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High throughput sample preparation in combination with gas chromatography coupled to triple quadrupole tandem mass spectrometry (GC–MS/MS): A smart procedure for (ultra)trace analysis of brominated flame retardants in fish

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ABSTRACT

In this study, gas chromatography (GC) coupled to triple quadrupole tandem mass spectrometry (MS/MS) operated in electron ionisation mode (EI) has been shown to be an effective tool for the (ultra)trace analysis of several representative brominated flame retardants (BFRs) including polybrominated diphenyl ethers (PBDEs), pentabromotoluene (PBT), pentabromoethylbenzene (PBEB), etc. in complex food and environmental matrices. Using this type of instrumentation, improved selectivity and sensitivity of the instrumental analysis was achieved. In addition to GC–MS/MS (EI), a GC–MS method employing QqQ as a single quadrupole in negative chemical ionisation (NCI) mode was also developed, as this technique might be preferred for those compounds where EI did not provide suitable (intensive enough) mass transitions (e.g., decabromodiphenyl ethane). Following the development of the GC–MS/MS method, a substantial simplification of the sample preparation method was achieved by employing an ethyl acetate QuEChERS-based extraction followed by silica minicolumn clean-up. Using this novel approach, six samples may be prepared in approx. one hour, thus significant time savings were achieved compared to routinely used methods. In addition, the method employs the reduced amounts of organic solvent and other chemicals. Under the optimised conditions, recoveries of all target analytes using both GC–MS/MS (EI) and GC–MS (NCI) were within the range of 70–119% and repeatabilities of the analytical procedure were $\leq$16% at all three spiking levels (0.1, 1 and 5 μg kg^{-1}). Regarding quantification limits (LOQs), as expected, a single quadruple operated in NCI provided significantly lower LOQs compared to EI. However, using the triple quadrupole mass analyser, comparable LOQs were achieved for both methods (0.005–1 μg kg^{-1} and 0.005–0.1 μg kg^{-1} for GC–MS/MS (EI) and GC–MS (NCI), respectively). Moreover, when highly selective mass transitions in GC–MS/MS (EI) were used for identification and quantification, a significant decrease of problematic interferences was observed compared to NCI where most of the compounds were quantified according to the less selective *m/z* 79 corresponding to a bromine atom.

1. Introduction

Clear evidence exists that fish consumption provides health benefits for the cardiovascular system and is suitable for secondary prevention in coronary heart disease. Being an important source of long chain *n*-3 polyunsaturated fatty acids, fatty fish, in particular, may significantly contribute to consumers' dietary exposure to several classes of contaminants. In addition to persistent organochlorine compounds, recent market basket studies have detected polybrominated diphenyl ethers (PBDEs) as ubiquitous contaminants of this important commodity and fish along with seafood are classified as the main food commodities responsible for their dietary intake [1]. With the exception of three commercial PBDEs mixtures, the usage of BFRs has until now mainly comprised of tetrabromobisphenol A (TBBPA) and hexabromocyclododecane (HBCD) [1]. As a result of their potential to bioaccumulate in the environment, the goods containing more than 0.1% of PentaBDE (brominated diphenyl ether) and OctaBDE technical mixtures have been prohibited in the EU since August 2004, and the ban was further extended to electrical and electronic goods with DecaBDE in July 2008 [2,3]. In response to these legislation acts, the 'alternative' BFRs suitable for commercial applications as an option

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to PBDEs have been introduced to the market. As might be assumed several of them such as bis(2,4,6-tribromphenoxy)ethane (BTBPE) and decabromodiphenyl ethane (DBDPE) have been already detected in the environment [4]. Moreover, the continuous release of PBDEs in to the environment from products that remain in use or from land fill sites cannot be avoided [5].

Based on the composition of PBDE technical mixtures and occurrence in the environment, the majority of studies to date have been mainly focused on eight PBDE congeners of primary interest (BDE 28, 47, 99, 100, 153, 154, 183 and 209), which were, together with HBCD and brominated biphenyl (BB) 153, included by the European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM Panel) into the core group of BFRs, that should be monitored and which are relevant for dietary exposure [6,7].

Taking into account all the above mentioned facts, a simple, inexpensive, rapid and highly sensitive analytical method, which enables collection of a large set of reliable data in a short time, is needed to fulfil the effectiveness for the control of food contamination.

As regards common laboratory practices, gas chromatography (GC) coupled to mass spectrometry (MS) represents the 'gold standard' determinative step for the analysis of BFRs in biotic matrices. Considering a poor tolerance of this technique to non-volatile matrix impurities, attention has to be paid to the proper choice of sample preparation strategy. In many cases, time consuming multi-step procedures including (i) non-selective isolation of lipids followed by (ii) various clean-up steps and fractionation are used. Typically, extraction in a Soxhlet apparatus with large volumes of non-polar or semi-polar organic solvents is carried out to isolate target analytes from the biotic matrices. Lipids and other co-extracts are further removed using gel permeation chromatography (GPC) and/or solid-phase extraction (SPE) with different sorbents [8–12]. A destructive clean-up technique such as sulphuric acid treatment is also applied in some laboratories. Alternatively, semi-automated techniques including microwave assisted extraction (MAE), pressurised liquid extraction (PLE) or super critical fluid extraction (SFE) are used [8–12]. Most recently, another novel approach derived from the QuEChERS (quick, easy, cheap, effective, rugged and safe) procedure [13,14] (originally developed for the analysis of pesticide residues in low fat-high moisture matrices), has been successfully adopted for the analysis of PBDEs and other organic pollutants in fish using GC–MS in electron ionisation (EI) mode with a time-of-flight (TOF) ion analyser [15].

Currently, GC–MS with unit resolution mass analysers operated both in EI or negative chemical ionisation (NCI) mode are most often employed for identification and quantification of PBDEs and other BFRs in complex food and environmental matrices [12,16,20]. When higher brominated compounds are included in the list of target analytes, NCI mode which enables monitoring of bromine ions $[Br]^-$, isotopes m/z 79 and 81, is the preferred option providing higher sensitivity compared to EI [10,12,16,20]. However, this detection approach is not selective enough, other co-eluting thermodegradable highly brominated compounds might interfere [16,18,19]. There is an increased risk of interferences occurring whenever relatively short capillary columns (10–15 m) and fast oven temperature programs intended for a 'gentler' GC separation are employed [12]. On the other hand, while operating in EI, more specific $[M]^{+\bullet}$ and $[M–Br_2]^+$ serve as identification ions, nevertheless, potential interferences with chlorinated compounds might occur [10,12,18,19]. In any case, the use of EI low-resolution (LR) MS is a good tool for the determination of brominated compounds only at relatively high concentration levels; on the other hand, it allows very accurate quantification, as ^{13}C-labelled standards might be used [10,12,16]. High-resolution (HR) instruments represent another reliable option in the analysis of brominated compounds offering higher sensitivity compared to 'traditional' LRMS. The detection limits (LODs) obtained by HRMS strongly depend on the type of ion analyser, for example, common HRTOF–MS instruments offering the possibility of retrospective data mining (as full spectral information is available), might not enable better LOD compared to conventional single quadrupoles (Q) [12,16,18,19].

In order to overcome the limitations discussed above, the use of tandem MS (MS/MS) using ion trap (IT) or triple Q (QqQ) analysers should be considered as the best alternative, minimising interferences by improved selectivity based on selection of appropriate precursor and product ions. Moreover, a significant decrease of chemical noise in the chromatogram is obtained, thus, thanks to the improved sensitivity, reliable determination of even (ultra)trace levels of BFRs required e.g., for human exposure studies, is feasible [16–19,21]. Several previous studies have been reported on the application of IT for the trace analysis of PBDE in different matrices [18,19,22]. On the contrary, the power of the QqQ up until now has been mainly demonstrated in pesticide residues analysis and/or organic contaminants other than BFRs [17,23–27]. There has been a very limited number of publications produces on BFRs, focusing mainly on water [28,29], human breast adipose tissue [17,19,21] and fish [18,30]. However, in the latter case, only PBDEs were included in the list of target analytes.

In the presented study, the application potential and suitability of GC–QqQ–MS/MS (EI) for the (ultra)trace analysis of BFRs in fish muscle tissue was evaluated and compared with GC–MS employing QqQ as a single quadrupole both in EI and NCI mode. A large number of BFRs including not only the above mentioned priority PBDEs (BDE 28, 47, 99, 100, 153, 154, 183 and 209), but also additional PBDE congeners (BDE 49, 66, 85, 196, 197, 203, 206 and 207) and alternative BFRs were included in the target analyte list. Integration of QqQ detection technique into BFRs analysis was expected to further improve an overall performance of the procedure based on a high throughput sample preparation approach originally developed for the multi-class analysis of persistent organic pollutants (POPs) and polycyclic aromatic hydrocarbons (PAHs) in fish [15].

2. Experimental

2.1. Standards

Certified standards of individual PBDE congeners (No. 28, 37, 47, 49, 66, 77, 85, 99, 100, 153, 154, 183, 196, 197, 203, 206, 207, 209), ^{13}C-BDE 209, hexabromobenzene (HBB), pentabromotoluene (PBT), pentabromoethylbenzene (PBEB), bis(2,4,6-tribromophenoxy)ethane (BTBPE), octabromo-1-phenyl-1,3,3-trimethylindane (OBIND) and decabromodiphenyl ethane (DBDPE) (all with declared purity $>98\%$) were supplied by Wellington Laboratories (Guelph, Ontario, Canada). Calibration solutions prepared in isooctane containing BDE 28–203, HBB, PBT, PBEB and BTBPE at concentration levels 0.05, 0.1, 0.5, 1, 5, 10, 50, 100 and 500 ng mL^{-1} and BDE 206, 207, 209, OBIND and DBDPE at 0.25, 0.5, 1, 5, 10, 50, 100, 500 and 1000 ng mL^{-1} were stored at 5 °C. Each calibration level contained surrogate standard BDE 37 at 10 ng mL^{-1} and syringe standards BDE 77 and ^{13}C-BDE 209 at 5 and 50 ng mL^{-1}, respectively. For the acquisition of full scan spectra and further MS/MS transition optimisation, individual standards of all compounds were prepared in isooctane (10,000 ng mL^{-1}) and stored as stated above. The standard reference material Lake Michigan Fish Tissue, SRM 1947 ($10.4 \pm 0.5\%$ (w/w) of fat) was supplied by National Institute of Standards and Technology (NIST, Gaithersburg, MD, USA).