Brominated Diphenyl Ether (BDE) Residues in Canadian Human Fetal Liver and Placenta

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Introduction

Certain chemicals known as POPs (persistent organic pollutants) such as Organochlorines (OCs), Polychlorinated biphenyls (PCB's) contaminate human foodstuffs, cross the placenta and can possibly interfere with the development of physiological systems in fetuses (e.g.immune, endocrine)[1]. Evidence shows that the levels of many POPs in breast milk have decreased due to their use being banned in North America[2,3]. A recent addition on the list of POPs is Brominated Diphenyl Ethers (BDEs). In contrast to OCs and PCBs, the levels of BDEs in the environment and in human milk have been increasing[4]. Ryan and Patry[5] and Ryan et al.[6] have reported that the median levels of total BDEs in breast milk collected from across Canada increased by about an order of magnitude (2.9 to 25 ppb milk lipid) from 1992 to 2002.

The present work investigated the levels of BDEs in 15 human placenta samples and in 13 human fetal liver samples obtained between 1998 and 2003.

Materials and Methods

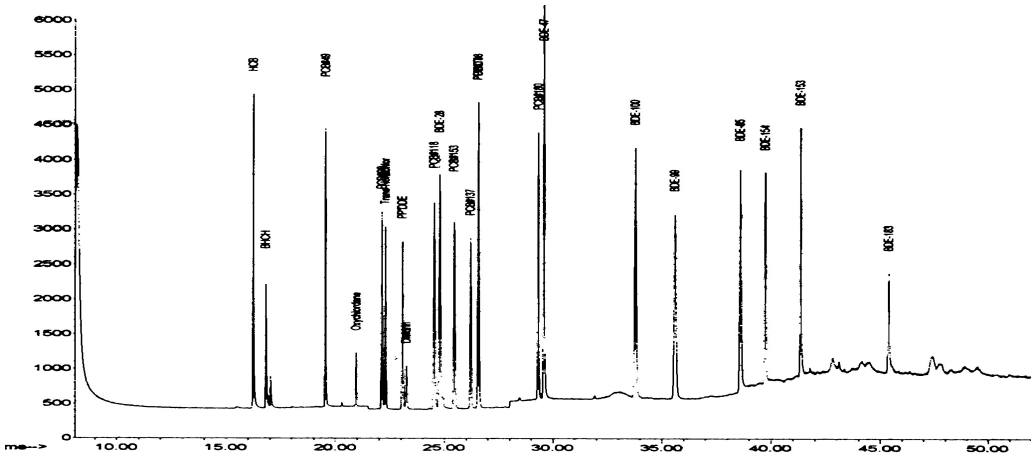
Sample Collection

Human fetal placenta and liver samples were obtained from elective terminations in the Montréal area of Canada. All tissues were obtained following informed consent. Ethical approval was obtained from both McGill University and Health Canada for the collection and use of human fetal tissues for BDE analysis. In all cases, no information was available concerning the tissue donors. The human fetal tissues were obtained at 15 to 20 weeks fetal age, stored at -80°C at McGill University, transferred to Health Canada Laboratories in dry ice and again stored at -80°C. When the samples were to be extracted and analysed, they were allowed to thaw at ambient temperature.

Analysis

Known weights of liver and placenta (~ 1g) were homogenized using a Polytron homogenizer in 20 ml acetone:hexane (2:1 v/v), filtered, dried over anhydrous sodium sulfate and evaporated to approximately 0.5 ml. Fat content determination was done by transferring the concentrated extract to a pre-weighed vial and

allowing the solvent to evaporate and then the vial containing the fat was re-weighed. Sample clean-up was done using a 6 g 2% deactivated florisil column. The column was eluted with 70 ml hexane and this fraction contained all of the BDE congeners (28,47,85,99,100,153,154, and 183), the PCB congeners (49,99,118,137,138,153 and 180) and most of the OCs (e.g. DDT, DDE, trans-Nonachlor, etc.). A second fraction was eluted with 60 ml of 30% dichloromethane in hexane and contained dieldrin and ß-hexachlorocyclohexane (ß-HCH). The first fraction extracts were concentrated and injected onto an Agilent GC-MS (EI) using a 30 m DB5 column. Sample batches included 2 laboratory blanks which were averaged and subtracted from the total in the samples. Sample batches also included a quality control which consisted of 150



mg corn oil spiked with all analytes of interest.

Target Compounds	Ret.time	target ion	area	Concentration	Qvalue
1) HCB	16.24	284	6720	21.00 ng/ml	100
2) BHCH	16.83	219	2529	23.40 ng/ml	100
3) PCB#49	19.54	292	5784	20.00 ng/ml	100
4) Oxychlordane	20.95	185	852	21.50 ng/ml	100
5) PCB#99	22.12	326	5984	22.40 ng/ml	100
6) Trans-Nonachlor	22.29	409	3992	21.00 ng/ml	100
7) PP'DDE	23.06	246	5524	21.90 ng/ml	100
8) Dieldrin	23.25	263	1241	25.60 ng/ml	100
9) PCB#118	24.52	326	7666	19.20 ng/ml	100
10) BDE-28	24.78	246	7610	48.00 ng/ml	100
11) PCB#153	25.45	360	6212	23.40 ng/ml	100
12) PCB#137	26.20	360	4890	20.00 ng/ml	100
13) PP'DDT	26.54	235	3882	21.00 ng/ml	100
14) PCB#138	26.56	360	5783	21.00 ng/ml	100
15) PCB#180	29.31	394	5549	19.20 ng/ml	100
16) BDE-47	29.58	326	8378	48.00 ng/ml	100
17) BDE-100	33.78	404	5454	48.00 ng/ml	100
18) BDE-99	35.59	404	5494	48.00 ng/ml	100
19) BDE-85	38.59	404	5637	48.00 ng/ml	100
20) BDE-154	39.73	484	4995	48.00 ng/ml	100
21) BDE-153	41.36	484	5128	48.00 ng/ml	100
22) BDE-183	45.39	562	2556	48.00 ng/ml	100

Results and Discussion

The BDE content of human fetal liver samples is presented in Table 1, and for placenta, in Table 2. Results are expressed as the mean and standard deviation (SD) for a given year and are on a lipid basis. The listing includes the levels of the two most prominent BDE congeners (47 and 99) as well as the sum of 8 BDE congeners (28, 47, 85, 99, 100, 153, 154 and 183).

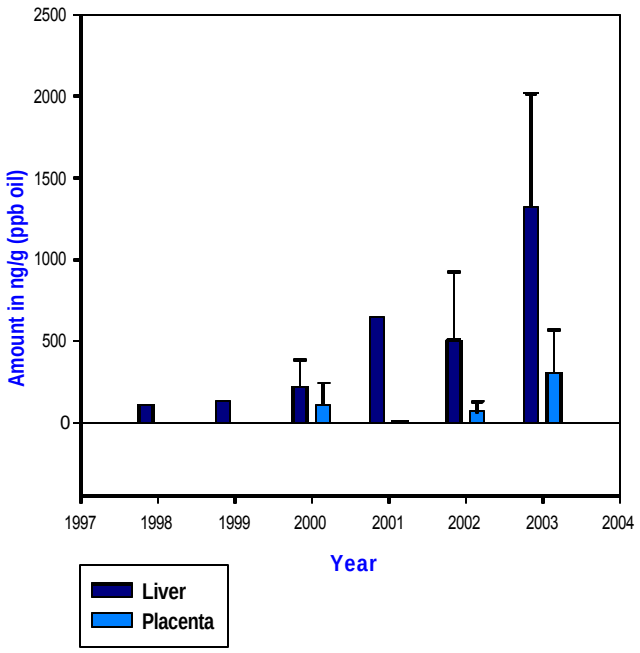
Table 1. BDE levels in human liver samples
Mean values on a lipid basis

year	1998	1999	2000	2001	2002	2003
number of samples	1	1	3	1	4	3
BDEs ng/g (*standard deviation*)						
? BDE(n= 8)	107.1 (0)	130.6 (0)	220.1 (163.7)	646.9 (0)	503.7 (417.3)	1324.7 (692.2)
Congener 47	44.39 (0)	0.00 (0)	67.0 (59.6)	180.4 (0)	97.9 (62.3)	217.8 (266.2)
Congener 99	62.7 (0)	130.6 (0)	129.9 (148.7)	466.54 (0)	227.8 (250.6)	526.6 (366.7)

Table 2. BDE levels in human placenta samples
Mean values on a lipid basis

year	1998	1999	2000	2001	2002	2003
number of samples	0	0	3	1	5	6
BDEs ng/g (*standard deviation*)						
? BDE(n= 8)	n/a	n/a	108.8 (135.2)	13.0 (0)	68.9 (61.4)	306.9 (261.9)
Congener 47	n/a	n/a	39.5 (43.5)	8.1 (0)	23.9 (19.4)	107.8 (95.6)
Congener 99	n/a	n/a	42.0 (53.1)	4.9 (0)	25.6 (30.5)	120.9 (107.5)

figure 1. Liver vs Placenta amounts



Although the number of samples analysed to date is limited, the tissue concentrations demonstrate a notable increase during the time period. This is especially true for the fetal liver which increased approximately 10 fold from 1998 to 2003. The period covered for the placenta is from 2000 to 2003 and while the levels of BDEs were lower than found in the liver, they also appeared to be increasing, albeit less obviously. In the liver, congener 99 was present in markedly higher quantities than congener 47 (approximately two fold). However, this was not the case for the placenta, where both congeners were present in approximately the same amounts. In most cases, the liver and placenta samples came from the same fetus. Figure 1 shows that the total amount of BDEs in fetal liver are higher than for the placenta samples. Furthermore, the mean BDE content of fetal liver tended to be higher than found for Canadian human milk (~ 45 ppb, Ryan et al.[6]) suggesting, that the fetal liver may be accumulating BDEs or the fetal liver is unable to metabolize BDEs. On the other hand, BDE levels in the placenta were similar to those found in maternal and cord serum from Indiana (~ 50 ppb, Mazdai et al.[7]).

Conclusions.

The amounts of BDEs in human fetal liver are increasing with time and, at present, appear to be greater than in human milk, maternal blood and fetal blood on a fat weight basis.

Future Directions.

We intend to analyse a greater number of fetal tissues from a longer time period in order to improve the BDE - fetal exposure database. While the human toxicity of BDEs remains to be determined, these data will assist in developing BDE exposure policies for the unborn fetus.

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