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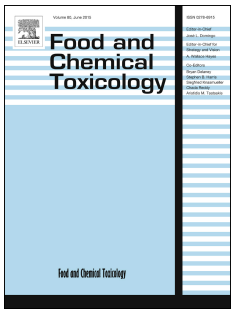


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# Human exposure to brominated flame retardants through the consumption of fish and shellfish in Tarragona County (Catalonia, Spain)

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ABSTRACT

The concentrations of 19 brominated flame retardants (BFRs) (8 polybrominated diphenyl ethers (PBDEs), 8 methoxylated PBDEs (MeO-PBDEs) and 3 emerging flame retardants) were determined in 10 species of fish and shellfish widely consumed in Tarragona County (Catalonia, Spain), by pressurized liquid extraction followed by gas chromatography coupled to tandem mass spectrometry. A higher occurrence of PBDEs was found in all the analyzed samples, while MeO-PBDEs were only detected in a few ones and the levels of emerging pollutants were relatively low. In contrast, hexabromobenzene was found in almost all samples at concentrations ranging between non detected and 0.2 ng $g^{-1}$ wet weight (w.w.). Salmon, sole, hake, cod and tuna showed the highest concentrations of ΣPBDEs (>0.8 ng $g^{-1}$ w.w.), while mussel was the species with the highest level of MeO-PBDEs (1.5 ng $g^{-1}$ w.w.). The dietary exposure of BFRs through consumption of these 10 species of fish and shellfish by the population of Tarragona County was estimated for different subpopulations, classified according to age and gender. Furthermore, calculations were performed in upper-, middle- and lower-bound risk scenarios. According to our data, the current concentrations of BFRs in fish and shellfish suggest no significant health risks for the consumers.

*Keywords:*
brominated flame retardants
fish and shellfish
GC-MS, PLE
dietary intake

## 1. Introduction

Consumption of fish and shellfish is an essential part of a healthy and well balanced diet (Domingo et al., 2007). However, this food group may also contain potentially high/moderate levels of a number of environmental contaminants, whose consumption can pose a risk to human health (Domingo, 2004, 2012, 2016). Brominated flame retardants (BFRs) are mixtures of man-made chemicals that are intentionally added to a wide variety of commercial products, such as plastics, textiles, and electronic/electrical equipment (Mackintosh et al., 2015; Fromme et al., 2016.). Due to their lipophilic, bioaccumulative and persistent nature, as well as their ubiquitous distribution and toxicity, the use of certain BFRs, such as hexabromocyclododecane (HBCD) or some polybrominated diphenyl ethers (PBDEs), has been recently banned or restricted in the European Union and/or North America (EFSA, 2011; Yuan et al., 2016). However, there is still some concern on the potential risk of these substances for the public health. BFR-treated products, either in use or as waste, may release small amounts of chemicals to the environment, being able to contaminate air, soil, and water (Cruz et al., 2015). These pollutants may also reach humans through their diets, mostly via intake of foodstuffs of animal origin (Domingo et al., 2008).

PBDEs, which form one of the most traditional families of BFRs, have been used in large amounts for many years. However, as we have mentioned before, penta- and octa-BDEs mixtures are already banned in the EU and the US. Furthermore, the production and use of deca-BDE has dramatically decreased in recent years (Sutton et al., 2015). PBDEs are ubiquitously present in the environment, being detected in air and dust (Fulara et al, 2012), sludge (Barón et al., 2014; Gorga et al., 2013; Law et al., 2014), sediments (Barón et al., 2014; Law et al., 2014), water (Law et al., 2014), and biota (Barón et al., 2014; Law et al., 2014; Munschy et al., 2011). PBDEs can reach the human body through different exposure pathways (EFSA, 2011). However, diet has been estimated to be the main route of PBDE entrance, being fish and shellfish one of the foodstuffs with higher PBDEs content (Domingo, 2012; Linares et al., 2015). In recent years, an increasing amount of information has been generated regarding the toxicity of PBDEs (Blanco et al., 2012; Heredia et al., 2012; Reverte et al., 2014). Toxicological studies have highlighted liver as a target organ for PBDEs (Fromme et al., 2016), and neurobehavioral and endocrine disrupting effects are also reported (Linares et al., 2015; Messer, 2010).

In biota, some PBDEs can be biotransformed to methoxylated PBDEs (MeO-PBDEs) through metabolic pathways (Wang et al., 2014; Weijs et al., 2009), or transformed by methylation (Losada et al., 2010). Moreover, some MeO-PBDEs have been suggested to occur naturally in marine ecosystems (Rotander et al., 2012; Weijs et al., 2009), being this the reason why increasing attention has been paid to the presence of MeO-PBDEs in wildlife (Jaspers et al., 2013; Dahlgren et al., 2016). Although toxicological information on these compounds is still limited, their structural similarity to PBDEs suggests that MeO-PBDEs may be also toxic for wildlife and humans (Ben Hassine et al., 2015).

In parallel to the restriction and ban of PBDEs, the usage of alternative BFRs, called emerging flame retardants, has been proposed (EFSA, 2012). Hexabromobenzene (HBB) is one of these compounds, with applications in the manufacture of paper and textiles. This chemical has been extensively used in Japan, while their production has not been reported in European countries. HBB is generated through the thermal degradation of deca-BDEs and other PBDEs. Recently, a number of studies have reported the wide occurrence of HBB in the environment (Munschy et al., 2011; Salamova et al., 2011; Gorga et al., 2013; Barón et al., 2014; Cruz et al., 2015). As for other emerging flame retardants, few data on the human toxicity of HBB are currently available, although a high exposure to HBB have been linked to liver effects (Feng et al., 2013). In any case, the production and use of HBB has not been regulated yet, while there is a lack of knowledge about the presence of this chemical in foodstuffs, and the potential role of the dietary intake as exposure pathway. In addition to HBB, decabromodiphenyl ethane (DBDPE) and pentabromoethyl benzene (PBEB) have been identified as other emerging BFRs of potential concern (EFSA, 2012). They were commercially introduced to replace PBDEs (Kierkegaard et al., 2004b; Liu et al., 2016), being currently detected in a wide range of environmental matrices (Barón et al., 2014; Egeback et al., 2012; Gorga et al., 2013; Santín et al., 2013). Despite the limited amount of human toxicity studies on emerging flame retardants (Nakari et al., 2010; Stieger et al., 2014), DBDPE is not expected to present a health risk for humans, at least considering data on ecotoxicological studies assessed in aquatic and sediment species (Hardy et al., 2012; Cruz et al., 2015).

The present study was aimed at determining the presence of 8 PBDEs, 8 MeO-PBDEs, as well as 3 emerging flame retardants (i.e., HBB, DBDPE and PBEB) in samples from 10 species of fish and shellfish widely consumed by the population of

Tarragona County (Spain). The concentrations were used to evaluate the exposure to those compounds through the intake of fish and shellfish, as well as to characterize the human health risks.

## 2. Materials and methods

### *2.1. Reagents and materials*

The concentrations of 8 different BDE congeners were determined in each sample. A standard stock solution with a mixture of 2,4,4'-tribromodiphenyl ether (BDE28), 2,2',4,4'-tetrabromodiphenyl ether (BDE47), 2,2',4,4',5-pentabromodiphenyl ether (BDE99), 2,2',4,4',6-pentabromodiphenyl ether (BDE100), 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE153), 2,2',4,4',5,6'-hexabromodiphenyl ether (BDE154), 2,2',3,4,4',5',6-heptabromodiphenyl ether (BDE183), at a concentration of 1 µg $mL^{-1}$, and decabromodiphenyl ether (BDE209) at 10 µg $mL^{-1}$, in nonane, was purchased from LGC Standards SLU (Barcelona, Spain). Similarly, for quantification by isotope dilution, a standard stock solution of $^{13}$C-labelled PBDEs ($^{13}$C-BDE28, $^{13}$C-BDE47, $^{13}$C-BDE99, $^{13}$C-BDE100, $^{13}$C-BDE154, $^{13}$C-BDE153, $^{13}$C-BDE183 and $^{13}$C-BDE209) at 1 µg $mL^{-1}$, and BDE209 at 10 µg $mL^{-1}$, in nonane, was also purchased from LGC Standards S.L.U (Barcelona, Spain). For analysis of MeO-PBDEs, a standard stock solution of native compounds containing 8 congeners (5-methoxy-2,2',4,4'-tetrabromodiphenyl ether (5-MBDE47), 6-methoxy-2,2',4,4'-tetrabromodiphenyl ether (6-MBDE47), 2,2',4',5-tetrabromo-4-methoxydiphenyl ether (4-MBDE49), 2'-methoxy-2,3',4,5'-tetrabromodiphenyl ether (2'-MBDE68), 5'-methoxy- 2,2',4,4',5-pentabromodiphenyl ether (5'-MBDE99), 5-methoxy-2,2',4,4',6-pentabromodiphenyl ether (5-MBDE100), 4-methoxy-2,2',4',5,5'-pentabromodiphenyl ether (4-MBDE101), and 2,2',4',5,6'-pentabromo-4-methoxydiphenyl ether (4-MBDE103)), at a concentration of 5 µg $mL^{-1}$ in nonane/toluene, was obtained from Wellington Laboratories Inc. (Guelph, ON, Canada). In addition, a standard stock solution with hexabromobenzene (HBB), decobromodiphenylethane (DBDPE) and pentabromoethylbenzene (PBEB) at levels of 50, 25 and 50 µg $mL^{-1}$, respectively, in toluene was also provided by Wellington Laboratories Inc.

Hexane, dichloromethane, toluene and sulfuric acid, all of them from J.T.Baker (Deventer, The Netherlands), were >99.9% grade purity. Diatomaceous earth was

supplied by Thermo Scientific (Barcelona) and filters for the PLE cell came from Dionex Corporation (Sunnyvale, CA, USA). Ultrapure water was obtained by using a purification system from Veolia Water (Sant Cugat del Vallès, Barcelona), while the purity of helium gas (Carburos Metálicos, Tarragona, Spain) for the chromatographic analysis was 99.999%.

*2.2. Sample preparation*

Ten species of fish and shellfish were selected among the most consumed species by the Catalan population (ENCAT, 2003): sole (*Solea solea*), hake (*Merluccius merluccius*), sardine (*Sardina pilchardus*), tuna (*Thunnus thynnus*), codfish (*Gadus morhua*), shrimp (*Aristeus antennatus*), salmon (*Salmo salar*), mackerel (*Scomber scombrus*), squid (*Loligo vulgaris*), and mussel (*Mytilus galloprovincialis*). Samples of each species were purchased at various establishments (supermarkets, local markets and fish stores) from Tarragona County (Catalonia, Spain). After collection, samples were immediately preserved in a refrigerator box. Once in the laboratory, they were kept at -20ºC until their pre-treatment. Thus, lateral fillets were dissected from the fish, while the shells of mussels and shrimps were taken off. Subsequently, samples were homogenized, lyophilized by means of a freeze-drying system (Labconco, Kansas City, MO, USA), and finally grinded. In addition, mussels were also sieved through a 125 µm mesh screen to homogenize the diameter of the particles. Each analyzed sample was, in fact, a composite sample prepared by mixing equal amounts from each species purchased from the three commercial establishments.

*2.3. Analytical method*

A mixture solution in toluene containing all the $^{13}$C-labelled PBDEs and $^{13}$C-BDE209 at levels of 0.2 and 2 µg mL$^{-1}$, respectively, was prepared. A set of seven calibration standard solutions, containing a mixture of all congeners at concentrations ranging from 1 to 600 ng mL$^{-1}$ for PBDEs, from 10 to 6000 ng mL$^{-1}$ for BDE209, from 1 to 750 ng mL$^{-1}$ for MeO-PBDEs, HBB and PBEB, and from 3 to 2250 ng mL$^{-1}$ for DBDPE, was prepared by dilution of the corresponding standard stock solutions in toluene. In addition, an appropriate amount of surrogate mixture solution was added to

the calibration standard solutions to obtain a concentration of 100 ng $mL^{-1}$ of each $^{13}C$-labelled PBDEs, excepting $^{13}C$-BDE209, whose concentration was 1000 ng $mL^{-1}$.

A more detailed description of the method for extraction and clean-up has been previously given (Barón et al., 2014). Briefly, 1.5 g of lyophilized sample was fortified at 2 μg $g^{-1}$ with a surrogate mixture standard ($^{13}C$-PBDEs), being kept in the fridge overnight to equilibrate. Then, a pressurized liquid extraction (PLE) (ASE 200, Dionex, Sunnyvale, CA, USA) with hexane/dichloromethane (1:1, v:v), followed by gravimetric determination of the lipid content, was done. The residue was dissolved again with 10 mL of hexane and subjected to solid phase extraction (SPE) with Al-N cartridges (5 g) (Symta, Madrid, Spain). The final extract was evaporated to dryness, re-dissolved with 40 μL of toluene, and analyzed by gas chromatography-tandem mass spectrometry (GC-MS/MS).

The chromatographic analysis was performed by using a Varian ion trap GC-MS system (Varian, Walnut Creek, CA, USA), following an adaptation of a previously developed method (Barón et al., 2014). The system was equipped with a 3800 gas chromatograph, a 4000 ion trap mass detector, and a CombiPal autosampler (CTC, Analytics, Zwigen, Switzerland) equipped with a 10 μL syringe of 23 gauge and point style 5 (Hamilton, Bonaduz, Switzerland). The mass spectrometer was operated in the electron ionization (EI) mode (70 eV), being the whole system controlled by means of the Varian MS Workstation v.6.9 software. The chromatographic separation was carried out on a ZB-5 analytical column (5% phenyl 95% dimethylpolysiloxane, 15m x 0.25 mm i.d.; 0.1 μm film thickness) from Micron Phenomenex (Torrance, California, USA). The injected volume was 1 μL, using splitless injection mode for 1 min at 280 ºC. The oven initial temperature was 140ºC, being held for 2 min, and then raised again at 10ºC/min until 310ºC, which was kept for 10 min. Helium was used as a carrier gas, at a constant flow rate of 1 mL $min^{-1}$. The whole time for the separation of the target compounds was 21 min. Transfer line, manifold, and trap temperatures were 280°C, 50°C and 200°C, respectively. Tandem mass spectrometry (MS/MS) mode was applied for the quantitative analysis. The retention time and the optimal MS parameters for each compound are summarized in Table 1.

*2.4. Quality assurance and quality control*

Quality control criteria used to ensure the correct identification of the target compounds consisted in the following: (1) the retention time should match that of the standard compound within ± 1s, (2) the signal-to-noise ratio (S/N) should be ≥ 3, and (3) the deviation of the two monitored ions intensities ratio should be within 15% of that of the standard compound.

Quantification of the target compounds was carried out by internal standard procedure with $^{13}$C-labelled BFRs. As mentioned before, multi-level calibration curves were performed for the quantification and good linearity was achieved ($R^2$ > 0.998). The instrumental limits of detection (LODs) calculated as three times the signal-to-noise ratio, ranged from 0.3 to 16.7 μg $L^{-1}$ for the analyzed compounds. The instrumental limits of quantification (LOQs) were defined as the lowest calibration point and ranged from 10 to 50 μg $L^{-1}$. Intra-day and inter-day repeatability expressed as relative standard deviation (RSD) (n=5, 1 μg $mL^{-1}$), were lower than 21% for all compounds.

*2.5. Exposure assessment and risk characterization*

The dietary intake of the 19 BFRs by the population of Tarragona County was estimated by using a deterministic method, which combines consumption and concentration data. Human exposure was assessed by applying the following equation:

$$E_t = \sum_{f=1}^{p} C_f X_{t,f} \qquad \text{Eq. 1}$$

Where $E_t$ is the dietary exposure to the BFR $t$ (ng kg $bw^{-1}$ $day^{-1}$), $C_f$ is the mean consumption of the individual species of fish or shellfish $f$ by the population (g kg $bw^{-1}$ $day^{-1}$), and $X_{t,f}$ is the concentration of the BFR $t$ in the fish or shellfish species $f$ (ng $g^{-1}$). The mean consumption of each age/gender population subgroup was previously normalized by dividing the dietary intake by the mean body weight. Data on BFR levels in fish and shellfish were based on fresh weight.

Calculations, for those not detected or presented at concentrations lower than their limit of quantification, were conducted under 3 different scenarios (upper-, middle- and lower-bound; UB, MB, LB, respectively), according to their limit of quantification (LOQ) and limit of detection (LOD) (IPCS, 2009). The UB scenario was estimated by

assuming the respective concentrations of LOD or LOQ. In the MB scenario, the concentrations were assumed to be one-half of the LOD or LOQ, and in the LB scenario a concentration of zero for non-detected BFRs and a concentration equal to the LOD for analytes with their levels below the LOQ were assumed. The intake of BFRs under these 3 scenarios was estimated for adolescents, adults and seniors (aged 10-19, 20-65 and >65, respectively) of both genders.

Currently, there is no international scientific consensus on the best system to estimate the risk assessment through food consumption, being several approaches commonly applied (COC, 2012; EFSA, 2005; Lachenmeier et al., 2012). In the present study, the health risks due to the intake of BFRs through fish and shellfish were calculated by using the MOE (Margin of Exposure) approach, according to the following equation:

$$MOE_t = \frac{BMDL_t}{E_t} \qquad \text{Eq. 2}$$

Where $MOE_t$ is the margin of exposure for the dietary exposure to the BFR *t*, $E_t$ is the dietary intake of the BFR *t* (ng kg $bw^{-1}$ $day^{-1}$), and *BMDL* (Benchmark dose confidence limit) is the point on the dose-response curve corresponding to a specific change due to the adverse response by the effect of BFR *t* (ng kg $bw^{-1}$ $day^{-1}$). The BMDL estimates the dose that causes a low, but measurable response, typically chosen in the range of 1-10% incidence above the control (EFSA, 2011; USEPA, 1995).

*2.6. Study population and data collection*

Consumption data were collected from a nutritional survey conducted in Catalonia, Spain, between 2002 and 2003 (ENCAT, 2003). A food frequency questionnaire (FFQ) was carried out with 2160 individuals (54% female and 46% males) aged between 10 and 80, covering 83 towns representing the whole population in Catalonia. Of the selected individuals invited to participate in the study, 66% agreed to take part of it. Twenty-six trained interviewers visited cases and controls at home seven days per week to check the answers to the FFQ, and they clarified and helped participants to answer questions. Thus, the consumption data were provided by means of a 3-day dietary record, a 24 h record, and a food frequency questionnaire. Usual dietary intake was

estimated from food frequencies and quantities reported by participants for the 15 months prior to the interview. Interviewers also obtained information via a structured interview on participants' medical history, lifetime smoking history, chronic disease history, nutritional supplement intake, healthy lifestyles, and social status, among others. Moreover, an anthropometric study was developed in order to control different human parameters. The seafood species were selected among those most consumed of the population. The consumption rates of the general population to each one of the analyzed species (hake, cod, sole, squid, shrimp, mussel, tuna, mackerel, salmon and sardine) are summarized in Table 2.

## 3. Results and discussion

### *3.1. Occurrence of BFRs in commercial samples of fish and shellfish*

The average concentrations of BFRs in each species of fish and shellfish, expressed in wet weight (w.w.), are shown in Table 3. For those not detected or present at concentration lower than their limit of quantification, specific values <LOD or <LOQ have been indicated, respectively. Moreover, values corresponding to one-half of the LOD or LOQ have been assumed to calculate total amount of each BFR's group. Among the 3 groups of analyzed BFRs, PBDEs showed the highest concentrations. Quantifiable amounts of PBDEs were found in most samples, being BDE28 and BDE47 determined in all the analyzed species. BDE47 was the congener with the highest contribution to the total level of PBDEs (ΣPBDEs). In contrast, BDE100, BDE183 and BDE209 were not detected in any sample, while BDE154 was identified only in mackerel at a concentration below its LOQ. The highest level of total PBDEs (ΣPBDEs) was found in salmon (1.3 ng $g^{-1}$ (w.w.)), which is the species with the highest lipid content (25%). In addition, sole, tuna, cod and hake also presented relatively high concentrations of ΣPBDEs (1.2, 0.8, 0.8 and 0.9 ng $g^{-1}$ (w.w.)). On the other hand, squid and shrimp, two species with low lipid content, showed the lowest values of ΣPBDEs (Table 3).

The levels of MeO-PBDEs were comparatively lower than those corresponding to PBDEs. Some MeO-PBDEs, such as 5-MBDE47, 4-MBDE49, 4-MBDE103, 5-MBDE99 and 4-MBDE101 were not detected in any of the samples. Mussels and tuna showed the highest concentration of total MeO-PBDEs (ΣMeO-PBDEs), with mean

values of 1.5 and 1.0 ng $g^{-1}$ (w.w.), respectively. In contrast, hake, cod and squid had values below the LOD/LOQ for all MeO-PBDEs.

Regarding emerging BFRs, neither traces of PBEB nor DBDPE were found in any of the analyzed samples, which is in agreement with recent data from the scientific literature (Barón et al., 2014; Papachlimitzou et al., 2012). HBB was the only emerging pollutant with concentrations above its LOD. This compound was identified in most samples, showing concentrations of up to 0.2 ng $g^{-1}$ (w.w.), in 5 different species (Table 3). Only hake, cod, sole, mussel and shrimp, which are species with a low content of fat, showed the maximum level of HBB (0.20 ng $g^{-1}$ (w.w.), also in accordance with previous results (Munschy et al., 2011).

The predominance of PBDEs in fish and shellfish with respect to other BFRs has been previously reported. Losada et al. (2010) also identified sole as the species with the highest concentration of ΣPBDEs (22.3 ng $g^{-1}$ (l.w.)), and BDE47 as the main congener. In fact, the high contribution of BDE47 on the total concentration of PBDEs in fish and shellfish has been found in a number of investigations. When analyzing BFRs in fish, Barón et al. (2014) observed that BDE47 was the most abundant congener among 19 brominated compounds. Similarly, in an investigation in which concentrations of BFRs in European farmed salmon were found to be higher than those from North and South America, Lyche et al. (2015) reported that BDE47 was the predominant compound in salmon. Although in recent years the occurrence of PBDEs has been investigated in a large number of aquatic species, mussels and salmon have been the most frequently studied, especially in dietary intake surveys (Cruz et al., 2015).

With respect to MeO-PBDEs, the concentrations in samples of fish and shellfish from Tarragona County are similar to those reported in the literature (Kierkegaard et al., 2004a; Losada et al., 2010). Furthermore, the same chemical profile has been observed, being 2-MBDE68 and 6-MBDE47 the predominant compounds. For comparison purposes, Losada et al. (2010) found that the levels of 6-MBE47 and 2-MBDE68 in samples of salmon from the Mediterranean Sea were 5.55 and 2.15 ng $g^{-1}$ (l.w.)), respectively. However, in contrast to our results, no MeO-PBDEs could be quantified in mussels.

*3.2. Dietary intake of BFRs and risk assessment*

The total dietary exposure of BFRs through consumption of fish and shellfish by the population of Tarragona, as well as the dietary exposure of ΣPBDEs, ΣMeO-PBDEs, PBEB, HBB and DBDPE, are depicted in Fig. 1. Human exposure was assessed for 6 population subgroups, based on age and gender, and under 3 scenarios: upper-, middle- and lower-bound intake. For all scenarios and subpopulations, the highest contribution to the intake of BFRs corresponded to ΣPBDEs (48%-68%), followed by ΣMeO-PBDEs, in the upper- and middle-bound scenarios, and HBB in the lower-bound scenario. In the upper- and middle-bound scenarios, senior men presented the highest exposure to BFRs (1.38 and 1.08 ng kg $bw^{-1}$ $day^{-1}$), while adult women showed the highest exposure in the lower-bound scenario (0.83 ng kg $bw^{-1}$ $day^{-1}$). Estimations were performed for the general adult population of Tarragona County. Among them, high fish consumers would be obviously the group with the highest intake of BFRs. However, as no current consumption data were available for this particular subpopulation group, no calculations were conducted for them.

In recent years, there has been an increasing concern among scientists for the analysis of BFRs, mainly PBDEs, in fish and shellfish, as well as in other foodstuffs. Furthermore, these data have been frequently used in order to assess the dietary intake of these chemicals by the general population. Details and results of some of these investigations are summarized in Table 4. It must be highlighted that the comparability between studies is difficult, and data interpretation must be performed with special caution. This is basically due to the potentially high number of different factors involved in a total diet study (e.g., analytical method, consumption data, exposure assessment model, food groups covered, congeners considered, etc.). In addition, concentration values refer to raw fish, disregarding the potential effect of cooking (Perelló et al., 2009; Domingo, 2016) and/or the bioavailability of these compounds (Yu et al., 2011).

Since 2000, our laboratory has been periodically performing a surveillance program to evaluate the dietary intake of chemical pollutants by the population living in Catalonia (Spain). In a first survey, total dietary exposure of ΣPBDEs was estimated in 97.3 ng $day^{-1}$, in a middle-bound scenario, and 81.9 ng $day^{-1}$, in a lower-bound scenario (Bocio et al., 2003). Fish and shellfish were the food group with the highest contribution (30% of the total), being the intake of ΣPBDEs through the consumption of 3 marine species (hake, sardine, and mussels) 30.7 ng $day^{-1}$ (or 0.44 ng kg $bw^{-1}$ $day^{-1}$). In the present study, the intake of ΣPBDEs through the consumption of 10 marine species was

found to be 0.45 ng $kg^{-1}$ bw $day^{-1}$ (or 31.2 ng $day^{-1}$), a value very close to that firstly reported (Bocio et al., 2003). A more extensive study was subsequently performed. The occurrence of PBDEs was investigated in a more extensive number of species (Domingo et al., 2006). The dietary intake of ΣPBDEs through the ingestion of 14 edible marine species widely consumed by the Catalan population was calculated to be 20.8 ng $day^{-1}$, with tuna and salmon being the highest contributors (Domingo et al., 2006). In the last survey of the series, the intake of ΣPBDEs through food decreased 23% with respect to the first study, being the total dietary exposure 75.4 ng $day^{-1}$ (Domingo et al., 2008). Considering only the group of fish and shellfish, the total intake was reduced to 26.5 ng $day^{-1}$ (Domingo et al., 2008).

Also in Spain, Pardo et al. (2014) analyzed the PBDE content in fish and shellfish marketed in the Region of Valencia over the period 2007–2012, estimating a daily intake of 0.137 ng kg $bw^{-1}$ $day^{-1}$ (9.59 ng $day^{-1}$) for the adult population. More recently, Aznar-Alemany et al. (submitted) analyzed the levels of PBDEs, those of some emerging brominated flame retardants (PBEB, HBB and DBDPE), as well as MeO-PBDEs in commercial seafood samples from European countries. The dietary intake of some specific BDE congeners was of the same order of magnitude as that calculated for the inhabitants of Tarragona County. In fact, similar exposure levels have been also found in other European countries: 19.3 ng $day^{-1}$ in Sweden (Tornkvist et al., 2011) and 20.3 ng $day^{-1}$ in Italy (Martellini et al., 2016). Data corresponding to a number of Asian countries are also similar (Yu et al., 2011; Sunggyu et al., 2013; Gong et al., 2015), with mean exposure levels of 41 ng $day^{-1}$ through fish consumption, and 15 ng $day^{-1}$ through shellfish ingestion.

With respect to MeO-PBDEs, information on their dietary intakes is extremely limited. In one of the very few studies, Wang et al. (2011) studied the dietary exposure of MeO-PBDEs of Hong Kong residents through fish consumption, finding values in the range 0.5-4.3 ng kg $bw^{-1}$ $day^{-1}$, well above the intake estimated for the population of Tarragona County (0.22 ng kg $bw^{-1}$ $day^{-1}$). Covaci et al. (2007) investigated the occurrence of MeO-PBDEs in fish oil dietary supplement. They calculated an intake of these chemicals of 10 ng $day^{-1}$ through the ingestion of these supplements, being the median intake of MeO-PBDEs between 3 and 6 times higher than the median intake of PBDEs.

Most studies regarding the dietary exposure of emerging BFRs have been conducted in China. Labunska et al. (2015) reported values of HBB in fish (0.05 ng kg

bw $^{-1}$day$^{-1}$), as well as PBEB and DBDPE in shrimp (0.03 and 0.20 ng kg bw$^{-1}$ day$^{-1}$, respectively). On the other hand, Peng et al. (2015) showed a dietary intake of PBEB (0.3 pg kg bw$^{-1}$ day$^{-1}$), HBB (53 pg kg bw$^{-1}$ day$^{-1}$), and DBDPE (640 pg kg bw$^{-1}$ day$^{-1}$) through consumption of fish and shellfish in a Chinese production area of BFRs.

*3.3. Risk assessment*

Data on the human toxicity of BFRs is still quite limited. Moreover, most of the information refers to PBDEs, while there is a very notable lack of toxicological data on the potential hazard of other BFRs. Because of these limitations, in the current study the risk could be only assessed for a few BDE congeners. Values of BMDL of 309000, 12000, 83000 and 1700000 ng kg$^{-1}$ bw were used for the risk characterization of BDE47, BDE99, BDE153 and BDE209, respectively (EFSA, 2011). Due to the NOAEL (no observed adverse effect level) limitations, described be Filipsson et al. (2003), BMDL has been pointed out as a viable alternative (EFSA, 2011). The MOEs to each one of these 4 congeners, for every population subgroup are shown in Table 5. No health risks were associated to the intake of BFRs through fish and shellfish consumption, in any of the 3 exposure scenarios.

## 4. Conclusions

Nineteen BFRs, including MeO-PBDEs and 3 emerging compounds, were analyzed in samples of 10 fish and shellfish species widely consumed in Tarragona County (Catalonia, Spain). BDE28 and BDE47 were the BDE congeners with the highest concentration. Salmon, sole and hake showed the greatest levels of ΣPBDEs, while mussels and tuna presented the highest values of ∑MeO-PBDEs. Moreover, 2-MBDE68, 6-MBDE47 and 5-MBDE100 were the most predominant congeners. Regarding the emerging compounds, HBB was identified in most samples, while PBEB and DBDPE were not detected in any sample. The daily intake of BFRs via ingestion of the 10 species of fish and shellfish was estimated under 3 different exposure scenarios. No health risks were associated to the intake of BFRs through the consumption of fish and shellfish. Furthermore, the current levels of exposure for the population living in Tarragona County are similar to those reported in the scientific literature for a number of European and Asian countries.

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586

**Table 1**
Retention times and MS conditions in the chromatographic analysis of BFRs in fish and shellfish.

| Compound | | Retention time (min) | Parent ion | Product ions [a] | CID Amplitude (V) | CID Storage level (m/z) | m/z range | Scan time |
|---|---|---|---|---|---|---|---|---|
| PBDEs | BDE28 [b] | 7.16 | 408 | **248,** 246, 409 | 0.4 | 179.7 | 190-418 | 0.38 |
| | BDE47 | 9.19 | 486 | **326,** 328, 484 | 0.8 | 214.4 | 224-496 | 0.58 |
| | BDE100 [e] | 10.63 | 406 | **405,** 323, 282 | 1.3 | 178.9 | 189-416 | 0.27 |
| | BDE99 [e] | 11.06 | 406 | **405,** 403, 371 | 0.2 | 178.9 | 189-416 | 0.27 |
| | BDE154 [g] | 12.21 | 644 | **483,** 643, 347 | 0.8 | 283.7 | 294-654 | 0.32 |
| | BDE153 [g] | 12.77 | 644 | **643,** 536, 516 | 0.1 | 283.7 | 294-654 | 0.32 |
| | BDE183 | 14.36 | 721 | **548,** 631, 418 | 0.2 | 317.6 | 328-731 | 0.53 |
| | BDE209 | 20.20 | 798 | **616,** 461, 776 | 0.1 | 351.5 | 352-808 | 0.53 |
| MeO- | 2-MBDE68 [d] | 10.01 | 516 | **515,** 517, 420 | 0.1 | 227.3 | 237-526 | 0.53 |
| | 6-MBDE47 [d] | 10.32 | 516 | **356,** 513, 424 | 0.3 | 227.3 | 237-526 | 0.53 |
| | 5-MBDE47 [e] | 10.77 | 516 | **358,** 479, 432 | 1.1 | 227.3 | 237-526 | 0.27 |
| | 4-MBDE49 [e] | 10.85 | 516 | **356,** 358, 500 | 0.3 | 227.3 | 237-526 | 0.27 |
| | 5-MBDE100 [f] | 11.78 | 596 | **497**, 419, 587 | 0.1 | 262.6 | 272-606 | 0.54 |
| | 4-MBDE103 [f] | 11.90 | 596 | **435,** 595, 435 | 0.6 | 262.6 | 272-606 | 0.54 |
| | 5-MBDE99 [g] | 12.42 | 596 | **558,** 381, 419 | 0.2 | 262.6 | 273-606 | 0.32 |
| | 4-MBDE101 [g] | 12.52 | 596 | **595,** 277, 463 | 0.7 | 262.6 | 273-606 | 0.32 |
| Emerging | PBEB [b] | 7.51 | 501 | **499,** 420, 486 | 0.4 | 220.7 | 231-511 | 0.38 |
| | HBB [c] | 8.57 | 551 | **549,** 415, 538 | 0.6 | 242.7 | 253-561 | 0.58 |
| | DBDPE [c] | 8.75 | 117 | **115,** 116, 91 | 0.4 | 51.5 | 62-127 | 0.58 |

[a] Quantification ions (m/z) in bold.
[b-g] Compounds were separated using the Multiple Reaction Monitoring mode.

**Table 2**
Mean consumption (g $day^{-1}$) of the 10 species of fish and shellfish selected among those species most widely consumed by the population of Tarragona County, classified according to gender and age.

| | **Foodex1 code** | Boys (10-19) | Adult men (20-65) | Senior men (>65) | Girls (10-19) | Adult women (20-65) | Senior women (>65) |
|---|---|---|---|---|---|---|---|
| Hake | A.01.000895 | 7.82 | 15.03 | 23.02 | 10.84 | 14.49 | 14.56 |
| Sole | A.01.000899 | 6.22 | 4.84 | 3.65 | 2.44 | 5.28 | 5.17 |
| Cod | A.01.000894 | 2.13 | 4.18 | 8.08 | 0.60 | 4.61 | 8.15 |
| Shrimp | A.01.000923 | 2.71 | 2.83 | 2.42 | 2.94 | 3.44 | 1.68 |
| Squid | A.01.000928 | 1.88 | 3.17 | 3.18 | 5.18 | 3.17 | 0.77 |
| Salmon | A.01.000883 | 3.30 | 1.80 | 2.23 | 1.00 | 3.00 | 1.14 |
| Tuna | A.01.000891 | 0.71 | 1.62 | 1.07 | 0 | 1.45 | 0.52 |
| Mackerel | A.01.000890 | 0.36 | 1.13 | 0.50 | 0.32 | 1.27 | 2.86 |
| Sardine | A.01.000880 | 0.99 | 2.92 | 2.60 | 2.08 | 2.69 | 4.70 |
| Mussel | A.01.000934 | 1.26 | 0.97 | 2.06 | 0 | 1.84 | 0.67 |

**Table 3**
Concentration of 19 brominated flame retardants (in ng $g^{-1}$ (w.w.)) in samples of 10 edible marine species widely consumed in Tarragona County (Catalonia, Spain).

| | | Hake (2%) | Sole (6%) | Cod (1%) | Shrimp (2%) | Squid (6%) | Salmon (25%) | Tuna (16%) | Mackerel (17%) | Sardine (14%) | Mussel (8%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **PBDEs** | BDE28 | 0.2 | 0.3 | 0.1 | 0.1 | 0.1 | 0.3 | 0.2 | 0.1 | 0.1 | 0.2 |
| | BDE47 | 0.5 | 0.7 | 0.5 | 0.3 | 0.3 | 0.7 | 0.5 | 0.5 | 0.3 | 0.3 |
| | BDE100 | <0.002 | <0.002 | <0.002 | <0.002 | <0.002 | <0.001 | <0.001 | <0.001 | <0.001 | <0.002 |
| | BDE99 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.2 | 0.1 | <0.003 | 0.1 | 0.1 |
| | BDE154 | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | <0.01 | <0.01 | <0.04* | <0.01 | <0.02 |
| | BDE153 | <0.03* | <0.03* | <0.03* | <0.03* | <0.03* | <0.02* | <0.02* | <0.02* | <0.02* | <0.02* |
| | BDE183 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| | BDE209 | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | <0.01 | <0.01 | <0.01 | <0.01 | <0.02 |
| | *ΣPBDEs* | *0.9* | *1.2* | *0.8* | *0.6* | *0.6* | *1.3* | *0.8* | *0.7* | *0.4* | *0.6* |
| **MeO-PBDEs** | 2-MBDE68 | <0.01 | 0.1 | <0.01 | 0.1 | <0.01 | 0.1 | 0.8 | 0.1 | <0.01* | 0.7 |
| | 6-MBDE47 | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | <0.2* | <0.1 | <0.6 |
| | 5-MBDE47 | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | <0.01 | <0.01 | <0.01 | <0.01 | <0.02 |
| | 4-MBDE49 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| | 5-MBDE100 | <0.1* | <0.1* | <0.1* | <0.1* | <0.1* | <0.04* | <0.04* | <0.04* | 0.2 | <0.1* |
| | 4-MBDE103 | <0.002 | <0.002 | <0.002 | <0.002 | <0.002 | <0.001 | <0.001 | <0.001 | <0.001 | <0.002 |
| | 5-MBDE99 | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | <0.04 | <0.04 | <0.04 | <0.04 | <0.04 |
| | 4-MBDE101 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |
| | *ΣMeO-PBDEs* | *0.3* | *0.4* | *0.3* | *0.4* | *0.3* | *0.3* | *1.0* | *0.4* | *0.3* | *1.5* |
| **Emerging BFRs** | PBEB | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | <0.01 | <0.01 | <0.01 | <0.01 | <0.02 |
| | HBB | 0.2 | 0.2 | 0.2 | 0.2 | <0.02 | 0.1 | <0.01 | 0.1 | 0.1 | 0.2 |
| | DBDPE | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.004 | <0.004 | <0.004 | <0.004 | <0.01 |

<LOD.
In parenthesis, percentage of lipid weight basis.

**Table 4**
A summary of studies on the concentrations and dietary intake of PBDEs.

| Country | Matrix | Congeners analyzed | Concentration (in ng $g^{-1}$ w.w.) | Dietary exposure (in ng $day^{-1}$ or [ng kg $bw^{-1}$ $day^{-1}$]) | Remarks | References |
|---|---|---|---|---|---|---|
| Spain | Fish and shellfish from Catalonia, Spain | tetraBDE pentaBDE hexaBDE heptaBDE octaBDE | 0.33, fish<br>0.32, shellfish | 30.7 | Predominance of the homologues tetra- and pentaBDEs, followed by hexaBDE. | Bocio et al., 2003 |
| Spain | Fish and shellfish from Catalonia, Spain | tetraBDE pentaBDE hexaBDE heptaBDE octaBDE | 0.56, fish | 20.8 | The highest levels of PBDEs were found in salmon. The highest and lowest levels corresponded to BDE47 and BDE183, respectively. | Domingo et al., 2006 |
| Spain | Fish and shellfish from Catalonia, Spain | tetraBDE pentaBDE hexaBDE heptaBDE octaBDE | 0.56, fish and shellfish | 26.5 | BDE47 was the congener with the highest concentration. | Domingo et al., 2008 |
| Belgium | Fish and shellfish from Belgium | 28, 47, 99, 100, 153 and 154 | - | 59.5 [0.85] | BDE47 was the congener with the highest concentration. | Sioen et al., 2008 |
| Sweden | Fish and fish products from Sweden | 28, 31, 47, 66, 99, 100, 138, 153, 154 and 183 | 0.397<br>0.249 only BDE47 | 19.3 | Fish contributed 38% to the total PBDE intake | Törnkvist et al., 2011 |

| | | | | | | |
|---|---|---|---|---|---|---|
| China | Fish and shellfish from Shangai | 17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190 and 209 | 0.002-0.35, shellfish<br>0.003-1.25, fish | 15 shellfish<br>41 fish | TetraBDE was the most abundant homologue. Bioaccessibility of PBDEs was studied. | Yu et al., 2011 |
| Japan | Fish from South Korea | 17, 28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 183, 184, 184, 191, 196, 197, 206, 207 and 209 | 0.06 - 6.25, shellfish | 65.9 | Predominant congeners were BDE47, 99 and 100. | Sunggyu et al., 2013 |
| China | Carp from east-central china | 28, 47, 99, 100, 153, 154 and 183 | 0.047 | 11.9 [0.199] BDE47<br>3.7 [0.061] BDE99<br>38.5 [0.642] BDE153 | Standard adult of 60 kg body weight was used to calculate dietary exposure. | Gong et al., 2015 |
| Italy | Fish and mollusc from local Italy market | 7, 15, 17, 28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 156, 183, 184 and 191 | 0.52, fish<br>0.49, mussels | 20.3 [0.29] fish and mollusks | A high percentage of the BDE47, 99 and 100 congeners was observed. | Martellini et al, 2016 |
| Spain | Fish and shellfish from Catalonia, Spain | 28, 47, 99, 100, 153, 154, 183 and 209 | 0.8 fish and shellfish | [0.45] | Predominant PBDE congeners in fish and shellfish were BDE28 and BDE47. | This study |

Calculation for dietary exposure was done by assuming that non-detected values were one-half of the limit of detection.
Results are given for a male adult of 70 kg body weight.
w.w. wet weight. b.w. body weight.

**Table 5**
Risk characterization (MOE) of the exposure to 4 BDE congeners through consumption of fish and shellfish species by the population of Tarragona County.

| | | **BDE47** | **BDE99** | **BDE153** | **BDE209** |
|---|---|---|---|---|---|
| | BMDL (ng $kg^{-1}$ b.w) | 309000 | 12000 | 83000 | 1700000 |
| **Upper-bound** | Boys | 1.3E+06 | 2.4E+05 | 3.3E+06 | 7.6E+07 |
| | Girls | 1.4E+06 | 2.3E+05 | 3.1E+06 | 7.2E+07 |
| | Adult men | 1.2E+06 | 2.2E+05 | 2.9E+06 | 6.7E+07 |
| | Adult women | 8.8E+05 | 1.6E+05 | 2.1E+06 | 5.0E+07 |
| | Senior men | 8.8E+05 | 1.5E+05 | 2.1E+06 | 4.8E+07 |
| | Senior women | 9.5E+05 | 1.8E+05 | 2.4E+06 | 5.6E+07 |
| **Middle-bound** | Boys | 1.3E+06 | 2.4E+05 | 6.2E+06 | 1.5E+08 |
| | Girls | 1.4E+06 | 2.3E+05 | 5.7E+06 | 1.4E+08 |
| | Adult men | 1.2E+06 | 2.2E+05 | 5.5E+06 | 1.3E+08 |
| | Adult women | 8.8E+05 | 1.6E+05 | 4.0E+06 | 9.9E+07 |
| | Senior men | 8.8E+05 | 1.5E+05 | 3.9E+06 | 9.6E+07 |
| | Senior women | 9.5E+05 | 1.9E+05 | 4.6E+06 | 1.1E+08 |
| **Lower-bound** | Boys | 1.3E+06 | 2.4E+05 | 9.2E+06 | n.c. |
| | Girls | 1.4E+06 | 2.3E+05 | 8.6E+06 | n.c. |
| | Adult men | 1.2E+06 | 2.2E+05 | 8.2E+06 | n.c. |
| | Adult women | 8.8E+05 | 1.6E+05 | 6.0E+06 | n.c. |
| | Senior men | 8.8E+05 | 1.5E+05 | 5.8E+06 | n.c. |
| | Senior women | 9.5E+05 | 1.9E+05 | 6.8E+06 | n.c. |

n.c.: not calculated. The associated dietary exposure is 0. BMDLs were collected from the literature (EFSA, 2011).

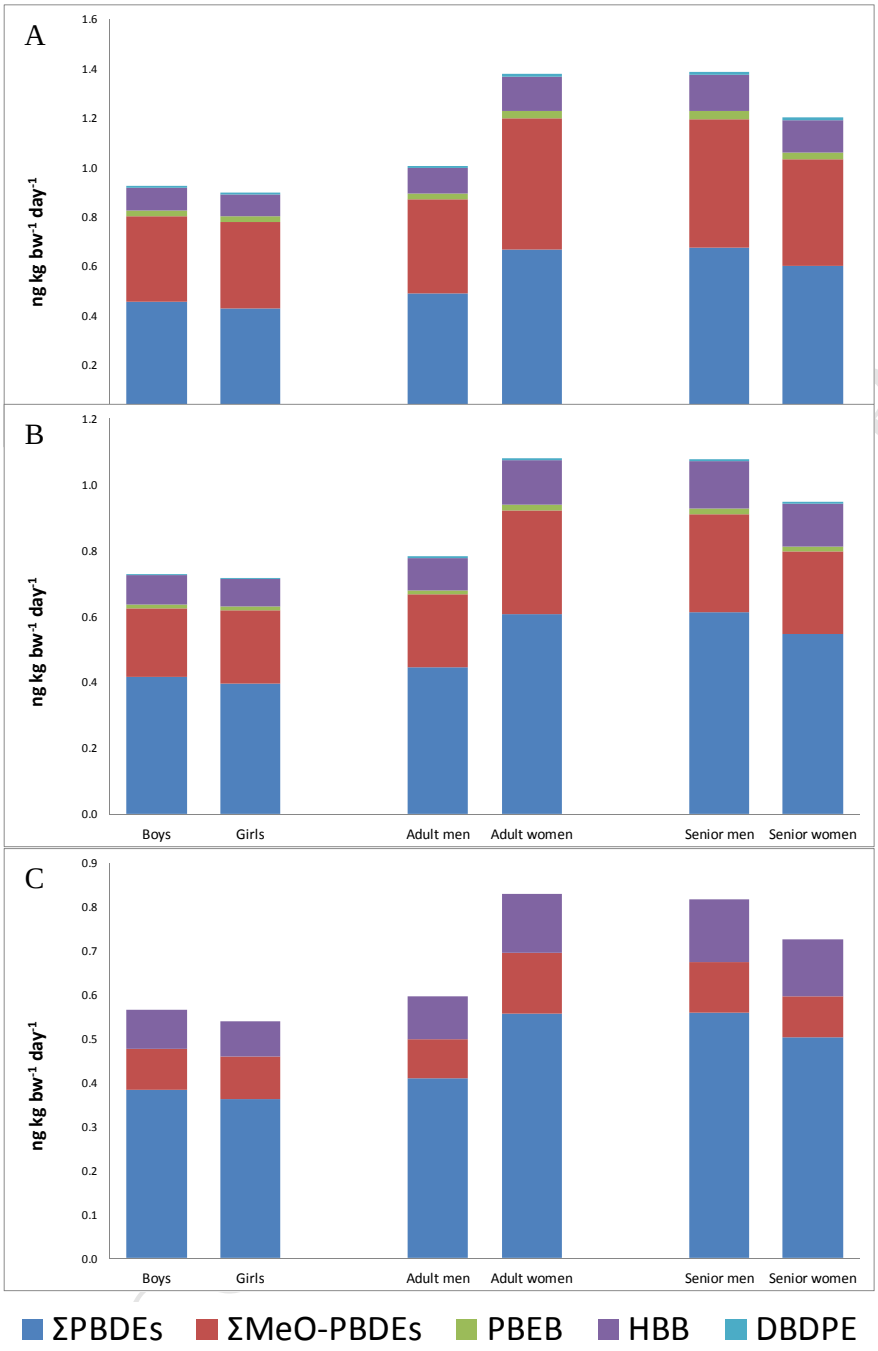


**Fig. 1.** Estimated dietary intake (ng $kg^{-1}$ bw $day^{-1}$) of ∑PBDEs, ∑MeO-PBDEs, PBEB, HBB and DBDPE for the general population of Tarragona County (Spain) according to gender and age. A) Upper-bound scenario. B) Middle-bound scenario. C) Lower-bound scenario.

HIGHLIGHTS

- A number of BFRs was found in fish and shellfish from Tarragona County market.
- BDE47 and 28 were the congeners with the highest levels in the analysed samples.
- Trace levels of some MeO-PBDEs were present in the main commercial fish species.
- HBB was identified in most samples, while PBEB and DBDPE were not detected in any.
- The dietary exposure to BFRs does not pose human health risks in Tarragona County.