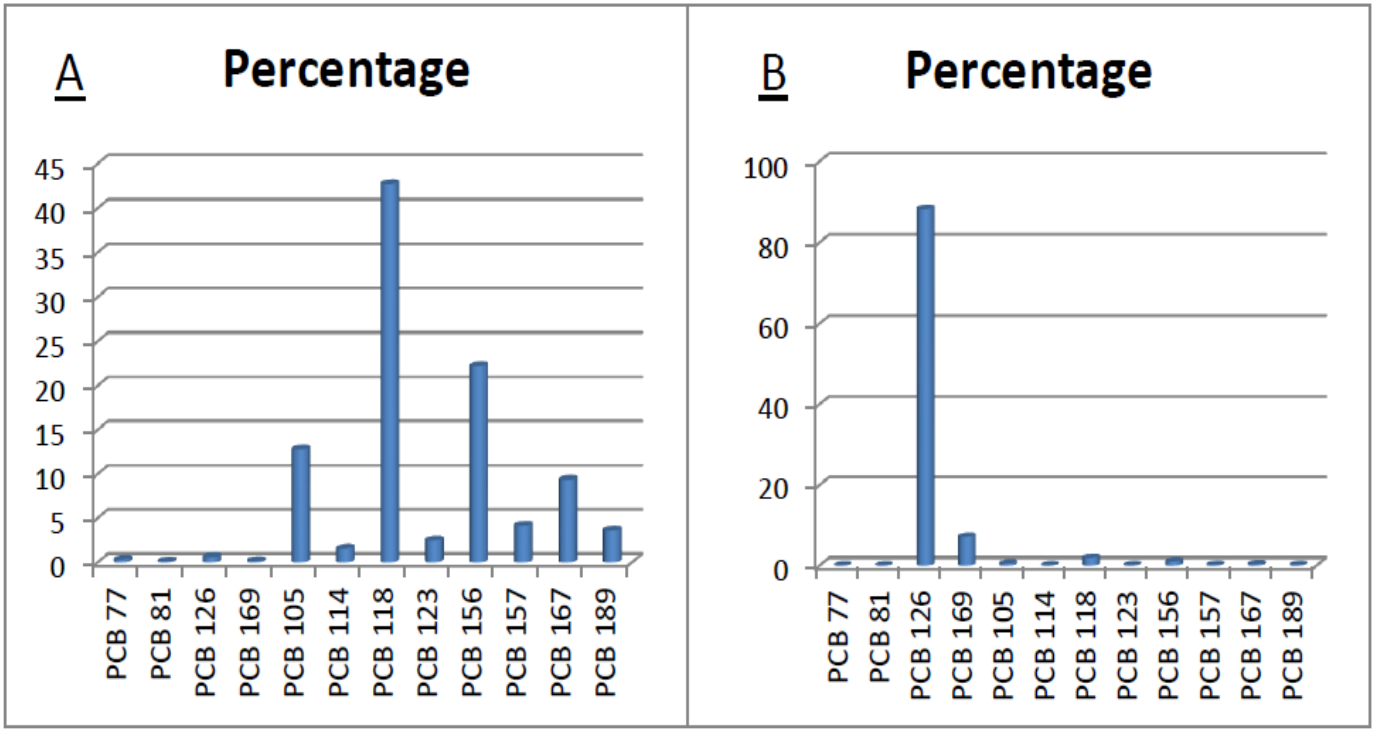

Fig.2. The contribution percentage of individual congener of dl-PCBs in pg/g lipid (A) and in pgTEQ/g lipid (B).

Table 1. The concentrations of dl-PCBs congeners in the collected breast milk samples.

Congener	TEF 2005	Homologs	Mean (pg/g lipid)	Range (pg/g lipid)	SD	Mean (pgTEQ2005/g lipid)	Range (pgTEQ2005/g lipid)	SD
PCB 77	0.0001	Non-ortho-PCBs	30.62	6.70-151.4	29.3	0.003	0.001-0.02	0.003
PCB 81	0.0003		11.1	2.17-39.8	9.4	0.003	0.001-0.01	0.003
PCB 126	0.10		59.8	17.66-87.6	16.7	6.04	1.77-9.41	1.72
PCB 169	0.03		16.3	2.44-30.8	7.1	0.49	0.07-0.9	0.21
PCB 105	0.00003	Mono-ortho-PCBs	1310.3	305.8-3498.6	857.2	0.04	0.01-0.1	0.03
PCB 114	0.00003		157.2	29.3-521.7	108.8	0.005	0.001-0.02	0.003
PCB 118	0.00003		4372.3	998.2-17893.8	3205.6	0.13	0.03-0.5	0.1
PCB 123	0.00003		257.4	33.1-1712.4	337.6	0.01	0.001-0.05	0.01
PCB 156	0.00003		2272	215.7-13814.9	2415.3	0.07	0.01-0.4	0.07

PCB 157	0.00003	425	84.6-1335.7	291.6	0.01	0.003-0.04	0.01
PCB 167	0.00003	956.3	207.1-4917.3	898.3	0.03	0.01-0.2	0.03
PCB 189	0.00003	370	32.-2302.7	429.9	0.01	0.001-0.07	0.01
SUM PCBs		10238.3	2387.6-43359	7820.4	6.8	2.5-10.34	1.72
∑Mono dl-PCBs		10120.5	2321.6-43240.8	7807.5	0.3	0.07-1.03	0.27
∑Non ortho dl-PCBs		117.8	66.1-243.4	38.2	6.5	2.5-10.3	1.91

Acknowledgment

We would like to thank all the staff in QCAP Egypt laboratory for a good environment during this study.

References

[1] J. Huang, T. Matsumura, G. Yu, S. Deng, M. Yamauchi, N. Yamazaki, R. Weber, Chemosphere Determination of PCBs , PCDDs and PCDFs in insulating oil samples from stored Chinese electrical capacitors by HRGC / HRMS, Chemosphere. 85, 239–246 (2011).

[2] H. Kanbe, M. Shibuya, Solvent cleaning of pole transformers containing PCB contaminated insulating oil, Waste Manage. 21, 371-380 (2001).

[3] A. Aota, Y. Date, S. Terakado, N. Ohmura, Screening of polychlorinated biphenyls in insulating oil using a microfluidic based pretreatment and immunoassay, Anal. Chem. Res. 3, 13–19 (2015).

[4] K. Kim, S. Hwan, K. Kim, K. Kim, Y. Kim, Environmental effects of supercritical water oxidation (SCWO) process for treating transformer oil contaminated with polychlorinated biphenyls (PCBs), Chem. Eng. J. 165, 170–174 (2010).

[5] C.S. Hernández, O. Pardo, F. Corpas-burgos, S.F. Fernández, A. López, C. Coscollà, M. Vento, V. Yusà, Science of the Total Environment Biomonitoring of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (dl-PCBs) in human milk : Exposure and risk assessment for lactating mothers and breastfed children from Spain, Sci. Total Environ. 744, 140710 (2020).

[6] Toxicology and Carcinogenesis Studies of a Mixture of 2,3,7,8-Tetrachlorodibenzop-Dioxin (TCDD) (Cas No. 1746-01-6), 2,3,4,7,8-Pentachlorodibenzofuran (PeCDF) (Cas No. 57117-31-4), and 3,3’,4,4’,5-Pentachlorobiphenyl (PCB 126) (Cas No. 57465-28-8) in Female Harlan SpragueDawley Rats (gavage studies) National Toxicology Program Technical Report Series, 526, 1–180 (2006).

[7] H. Parada, X. Sun, C. Tse, L.S. Engel, E. Hoh, A.F. Olshan, M.A. Troester, International Journal of Hygiene and Plasma levels of polychlorinated biphenyls (PCBs) and breast cancer mortality : The Carolina Breast Cancer Study, Int. J. Hyg. Environ. Health. 227, 113522 (2020).

[8] K. Pencíkova, L. Svrzkova, S. Strapacova, J. Neca, I. Bartonkova, Z. Dvorak, M. Hýzdalova, J. Pivnicka, L. Palkova, H-J Lehmler, X. Li, J. Vondracek, M. Machala, In vitro profiling of toxic effects of prominent environmental lower- chlorinated PCB congeners linked with endocrine disruption and tumor promotion, Environ Pollut. 237, 473-486 (2018).

[9] K. L. Bruner-Tran, K. G. Osteen, Dioxin-like PCBs and Endometriosis, Syst Biol Reprod Med. 56, 132–146 (2010).

[10] S.M. Bassem, M.I. Abd, E. Tawab, T.A. Temraz, W.K.B. Khalil, K. Farouk, G.H. Ali, Egyptian Journal of Chemistry, 63, 1787–1798 (2020).

[11] C. opez, A. Adelfio, A. M.Wall, B. Molloy, T. A.Holton, N. Khaldi, Human milk and infant formulae: Peptide differences and the opportunity to address the functional gap, Curr. Res. Nutr. Food Sci. 3, 217-226 (2020).

[12] É. Vigh, A. Colombo, E. Benfenati, H. Håkansson, M. Berglund, J. Bódis, J. Garai, Science of the Total Environment Individual breast milk consumption and exposure to PCBs and PCDD / Fs in Hungarian infants : A time-course analysis of the fi rst three

months of lactation, Sci. Total Environ. 449, 336–344 (2013).

[13] P. Ssebugere, M. Sillanp, H. Matovu, E. Mubiru, Human and environmental exposure to PCDD / Fs and dioxin-like PCBs in Africa : A review, Chemosphere. 223, 483-493 (2019).

[14] A. A. El-Kady, T. Kunisue, Comprehensive Strategies for Polychlorinated biphenyls Quantitative Analysis Specialized in Foodstuffs. Egyptian Journal of Chemistry, (2020). doi: 10.21608/ejchem.2020.26025.2519.

[15] R. Matsumoto, N. Phuc, C. Tu, S. Haruta, M. Kawano, I. Takeuchi, Polychlorinated biphenyl (PCB) concentrations and congener composition in masu salmon from Japan : A study of all 209 PCB congeners by high-resolution gas chromatography / high-resolution mass spectrometry (HRGC / HRMS), Reg. Stud. Mar. Sci. 3, 119-130 (2016).

[16] S. Gauthier, E. Alexander, S. Stefan, The performance of atmospheric pressure gas chromatography-tandem mass spectrometry compared to gas chromatography-high resolution mass spectrometry for the analysis of polychlorinated dioxins and PCBs in food and feed samples, J. Chromatogr. A.16, 76-90 (2016).

[17] T.H.E.E. Commission, L 320/18, 2011, 18–23 (2011).

[18] Method 1668B Chlorinated Biphenyl Congeners in Water , Soil , Sediment , Biosolids , and Tissue by HRGC / HRMS November 2008, (2008).

[19] I. Çok, B. Mazmanci, M.A. Mazmanci, C. Turgut, B. Henkelmann, K. Schramm, Analysis of human milk to assess exposure to PAHs , PCBs and organochlorine pesticides in the vicinity Mediterranean city Mersin , Turkey, Environ. Int. 40, 63–69 (2012).

[20] H. Pan, J. Li, X. Li, Y. Yang, Z. Qin, Transfer of dechlorane plus between human breast milk and adipose tissue and comparison with legacy lipophilic compounds, Environ. Pollut. 265 (2020).

[21] A. Polder, G.W. Gabrielsen, J.Ø. Odland, T.N. Savinova, A. Tkachev, K.B. Løken, J.U. Skaare, Spatial and temporal changes of chlorinated pesticides , PCBs , dioxins (PCDDs / PCDFs) and brominated flame retardants in human breast milk from Northern Russia, 91 (2007).

[22] U. Raab, M. Albrecht, U. Preiss, W. Völkel, U. Schwegler, H. Fromme, Chemosphere Organochlorine compounds , nitro musks and perfluorinated substances in breast milk – Results from Bavarian Monitoring of Breast Milk 2007 / 8, Chemosphere. 93, 461–467 (2013).

[23] D.F.K. Rawn, A.R. Sadler, V.A. Casey, F. Breton, W. Sun, T.E. Arbuckle, W.D. Fraser, Science of the Total Environment Dioxins / furans and PCBs in Canadian human milk : 2008 – 2011, Sci. Total Environ. 595, 269–278 (2017).

[24] T. Todaka, H. Hirakawa, J. Kajiwara, T. Hori, K. Tobiishi, Chemosphere Concentrations of polychlorinated dibenzo- p -dioxins , polychlorinated dibenzofurans , and dioxin-like polychlorinated biphenyls in blood and breast milk collected from 60 mothers in Sapporo City , Japan, 72, 1152–1158 (2008).

[25] M.M. Ulaszewska, E. Zuccato, E. Capri, R. Iovine, A. Colombo, G. Rotella, C. Generoso, P. Grassi, M. Melis, R. Fanelli, Chemosphere The effect of waste combustion on the occurrence of polychlorinated dibenzo- p -dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in breast milk in Italy, Chemosphere. 82, 1–8 (2011).

[26] I. Çok, M. Keski, M. Uner, E. Demirkaya, B. Henkelmann, H. Shen, J. Kotalik, K. Schramm, Chemosphere Polychlorinated dibenzo-p-dioxins , dibenzofurans and polychlorinated biphenyls levels in human breast milk from different regions of Turkey, Chemosphere. 76, 1563–1571 (2009).

[27] J. Focant, N. Fréry, M. Bidondo, G. Eppe, G. Scholl, A. Saoudi, A. Oleko, S. Vandentorren, Science of the Total Environment Levels of polychlorinated dibenzo- p -dioxins , polychlorinated dibenzofurans and polychlorinated biphenyls in human milk from different regions of France, Sci. Total Environ. 452–453, 155–162 (2013).

[28] D. Costopoulou, I. Vassiliadou, L. Leondiadis, Infant dietary exposure to dioxins and dioxin-like compounds in Greece, Food Chem. Toxicol. 59, 316–324 (2013)