# DETERMINATION OF PHENOLIC ORGANOHALOGENS IN HUMAN SERUM FROM A BELGIAN POPULATION AND ASSESSMENT OF PARAMETERS AFFECTING HUMAN CONTAMINATION

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## Introduction

Since several decades, the prevalence of thyroid diseases such like autoimmune hypo- and hyperthyroidism is increasing, and the diagnostic enhancement or migration factor cannot fully explain this phenomenon. The implication of environmental pollutants which may interfere with the normal thyroid hormone action is a plausible hypothesis that focuses the attention of many scientists. Among these pollutants, phenolic organohalogens (POHs) are a particular concern because of their structural resemblance to the thyroid hormones. Tetrabromobisphenol A (TBBPA), the most widely used brominated flame retardant, hydroxylated polybrominated diphenyl ethers (OH-PBDEs), the main metabolites of polybrominated diphenyl ethers (PBDEs), bromophenols (BPs), industrially produced for their flame retardant properties and also resulting from PBDE metabolism, the pesticide pentachlorophenol (PCP), and hydroxylated polychlorinated biphenyls (OH-PCBs) are POHs which are able to bind on transthyretin involved in the transport of thyroid hormones especially across the placenta and the blood-brain barrier. Moreover, these POHs are themselves able to cross these barriers and thus concentrate into the central nervous system or into the fetus. The determination of POHs in human population appears therefore to be a serious health concern. However, few large scale studies on the contamination of the general population by POHs have already been carried out. The aims of this study were to determine the background contamination of a Belgian general population, and assess some dietary habits or demographic parameters as sources of exposure. For these purposes, we measured the serum level of 4 BPs, 7 OH-PCBs, 3 OH-PBDEs, PCP and TBBPA in 274 non-occupationally exposed people aged between 18 and 76, living in Liege (Belgium) and the surrounding area, and collect their answers to a questionnaire about their life style, diet and home environment.

## Materials and Methods

The details about the recruitment and the characteristics of the study population were previously described [1]. Briefly, 274 volunteers aged from 18 to 76 years old and living in the Province of Liege were enrolled between February and May 2015, provided a blood sample in clot activator tubes, and answered to a questionnaire about their alimentary habits, life style and home environment during a face-to-face interview. The measurement of the POHs was performed using strong anion-exchange SPE followed by a rapid liquid liquid extraction prior to derivatization using trimethylsilyldiazomethane. The extract was then analyzed by GC-ENCI-MS operating in single ion monitoring. The whole procedure was detailed elsewhere [2].

## Results and Discussion

Table 1 presents the detection frequencies and the concentrations of target chemicals. PCP was the predominant POH in our population, whereas 2,3,6-TBP, 2,4,5-TBP and 5-OH-BDE 47 were never detected and the detection frequencies for 5'-OH-BDE 99, 6-OH-BDE 47 and 2,3,4,6-TeBP were very low. 4-OH-CB 107, 4-OH-CB 146 and 4-OH-CB 187 were detected in all samples and shared for 75% of the ΣOH-PCBs.

**Table 1:** LOQs, mean concentrations and standard deviations, median concentrations, ranges (pg mL-1) and detection frequencies (%) of POHs in human serum samples from Belgium.

| | LOQ | N>LOQ | Mean | SD | Median | Min | Max |
|---|---|---|---|---|---|---|---|
| PCP | 44.6 | 100.0 | 1165.5 | 2735.3 | 593.0 | 69.2 | 35869.1 |
| TBBPA | 4.1 | 31.0 | <LOQ | - | <LOQ | <LOQ | 43.6 |
| 5-OH-BDE 47 | 2.3 | 0.0 | <LOQ | - | <LOQ | <LOQ | <LOQ |
| 6-OH-BDE 47 | 2.5 | 2.6 | <LOQ | - | <LOQ | <LOQ | 8.2 |
| 5'-OH-BDE 99 | 2.0 | 2.2 | <LOQ | - | <LOQ | <LOQ | 4.5 |
| 2,3,6-TBP | 2.4 | 0.0 | <LOQ | - | <LOQ | <LOQ | <LOQ |
| 2,4,5-TBP | 5.0 | 0.0 | <LOQ | - | <LOQ | <LOQ | <LOQ |
| 2,4,6-TBP | 49.6 | 63.8 | 81.2 | 107.8 | 57.3 | <LOQ | 1276.6 |
| 2,3,4,6-TeBP | 4.1 | 11.8 | <LOQ | - | <LOQ | <LOQ | 51.1 |
| 4-OH-CB 107 | 3.2 | 100.0 | 56.1 | 52.2 | 43.7 | 6.6 | 361.8 |
| 3-OH-CB 138 | 3.1 | 90.8 | 16.3 | 20.0 | 11.5 | 2.7 | 261.4 |
| 4-OH-CB 146 | 2.2 | 100.0 | 34.6 | 29.8 | 26.9 | 4.4 | 195.5 |
| 3-OH-CB 153 | 3.0 | 67.5 | 14.5 | 20.1 | 8.9 | <LOQ | 208.2 |
| 4-OH-CB 172 | 2.0 | 88.2 | 11.0 | 10.2 | 8.3 | 1.8 | 68.9 |
| 3-OH-CB 180 | 2.1 | 52.8 | 3.3 | 4.1 | 2.1 | <LOQ | 31.9 |
| 4-OH-CB 187 | 2.0 | 100.0 | 47.0 | 29.3 | 39.4 | 10.4 | 228.4 |
| ΣOH-PCBs | | - | 182.9 | 142.8 | 143.7 | 31.5 | 1198.8 |
| ΣOH-PCBs/ΣPCBs | | | 0.25 | 0.16 | 0.21 | 0.04 | 1.43 |

The very low frequencies of detection of OH-PBDEs observed in our study were expected since according to the literature, they used to be detected only in countries where the populations are known to be particularly exposed to PBDEs such as in North America [3] or in Asia [4]. The human contamination levels by PCP and OH-PCBs observed in Belgium in 2015 seemed to be quite low compared to populations known to be particularly exposed [5, 6]. Nevertheless, the concentrations measured in our population are among the highest reported in the 5 last years, far above the background contamination of non-occupationally exposed populations [4, 7]. Although the current levels are much lower than those reported in another Belgian population recruited in 2000 [8], corroborating the global decrease of the OH-PCB and PCP serum levels observed this past decade, the reasons for such apparent high contamination in Belgium remain unclear. Multivariate analyses were used to identify some demographic parameters, dietary or daily lifestyle habits influencing the PCP and OH-PCB concentration in our population (Table 2). For PCP, lower levels were found in smokers likely due to the induction of phase II metabolization enzymes by the cigarette smoke and therefore an increasing elimination rate of PCP reducing the level measured in the smoker's serum. Higher PCP concentrations were also found in men compared to women suggesting gender differences in the toxicokinetic, and in people with university or short cycle higher education degree vs people having lower secondary level. Finally, significantly higher levels were observed in people who used to eat sea fish weekly compared to those who reported to never eat, growing the conflicting debate about the importance of the food intake in the PCP exposure pathways for human. The determination coefficient of the current multivariate regression for PCP was very weak ($R^2$=0.14) and therefore the model would only explain 14% of the PCP concentration variability. Thus the human exposure pathway to PCP still remains largely unknown. The multivariate model proposed for the ΣOH-PCBs seems to be more predictive ($R^2$=0.61) and included sea fish consumption, age and BMI. If the positive correlation between OH-PCBs and age and sea fish consumption has been previously reported [5, 9], the negative association with BMI was highlighted for the first time. This correlation would reflect the storage of PCBs in adipose tissues reducing the circulating blood PCB and thus OH-PCB levels, but also the potential reduction of PCB metabolism rate in obese people.

**Table 2:** Results of the Multivariate regression for PCP and OH-PCB concentrations

| Variable | N | log PCP | | log ΣOH-PCBs | |
|---|---|---|---|---|---|
| | | β coef. | p-value | β coef. | p-value |
| Intercept | 269 | 5.498 | *<0,001* | 4.086 | *<0,001* |
| Age (years) | | 0.004 | 0.341 | 0.036 | *<0,001* |
| Sex (men vs women) | | 0.418 | *0.001* | 0.080 | 0.157 |
| BMI (kg/m²) | | - | - | -0.035 | *<0,001* |
| Smoker status (smoker vs non-smoker) | | -0.278 | 0.059 | - | - |
| Sea fish consumption (<monthly vs | | 0.252 | 0.255 | 0.065 | 0.543 |
| (1-3x/month vs never) | | 0.318 | 0.135 | 0.142 | 0.166 |
| (1weekly vs never) | | 0.615 | *0.005* | 0.295 | *0.005* |
| (>weekly vs never) | | 0.255 | 0.327 | 0.203 | 0.100 |
| Level of education (Technical secondary vs lower secondary) | | 0.411 | 0.065 | - | - |
| (Short cycle higher education vs lower secondary) | | 0.524 | *0.016* | - | - |
| (Long cycle higher education vs lower secondary) | | 0.096 | 0.728 | - | - |
| (University vs lower secondary) | | 0.484 | *0.050* | - | - |
| (Post university vs lower secondary) | | 0.039 | 0.932 | - | - |
| Intercept | 125[a] | - | - | 4.059 | *<0,001* |
| Age (years) | | - | - | 0.042 | *<0,001* |
| BMI (kg/m²) | | - | - | -0.035 | *<0,001* |
| Number of children | | - | - | -0.078 | 0.057 |

[a]Women only

## Conclusion

We determined the concentrations of 16 phenolic organohaloganeted compounds (PCP, TBBPA, bromophenols, OH-PBDEs and OH-PCBs) in serum from 274 people aged from 18 to 76 years old living in Liege (Belgium) and the surrounding area. The main POH measured in serum was PCP followed by OH-PCBs and to a lesser extent 246-TBP and TBBPA. Gender, smoker status, sea fish consumption and level of education were the main determinants of PCP serum concentrations, while age, sea fish consumption and BMI were significantly associated with OH-PCB levels. Since the model computed for PCP was poorly predictive, the sources of human exposure to PCP still remain largely unknown and need to be further studied.

## References


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