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UV-filters and musk fragrances in seafood commercialized in Europe Union: Occurrence, risk and exposure assessment

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ABSTRACT

In the framework of the FP7 ECsafeSeafood project, 62 seafood samples commercialized in Europe Union from several representative species – mackerel, tuna, salmon, seabream, cod, monkfish, crab, shrimp, octopus, perch and plaice – were analysed for residues of 21 personal care products (PCPs), including 11 UV-filters (UV-Fs) and 10 musk fragrances (musks). PCPs analysis were performed by Quick, Easy, Cheap, Effective Rugged, Safe (QuEChERS), combined with liquid-liquid extraction (LLE) or dispersive solid-phase extraction (dSPE), followed by gas chromatography-tandem mass spectrometry (GC-MS/MS). The results showed the presence in a wide range of samples of nine out of eleven UV-Fs compounds analysed, namely 2-ethylhexyl salicylate (EHS), 2-ethylhexyl,4-methoxycinnamate (EHMC), 4-methylbenzylidenecamphor (4-MBC), benzophenone-1 (BP1), benzophenone-3 (BP3), isoamyl-4-methoxycinnamate (IMC), 2,2′-dihydroxy-4,4′-dimethoxybenzophenone (DHMB), homosalate (HS), and octocrylene (OC), whereas galaxolide (HHCB), galaxolide lactone (HHCB-lactone), and tonalide (AHTN) were the most found musks. The potential risks to human health associated with the exposure to eight of the more prevalent PCPs – EHS, EHMC, 4-MBC, BP1, BP3, IMC, HHCB, and AHTN - through seafood consumption were assessed for consumers from five European countries (Belgium, Ireland, Italy, Portugal and Spain). Results showed that the human exposure to UV-Fs and musks estimated from the concentration values found in seafood and the daily consumption of concerned seafood species, were far below toxicological reference values.

1. Introduction

The economic and industrial development of the world has rapidly increased in the last decades leading to a rise in threats to the oceans. Among these menaces, the organic contamination with personal care products (PCPs) has been of great concern in aquatic systems in the last few years (Halden, 2015), and their concentration in the oceans is likely to increase, particularly due to atmospheric temperature increase and ozone-depletion.

PCPs comprise a wide range of compounds such as UV-filters (UV-Fs) and musks, used in sunscreens to protect the skin against the harmful effects of ultraviolet radiation and in household products or cosmetics as fragrance ingredients, respectively. These compounds are widely employed, especially in developed countries for daily human

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hygiene and mostly end up in environmental waters. As a consequence, both UV-Fs and musks have been reported in surface waters (Homem et al., 2016; Tsui et al., 2014), ground water (Jurado et al., 2014; Pintado-Herrera et al., 2014), drinking water (Diaz-Cruz et al., 2012; Li et al., 2016), seawater (Magi et al., 2012; Panagiotou et al., 2009), and wastewaters (Cunha et al., 2015a; Homem et al., 2016; Kupper et al., 2004). Moreover, due to their lipophilic nature (log K_{OW} values between 4 and 8) and great stability in the environment, these compounds can easily bioaccumulate and biomagnify, reaching several trophic levels (Zhang et al., 2013). UV-Fs have been detected in various aquatic organisms, including fish (Gago-Ferrero et al., 2013), mussels, clams (Cunha et al., 2015b), and dolphins (Alonso et al., 2015), as well as in human fluids and tissues like breast milk (Rodriguez-Gomez et al., 2015), semen (Leon et al., 2010), and placenta (Valle-Sistac et al., 2016). The presence of musks have also been reported in fish (Cunha et al., 2015b), mussels (Trabalon et al., 2015), breast milk (Reiner et al., 2007) and human adipose tissue (Rimkus et al., 1994). Despite the importance of the above mentioned data, a large survey on the magnitude of PCPs contamination in fish consumed in Europe, a requisite to made an estimation of human intake of these compounds and associated risk, is missing as far as we know.

To date, numerous toxicological studies in aquatic organisms showed that several UV-Fs and musks exhibit endocrine disrupting properties (Downs et al., 2016; Kunz and Fent, 2006; Schlumpf et al., 2001). Yet, so far, the toxic effects in humans after such a prolonged low dose exposure to UV-Fs and musks have hardly been investigated. Kunz and Fent (2006) and Kunz et al. (2006) demonstrated that UV-Fs show anti-estrogenic, androgenic, and/or anti-androgenic activity through human estrogen and androgen receptor assays. The toxicity in aquatic organisms and also in humans raises legal and health concerns worldwide. Therefore, many regions (e.g., European Union (EU), The United States of America (USA), Japan and Australia) have UV-Fs and musks under strict legislation in terms of their manufacture and utilization in product formulation. For example, in EU a positive list of 25 organic UV-Fs is accepted in product formulations (1223/2009/EC, 2009), whereas these number is only 16 in USA, 26 in Australia, and 31 in Japan (Sanchez-Quiles and Tovar-Sanchez, 2015). Regarding environmental legislation, the levels of UV-Fs and musks are still not established. However, EHMC, was recently included in the Watch List as a priority pollutant in surface water under the Environmental Quality Standards Directive (2008/105/EC, 2013; Carvalho et al., 2015).

Seafood consumption, owing to its recognized value as part of an healthy diet, plays a significant role in the diet in many European countries, reaching a consumption of around 25,5 kg per capita per year on average in 2014 (Comission, 2016). Fish or seafood consumption has been reported to be the focal food category in the majority of food-related risk/benefit perception and communication studies from the past decades (Jacobs et al., 2015). Indeed, despite providing health benefits, mainly due to the presence of high value protein and Ω−3 fatty acids, seafood consumption can lead to the exposure to certain environmental contaminants and in some cases (of high exposure) can induce health risks, e.g. for methyl mercury (Jacobs et al., 2017). Considering human exposure to UV-Fs and musks, a combination of exposure routes can occur: (i) through the diet, (ii) ingestion/inhalation via environment, and (iii) dermal/inhalation intake. The dietary route, especially through contaminated seafood consumption, plays an important role in the overall human exposure; however, risk analysis is difficult as there are still no admissible limits for the presence of both UV-Fs and musks in food. Nevertheless, in this study an attempt has been made to assess the exposure to both UV-Fs and musks via seafood consumption and to evaluate the potential risks for human health. So far, a similar study for musks is only available for Catalan populations (Trabalon et al., 2015), far from representing all the European population.

The current study, conducted in the framework of the European ECsafeSEAFOOD FP7 project, was focused on the monitoring of UV-filters and musk fragrances in seafood at European scale. Data obtained in this large survey were analysed to answer to the following questions: what are the fish species more exposed to musks and UV-F? what is the magnitude of the exposure? where are located the sites with higher PCPs levels? In addition, the potential risks for human health associated with the exposure to a selection of UV-Fs and musks through seafood consumption was assessed for adults from five EU countries, namely Belgium, Ireland, Italy, Portugal and Spain. For such purposes sixty-two samples of seafood consumed in Europe were collected, covering different habitats, wild vs. farmed organisms, and from EU or extra-EU production.

2. Experimental procedure

2.1. Standards and reagents for UV-filters

2-Hydroxy-4-methoxybenzophenone (BP3; 98% purity), and 2-ethylhexyl 4-(dimethylamino)benzoate (EPABA; 98% purity) were purchased from Alfa Aesar (Heysham, Lancashire, UK). 3,3,5-trimethylcyclohexyl salicylate (HMS; 98% purity) 2,2′-dihydroxy-4,4′-dimethoxybenzophenone (DHMB, 99% purity) and isoamyl-4-methoxycinnamate (IMC, 95% purity) were purchased from TCI (Haven, Zwijndrecht, Belgium). Octocrylene (OC, 98% purity), 2-ethylhexyl 4-methoxycinnamate (EHMC, 100% purity), 2-ethylhexyl salicylate (EHS, 99% purity), hexyl 2-[4-(diethylamino)-2-hydroxybenzoyl]benzoate (DBENZO, 99% purity), 2,4-dihydroxybenzophenone (BP1, 99% purity) and 3-(4-methylbenzylidene)camphor (4-MBC, 98.5% purity), were purchased from Sigma-Aldrich (Steinheim, Germany). The internal standard (IS) Benzophenone-d10 (BPd_{10}-IS, 99 atom % D) was also purchased from Sigma-Aldrich.

Individual standard solutions of UV-filters were prepared in methanol (HPLC grade from Sigma-Aldrich) at concentrations of 2000 μg/mL. Working mixture solutions of 100 μg/mL were prepared in acetonitrile, solvent used in the extraction.

For QuEChERS extraction: acetonitrile (MeCN, gradient grade for HPLC; 78.6% purity), Z-sep + and anhydrous magnesium sulfate (anhydrous $MgSO_4$; 99.5% purity) were purchased from Sigma-Aldrich; hydrochloric acid (HCl; 37%) and sodium chloride (NaCl; 99.5% purity), were purchased from AppliChem Panreac ITW Co. (Barcelona, Spain). To ensure efficient removal of residual water, anhydrous $MgSO_4$ was treated for 5 h at 500 °C in a muffle furnace. Liquid-liquid extraction solvents n-hexane (gradient grade for HPLC), *tert*-butyl methyl ether (MTBE, pro-analysis), and benzene (pro-analysis) were purchased from Merck (Darmstadt, Germany). Derivatization reagent N,O-bis(trimethylsilyl)trifluoroacetamide with 1% TMCS (BSTFA + 1%TMCS, 99% purity grade) was obtained from Fluka.

Ultra high purity Helium (99.999%) and nitrogen (99.99%) for GC-MS/MS were purchased from Gasin (Maia, Portugal).

2.2. Standards and reagents for musk fragrances

The six polycyclic musk fragrances: 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5*H*)-indanone (DPMI, cashmeran), 4-acetyl-1,1-dimethyl-6-*tert*-butylindane (ADBI, celestolide), 6-acetyl-1,1,2,3,3,5-hexamethylindane (AHMI, phantolide), 5-acetyl-1,1,2,6-tetramethyl-3-isopropylindane (ATII, traseolide), 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-*(g)*-2-benzopyran (HHCB, galaxolide) and 7-acetyl-1,1,3,4,4,6-hexamethyl-1,2,3,4-tetrahydronaphthalene (AHTN, tonalide) were supplied by Promochem Iberia (Barcelona, Spain). 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-*(g)*-2-benzopyran-1-one (HHCB-lactone, galaxolidone) was provided by International Flavors & Fragrances Inc. (Barcelona, Spain). The nitro musk fragrances 2,4,6-trinitro-1,3-dimethyl-5-*tert*-butylbenzene (MX, musk xylene) and 1,1,3,3,5-pentamethyl-4,6-dinitroindane (MM, musk moskene) were purchased as 100 μg/mL individual solutions in

acetonitrile from Sigma-Aldrich and Riedel de Haën (Seelze, Germany), respectively. The standard 4-aceto-3,5-dimethyl-2,6-dinitro-tertbutylbenzene (MK, musk ketone) was provided by Fluka while the internal standard (IS) d_{15}-musk xylene (MXd_{15}) came as a 100 μg/mL solution in acetone from Symta (Madrid, Spain).

Individual standard solutions of the synthetic musk fragrances were prepared in acetone at concentrations of 4000 μg/mL for polycyclic musks and 1000 μg/mL for MK and HHCB-lactone. A working mixture solution of 100 μg/mL was prepared in ethyl acetate except for MX, MM and MXd_{15} which were supplied directly at a concentration of 100 μg/mL in acetonitrile and used as received. Acetone and ethyl acetate were GC grade with purity > 99.9% from Prolabo (VWR, Llinars del Vallès, Barcelona, Spain).

The extraction solvent acetonitrile was purchased from Prolabo and the extraction salt packet for QuEChERS was purchased from Scharlab. Florisil was provided by Sigma-Aldrich. Ultrapure water was obtained using an ultrapure water purification system from Veolia Water (Sant Cugat del Vallés, Barcelona, Spain). Helium gas with a purity of 99.999% was used for the chromatographic analysis (Carburos Metálicos, Tarragona, Spain).

2.3. Sampling

In order to assess the levels of contaminants of emerging concern in the most relevant commercially available seafood species, two sampling seasons were undertaken in April–June 2014 and September–January 2015. The species selection was based on the following criteria: a) being among the most common species consumed in Europe; b) species that potentially accumulate high concentrations of contaminants; c) species with wide geographic distribution; d) species from different habitats; e) species from extra-EU origin or from EU production; and f) species from wild or farmed origin.

A total of 62 samples of seafood species consumed in Europe were collected including 6 species from the Mediterranean Sea (FAO Fishing Area 37) and the North Sea (FAO Fishing Area 27 IV), 1 species from the North-East Atlantic Ocean (FAO Fishing Area 27), Atlantic Southeast (FAO Fishing Area 47) and Atlantic Southwest (FAO Fishing Area 41), 3 samples imported from the Pacific Ocean and one from Asia and 3 canned seafood. The species were crab (3), cod (3), hake (4), mackerel (11), monkfish (4), mussel (11), Nile perch (1), octopus (2), plaice/sole (10), salmon (3), sardine (1), seabream (2), shrimp (1) and tuna (6).

In each sampling site, at least 25 specimens per species were sampled and pooled, reaching a minimum of 800 g of edible tissue. For mussels all edible content was sampled, fish muscle tissue was collected without skin from the thickest part of the fillets, and for shrimp abdomen muscle tissue was used without the exoskeleton. The fat layer of fish was not removed with the skin. All species were of uniform average commercial sizes and weights. Fifty-five samples were analysed to determine the presence of eleven UV-Fs, while forty-five samples were analysed to determine the presence of ten polycyclic and nitromusks (see Table S1 for further details). All samples were homogenized and freeze dried.

2.4. Sample extraction

2.4.1. Extraction of UV-filters

Sample preparation was based on a previously described methodology (Cunha et al., 2015a) with some modifications: weigh 2 g of freeze-dried sample into a 40 mL amber glass vial tube; add 100 μL of BPd_{10} (IS, 2000 μg/L); add 7 mL of deionized water and 10 mL of MeCN; vortex and place on a wrist action shaker for 10 min; add 4 g of anhydrous $MgSO_4$ and 1 g of NaCl; shake vigorously by hand for 5 min; centrifuge the tube at 4736*g* for 3 min; transfer 3 mL of the MeCN extract to a 20 mL vial tube and add 7 mL of deionized water; add 4 mL of hexane:*tert*-butylmethylether (3:1 v/v); shake gently by hand for 30 s; centrifuge at 4736*g* for 1 min to remove the organic phase; add 4 mL of hexane:benzene (3:1 v/v); combine the organic phases and add 200 mg of Z-Sep+; vortex for 1 min; centrifuge at 4736*g* for 3 min; evaporate the top layer to dryness using a gentle nitrogen stream at room temperature; finally, silylate the dry extracts with 50 μL of BSTFA + 1% TMCS during 5 min in a household microwave (600 W); the derivizated extracted was placed in a glass insert and 1 μL of the extract was injected to be analysed by GC-MS/MS.

2.4.2. Extraction of musk fragrances

Musks present in the different matrices were extracted using the following procedure based on QuEChERS extraction, which was described in more detail by Trabalon et al. (2015). In summary: 0.5 g of freeze-dried sample, 10 mL of ultrapure water and 10 mL of acetonitrile were mixed. Then, an extraction salt packet of QuEChERS according to the Standard Method EN15662 was added and centrifuged. The acetonitrile layer (supernatant) was transferred to a 15 mL centrifuge tube containing 2 *g* of florisil for the dSPE clean-up. The tube was centrifuged and the supernatant was removed and further evaporated under a gentle stream of nitrogen to a final volume of approximately 1 mL. The internal standard (MXd_{15}) was added and the extract was reconstituted to 2 mL with ethyl acetate. Extracts were filtered through a 0.22 mm PTFE syringe filter and analysed by GC-MS/MS.

2.5. GC-MS conditions

2.5.1. Determination of UV-filters by GC-MS/MS

The GC-MS/MS equipment consisted of an Agilent 7890B chromatograph (Agilent Technologies, Palo Alto, CA, USA) equipped with 7693 autosampler (Agilent Technologies) and coupled to a triple quadrupole mass spectrometer Agilent 7000 C MS (Agilent Technologies). GC separation was performed on a DB-5MS capillary column (30 m × 0.25 mm I.D., 0.25 μm film thickness; J&W, USA), which was maintained initially at 95 °C for 1 min, increased at 40 °C/min to 180 °C, then increased at 5 °C/min to 230 °C, and finally increased to 290 °C at 25 °C/min and held for 4.47 min. The injector was maintained at 250 °C and 1 μL of extract was injected in splitless mode (purge time of 1 min and purge flow of 64 mL/min). The temperatures of the transfer line, ion source, 1st and 2nd quadrupole were 250, 230, 150 and 150 °C, respectively. The collision cell gases were nitrogen (1.5 mL/min) and helium (2.25 mL/min). The triple quadrupole MS was operated in multiple reaction monitoring (MRM) mode detecting two transitions per analyte (Table S2). Dwell times were adjusted to 50 ms to achieve 5 cycles/s (Hz) per time window. MassHunter quantitative analysis software (v. B.02.03) (Agilent Technologies) was used for the data processing.

2.5.2. Determination of musk fragrances by GC-MS/MS

Following the method described by Trabalon et al. (2015), the GC-IT-MS/MS analyses were performed using a Varian ion trap GC-MS system (Varian, Walnut Creek, CA, USA), equipped with a 3800 gas chromatograph, a 4000 ion trap mass detector, a 1079 programmable vaporising temperature injector and a CombiPal autosampler (CTC Analytics, Zwigen, Switzerland). The chromatographic separation was carried out on a ZB-50 analytical column (30 m × 0.25 mm i.d. × 0.25 μm film thickness) from Micron Phenomenex. The oven temperature program was as follows: 70 °C hold for 3.5 min, 50 °C/min to 200 °C, then 5 °C/min to 240 °C and finally 20 °C/min to 290 °C (hold 3.4 min). Helium was used as carrier and collision gas at a constant flow rate of 1 mL/min. During the injection of the 10 μL of the QuEChERS extract, the 1079 injector operated in large volume injection (LVI) mode and a 2 mm i.d. insert liner packed with glass wool (Varian) was used. During injection in split mode at a rate of 50 mL/min the 1079 injector temperature was set at 70 °C. The ethyl acetate was purged out with a vent flow of 100 mL/min within 0.5 min (vent time). The splitless mode was then programed for 2.5 min, while temperature was

increased at 100 °C/min to 300 °C for 5 min. Transfer line, manifold and trap temperatures were 280 °C, 50 °C and 200 °C, respectively. The mass spectrometer was operated in the electron ionisation (EI) mode (70 eV) with a filament-multiplier delay of 3 min to prevent instrument damage. For quantitative analysis of the target fragrances, MS/MS mode was applied. Retention times, as well as optimal MS parameters of the target fragrances are summarized in Table S3.

2.6. Risk assessment

2.6.1. Concentration and consumption data

A risk assessment was performed for a selection of contaminants for which the highest concentration levels were measured within this study. With regards to UV-Fs, a database file for BP1, BP3, EHS, 4-MBC, EHMC, and IMC concentrations was compiled based on the data obtained and presented in this study. For musks, a database file for HHCB and AHTN concentrations was compiled combining the data obtained and presented in this study with additional data from a peer-reviewed publication (Foltz et al., 2014), that reports results of samples outside Europe which was included to have higher data availability.

Data for UV-Fs and musks included raw samples of species of commercial importance in Europe. To obtain an estimation of the contaminant intake based on the overall seafood diet, missing concentration data for frequently consumed species were completed by a mean value based on the fish group or, when applicable, based on crustaceans and shellfish groups.

In 2013, ECsafeSEAFOOD performed a consumer survey in five European countries: Belgium, Ireland, Italy, Portugal and Spain (Jacobs et al., 2015). These countries were selected to cover western, northern and southern Europe, covering a heterogeneous population in terms of seafood consumption and habits. The samples were nationally representative regarding gender, region and age within the range of 18–75 years. The consumption frequency of 32 seafood species, selected based on the consumption patterns in the five countries and on the susceptibility of species to contain relevant concentrations of environmental contaminants, was inquired using self-reported items. For each country, at least 85% of the total seafood diet (based on the median) was represented by the 15 most consumed species. Therefore, only the 15 most consumed species per country were considered for the exposure assessment. The body weight (bw) of participants was also requested in the survey.

2.6.2. Exposure assessment

For each country, a distribution was fitted to the consumption data of each species and to the body weight data using @RISK version 6 (Palisade Corporation, US). The seafood consumption distributions were divided by the body weight distributions, resulting in a consumption dataset (expressed in kg/(kg bw)/day) for each country. More detailed information on the methodology and on the results regarding the consumption data and body weight data is described by Jacobs et al. (2017).

To estimate the exposure to selected contaminants through the seafood diet, the consumption data of species were combined with the concentration data of contaminants in samples according to the following formula:

$$Y_{i,c} = \sum_{v=1}^{v=15} C_{c,v} \times X_{i,v}$$

$C_{c,v}$ = concentration of contaminant c in seafood species v [μg/kg ww]
$X_{i,v}$ = consumption of seafood species v by individual i [kg/(kg bw)/day]
$Y_{i,c}$ = exposure to contaminant c for individual i [μg/(kg bw)/day]

This model combines species-specific seafood consumption data with contaminant concentration data. A probabilistic approach was applied for the consumption and the body weight data in order to take into account the variability and uncertainty for these parameters. Detailed information on the concentration of contaminants in seafood species expressed in wet weight (ww) was published in the report D2.4 (http://www.ecsafeseafood.eu/) (ecsafeseafood, 2017). When considering the concentration data, only for HHCB it was possible to fit a distribution to the concentration data for one species only, namely mackerel. For the concentration data of the other species for the selected contaminants, a deterministic approach (which is less informative compared to a probabilistic approach) was used due to low data availability or because it was not possible to reach a good model fit.

The first order Monte Carlo simulations were performed considering 100,000 iterations to estimate contaminant intakes through the seafood diet for the lower and upper bound scenarios. Non-detected (< LOD) were considered zero and non-quantified (< LOQ) were considered as LOD or LOQ for lower bound (LB) or upper bound (UB) scenario, respectively. More detailed information on the methodology is described by Jacobs et al. (2017).

2.6.3. Risk assessment

To evaluate the risk for the considered population groups, no established health based guidance value is available for the selected contaminants. However, NOAEL (No Observed Adverse Effect Level) values are available for these contaminants (Table 1). Based on these NOAEL values a TWI_calc (calculated Tolerable Weekly Intake) value was determined by applying an uncertainty factor of 100 (to account for species differences and human variability). When the exposure exceeds the TWI, recommendations for risk reduction (i.e. risk management) and related communication (i.e. risk communication) can be set forth. The determination of priorities can be based on the extent to which the TWI is exceeded (Gillespie et al., 2011).

Table 1
Hazard identification and NOAEL values for the selected musks and UV-Fs.

Group	Compound	Hazard identification	NOAEL value (mg/kg bw/day)	Ref.
Musks	HHCB	Developmental toxicity/teratogenicity	50–150	ECHA (15/03/2016)
	AHTN	Haematological effects (based on 90-day repeated dose study with rats)	5	ECHA (2008b)
UV-Fs	BP1	Probably carcinogenic (Group 2B), reproduction toxicity rats (oral, subcutaneous and intraperitoneal)	100	ECHA (15/03/2016)
	BP3	Probably carcinogenic (Group 2B), maternal and prenatal developmental toxicity (rats, oral)	200	ECHA (15/03/2016)
	EHS	Reproduction toxicity rats (oral)	25	ECHA (15/03/2016)
	4-MBC	Repeated dose toxicity rats (oral), thyroid effects	25	EC (2008)
	EHMC	Subchronic oral toxicity rat, effects on liver, kidney	450	EC (1991)
	IMC	Fertility and reproductive performance, for systemic parental and developmental toxicity (rat, oral)	450	ECHA (15/03/2016)

3. Results and discussion

3.1. Analytical performance of UV-filters

Performance characteristics of the method were established through the following parameters: matrix effect, linearity, recovery, repeatability, limits of quantification (LOQs) and detection (LODs).

Matrix effect was evaluated by comparing the calibration curves obtained from spiked blank extracted mackerel with that obtained by the use of standard solutions. It was noted that the slope ratios matrix/solvent for each compound were significant different (data not shown). Therefore, to compensate the suppression effect observed, matrix matched calibration was used for quantification purposes. Linearity was evaluated by spiking extracted mackerel samples with seven different concentrations of UV-filters ranging from 5 to 200 μg/kg d.w. for HS, BP3 and EHMC; from 10 to 400 μg/kg d.w. for EHS, IMC, 4-MBC, BP1 and OC; from 12 to 400 μg/kg d.w. for DHMB, EPABA, and from 40 to 800 μg/kg d.w. for DBENZO. Benzophenone-D_{10} was used as IS due to its similar physico-chemical properties with some UV-filters. Determination coefficient (R^2) values were higher than 0.996 for all compounds.

Recovery studies were carried out at two concentration levels (25 and 100 μg/kg), performing 6 replicates at each level (Table 2). The recovery values ranged from 57% to 108% (25 μg/kg) and 61–107% (100 μg/kg). Although for some compounds, these recoveries were not close to 100%, most of them achieved an acceptable range (70–120%) according to the guidelines established by the EU (SANTE/11945/2015, 2015).

Repeatability was evaluated at the two concentration levels of the recovery studies, performing six replicates at each level. Repeatability values (expressed as percentage of relative standard deviation, RSD%) were always lower than 20%.

Quantification and detection limits were estimated as the lowest concentration giving a response of ten and three times the average of the baseline noise, respectively. LOD ranged between 0.5 and 7 μg/kg whereas LOQ ranged between 1 and 20 μg/kg. Both, LOD and LOQ obtained were better than those previously obtained using QuEChERS followed by dispersive liquid–liquid microextraction (DLLME), with LOD and LOQ lower than 23 μg/kg and 100 μg/kg, respectively (11). In any case, results were similar to those reported in literature for a similar matrix (Bachelot et al., 2012; Gago-Ferrero et al., 2013).

3.2. UV-filters in seafood

The average concentrations of the eleven UV-Fs compounds, expressed as dry weight d.w., range, and frequency of detection in seafood samples are presented in Table 3; all the samples were analysed in triplicate.

No detectable contamination levels were observed for EPABA and DBENZO. Among all UV-Fs found, 4-MBC presented the highest frequency of detection (near of 100%), although below the LOQ in most samples. The maximum level of 4-MBC (56.2 μg/kg d.w.) was found in wild mussels. Overall, the concentrations of this compound are greater than those reported in literature, with detected levels ranging from 0.2 to 2.3 μg/kg d.w. in wild fish from China (Peng et al., 2015) or undetected in seafood from European hotspots (Cunha et al., 2015a) or commercialized in Spain (Gago-Ferrero et al., 2013).

Benzophenones, namely BP3 and BP1, were also frequently detected in seafood samples analysed, with concentrations ranging from < LOQ to 98.7 μg/kg d.w. and from < LOQ to 98.9 μg/kg d.w., respectively. BP3 levels herein reported are in agreement with Emnet et al. (2015) which reported levels ranging from < 6.6 to 108 μg/kg d.w and by Langford et al. (2015) who found levels ranging from < 5 to 182 μg/kg d.w. Lower BP3 levels than those found in this study were described by Peng et al. (2015) and Gago-Ferrero et al. (2013) with levels ranging from 0.106 to 1.52 μg/kg d.w and from 16.5 to 24.3 μg/kg d.w, respectively. Concerning BP1, the levels were higher in this study than those found by Tsai et al., ranging from 0.7 to 3.6 μg/kg d.w. (Tsai et al., 2014).

The maximum concentration value of UV-Fs was found for OC with 103.3 μg/kg d.w. in a farmed seabream sample. This compound is highly lipophilic with log K_{ow} = 6.9, therefore with a high tendency to bioaccumulate. Higher levels of OC than those herein reported were found by Groz et al. (2014) in mussel samples collected in Portugal, with a maximum level of 3992 μg/kg d.w.

Salicylate derivatives, namely HS and EHS were found in less than 50% of analysed samples, which is in agreement with literature (Tsai et al., 2014). The highest levels of HS were found in wild tuna (58.5 μg/kg d.w), while wild mussels presented the maximum level of EHS (72.1 μg/kg d.w).

Cinnamates derivatives IMC and EHMC were observed for a wide range of samples, with levels ranging between < LOQ and 74.4 μg/kg d.w., and between 2.5 and 66.7 μg/kg d.w, respectively. These levels are similar to those reported in literature. Langford et al. (2015) found EHMC levels between < 20 and 36.9 μg/kg d.w., Cunha et al. (2015a) reported levels < 20 μg/kg and Gago-Ferrero et al. (2013) found levels between < 16.7 and 241.7 μg/kg d.w.

Farmed seabream showed the highest average total concentration of UV-Fs (196 μg/kg d.w.), while wild octopus, plaice/sole and crab were less contaminated, all presenting levels < LOQ. In general, the levels reported for the species analysed are in agreement with data previously reported in literature (Cunha et al., 2015a; Langford et al., 2015).

Table 2
Average of recovery (%) and repeatability (%RSD), for the UV-filters in study, obtained in fillet mackerel spiked samples using QuEChERS followed by LLE and GC–MS/MS analysis (n = 6). (–) not determined.

Target compounds	Determination coefficient R^2	25 μg/kg spiking level		100 μg/kg spiking level		LOQ μg/kg	LOD μg/kg
		%recovery	repeatability %RSD	%recovery	repeatability %RSD		
EHS	0.9965	70	18	82	14	5	2
HMS	0.9980	108	17	92	18	5	2
IMC	0.9994	68	20	77	17	5	1
4-MBC	0.9987	57	7	88	15	5	2
BP3	0.9955	77	5	72	17	2	0.5
BP1	0.9992	67	12	78	11	5	3
DHMB	0.9963	64	10	68	11	12	7
EPABA	0.9984	61	9	61	7	5	2
EHMC	0.9989	90	14	107	10	1	0.5
OC	0.9983	79	18	77	17	10	3
DBENZO	0.9970	–	–	82	14	20	7

Table 3
Levels of UV-Fs in seafood.

Origin	Common class	Species		EHS (μg/kg)	HS (μg/kg)	4-MBC (μg/kg)	BP3 (μg/kg)	BP1 (μg/kg)	DHMB (μg/kg)	EHMC (μg/kg)	IMC(μg/kg)	OC (μg/kg)	DBENZO (μg/kg)	EPABA (μg/kg)
Industrial	Canned	Mackerel (n = 2)	Average	24.1	2.6	11.3	1.3	23.4	3.0	1.3	24.5	9.2	n.d.	n.d.
			Range	n.d. – 48.1	n.d. – 5.1	5.0–17.5	n.d. – 5.0	5.0–41.8	n.d. – 6.0	n.d. – 2.5	5.0–43.9	n.d. – 18.5	n.d.	n.d.
			% Frequence	50	50	100	50	100	50	50	100	50	0	0
		Sardine				14.09	55.72						n.d.	n.d.
		Tuna (n = 2)	Average	6.9	5.2	5.0	13.8	22.0	3.0	32.7	2.5	28.8	n.d.	n.d.
			Range	n.d. – 13.8	n.d. – 10.4	5,0–5,0	n.d. – 27.6	5.0–39	n.d. – 6.0	n.d. – 65.4	n.d. – 5	n.d. – 57.6	n.d.	n.d.
			% Frequence	50	50	100	50	100	50	50	50	50	0	0
Aquaculture	Crustacean	Shrimp		37.1	n.d.	43.9	14.7	23.8	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Fish	Pangasius		13.6	n.d.	5.0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
		Salmon (n = 3)	Average	7.7	5.1	5.0	0.8	1.7	2.0	0.8	1.7	1.7	n.d.	n.d.
			Range	n.d. – 23	n.d. – 15.3	5,0–5,0	n.d. – 2,5	n.d. – 5.0	n.d. – 6.0	n.d. – 2.5	n.d. – 5	n.d. – 5	n.d.	n.d.
			% Frequence	33	33	100	33	33	33	33	33	33	0	0
		Seabream (n = 2)	Average	21.4	16.7	2.5	2.5	49.4	n.d.	1.3	35.9	66.6	n.d.	n.d.
			Range	n.d. – 42.9	n.d. – 33.4	n.d. – 8	n.d. – 5.0	n.d. – 98.9		n.d. – 2.5	5–66.7	30–103.3	n.d.	n.d.
			% Frequence	50	50	50	50	50	0	50	100	100	0	0
Lake	Fish	Perch		n.d.	n.d.	5.0	32.3	17.2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
Sea	Bivalves	Mussels (n = 11)	Average	14.7	3.7	12.7	9.1	25.5	3.3	4.5	6.1	10.7	n.d.	n.d.
			Range	n.d. – 72.1	n.d. – 19.1	n.d. – 56.2	n.d. – 85.5	n.d. – 94.2	n.d. – 6.0	n.d. – 34.2	n.d. – 37.3	n.d. – 56.0	n.d.	n.d.
			% Frequence	73	55	91	64	82	55	64	64	64	0	0
	Cephalopod	Octopus (n = 2)	Average	n.d.	n.d.	5.0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			Range			5,0–5,0							n.d.	n.d.
			% Frequence	0	0	100	0	0	0	0	0	0	0	0
	Crustacean	Crab (n = 3)	Average	n.d.	n.d.	5.0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			Range			5,0–5,0							n.d.	n.d.
			% Frequence	0	0	100	0	0	0	0	0	0	0	0
	Fish	Cod (n = 3)	Average	8.9	0.8	5.0	n.d.	n.d.	n.d.	n.d.	n.d.	13.0	n.d.	n.d.
			Range	n.d. – 26.7	n.d. – 2.5	5,0–5,0						n.d. – 39.1	n.d.	n.d.
			% Frequence	33	33	100	0	0	0	0	0	33	0	0
		Mackerel (n = 9)	Average	9.0	1.3	5.6	15.7	2.2	2.7	4.3	8.4	6.5	n.d.	n.d.
			Range	n.d. – 49.1	n.d. – 6.4	n.d. – 15.7	n.d. – 82.2	n.d. – 5.0	n.d. – 6.0	n.d. – 28.7	n.d. – 55.5	n.d. – 43.2	n.d.	n.d.
			% Frequence	56	33	89	78	44	44	56	56	44	0	0
		Monkfish (n = 4)	Average	3.8	22.1	8.9	40.6	11.5	27.1	28.3	2.5	7.8	n.d.	n.d.
			Range	n.d. – 15.3	n.d. – 54	5.0–20.4	5.0–98.7	n.d. – 36.1	n.d. – 90.7	2.5–74.4	n.d. – 5.0	n.d. – 19.3	n.d.	n.d.
			% Frequence	25	100	100	100	75	50	100	50	50	0	0
		Plaice/Sole (n = 6)	Average	n.d.	n.d.	5.0	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
			Range			5,0–5,0							n.d.	n.d.
			% Frequence	0.00	0.00	100.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0
		Tuna (n = 4)	Average	2.5	20.2	2.5	1.3	15.9	1.5	1.3	2.5	2.5	n.d.	n.d.
			Range	n.d. – 5.0	n.d. – 58.5	n.d. – 5,0	n.d. – 2,5	5.0–34.2	n.d. – 6.0	n.d. – 2.5	n.d. – 5.0	n.d. – 5.0	n.d.	n.d.
			% Frequence	50	50	50	50	100	25	50	50	50	0	0

* LOQ values were considered as half of LOD. (n.d. – not detected).

Table 4
Levels (μg/kg d.w.) of musks in seafood.

Origin	Class	Species		Polycyclic musks							ΣPolycyclic musk (dw)	Nitro musks		
				DPMI (μg/kg)	ADBI (μg/kg)	AHMI (μg/kg)	ATII (μg/kg)	HHCB (μg/kg)	AHTN (μg/kg)	HHCB-Lactone (μg/kg)		MX (μg/kg)	MM (μg/kg)	MK (μg/kg)
Industrial	Fish	Mackerel (n = 1)		5.0	n.d.	n.d.	n.d.	2.5	2.5	n.d.	**10.0**	n.d	n.d	n.d
Aquaculture	Crustaceans	Shrimp (n = 1)		n.d.	n.d.	n.d.	10.9	25.5	7.1	58.1	**101.7**	n.d.	n.d.	n.d.
	Fish	Pangasius (n = 1)		5.0	n.d.	n.d.	n.d.	27.2	2.5	75.3	**109.9**	n.d.	n.d.	n.d.
		Seabream (n = 1)		n.d.	n.d.	n.d.	n.d.	11.6	2.5	n.d.	**14.1**	n.d.	n.d.	n.d.
		Salmon (n = 2)	Average	n.d.	n.d.	n.d.	n.d.	20.3	3.7	n.d.	**24.0**	n.d.	n.d.	n.d.
			Range					17.8–23.2	2.5–5.5					
			% Frequency	0	0	0	0	100	100	0		0	0	0
Lake	Fish	Perch (n = 1)		n.d.	n.d.	n.d.	n.d.	22.4	7.2	n.d	**29.6**	n.d.	n.d.	n.d.
Sea	Bivalves	Mussels (n = 7)	Average	4.27	1.43	1.43	n.d.	22.30	n.d.	n.d.	**29.4**	n.d.	n.d.	n.d.
			Range	5–14.9	n.d. – 5	n.d. – 5		n.d. – 109.8						
			% Frequency	57	29	29	0	57	0	0		0	0	0
	Cephalopoda	Octopus (n = 2)	Average	2.5	n.d.	n.d.	n.d.	52.4	9.0	52.1	**116.0**	n.d.	n.d.	n.d.
			Range	n.d. – 5				41.5–66.2	6.6–12.2	36.5–74.5				
			% Frequency	50	0	0	0	100	100	100		0	0	0
	Crustaceans	Crab (n = 3)	Average	n.d.	n.d.	n.d.	13.20	19.02	8.94	n.d.	**41.2**	n.d.	n.d.	n.d.
			Range				n.d. – 39.6	n.d. – 28.8	n.d. – 14.1					
			% Frequency	0	0	0	33	67	67	0		0	0	0
	Fish	Cod (n = 2)	Average	n.d.	n.d.	n.d.	3.6	16.9	7.0	8.2	**35.6**	n.d.	n.d.	n.d.
			Range				2.5–4.6	15.3–18.5	6.3–7.6	n.d. – 16.3				
			% Frequency	0	0	0	50	100	100	50		0	0	0
		Hake (n = 4)	Average	n.d.	n.d.	n.d.	6.4	19.1	6.1	9.3	**41.0**	n.d.	n.d.	n.d.
			Range				n.d. – 15.5	14.7–29.3	5.7–6.6	n.d. – 37.3				
			% Frequency	0	0	0	50	100	100	25		0	0	0
		Mackerel (n = 6)	Average	3.3	n.d.	n.d.	n.d.	23.7	4.5	124.5	**156.0**	n.d.	n.d.	n.d.
			Range	n.d. – 5				2.5–90.9	n.d. – 9.3	n.d. – 228.5				
			% Frequency	67	0	0	0	100	83	67		0	0	0
		Monkfish (n = 2)	Average	6.1	1.3	n.d	5.0	38.0	7.9	55.8	**114.2**	n.d.	n.d.	n.d.
			Range	4.7–7.6	n.d. – 2.5		4.5–5.6	37.3–38.7	7.5–8.4	47.3–64.2				
			% Frequency	100	50	0	100	100	100	100		0	0	0
		Plaice (or Sole) (n = 10)	Average	1.2	n.d.	n.d.	0.3	58.8	6.4	8.7	**75.3**	n.d.	n.d.	n.d.
			Range	n.d. – 9.3			n.d. – 2.5	12.3–414.4	5.9–7.3	n.d. – 48.7				
			% Frequency	22	0	0	10	100	100	20		0	0	0
		Tuna (n = 2)	Average	5.0	n.d.	n.d.	n.d.	12.8	2.5	56.6	**76.9**	n.d.	n.d.	n.d.
			Range	5.0–5.5				9.0–16.7	2.5–2.5	55.5–57.6				
			% Frequency	100	0	0	0	100	100	100		0	0	0

* LOQ values were considered as half of LOQ. (n.d. – not detected).

3.3. Analytical performance of musk

The results have shown good linear response with coefficient of determination (R^2) > 0.995 for all the analysed musks (Trabalon et al., 2015)). Limits of detection (LOD) and limits of quantification (LOQ) were 4 and 10 μg/kg (DPMI), 4 and 5 μg/kg (ADBI and AHMI), 2 and 5 μg/kg (ATII), 1 and 5 μg/kg (HHCB and AHTN), 10 and 20 μg/kg (MX, MM, and MK), and 5 and 10 μg/kg (HHCB-lactone), respectively (See Supplementary Table S3).

3.4. Musks in seafood

The range and average concentrations of ten polycyclic and nitromusks, expressed as dry weight (d.w.), and frequency of detection in seafood species are gathered in Table 4; all the samples were analysed in triplicate.

As expected, none of the nitromusks (MX, MM and MK) was detected in any sample, since the current regulations limit or prohibit their use in cosmetics (98/62/EEC, 1998, 1223/2009/EC, 2009). These results are in agreement with previous results in the screening of samples collected in several European hotspots (Cunha et al., 2015a), as well as those reported in recent literature for seafood (Trabalon et al., 2015; Vallecillos et al., 2015), although contrasting with literature published before the establishment of policy regulations (Gatermann et al., 1999).

All polycyclic musks, which are presently the musks that dominate the global market (Homem et al., 2016), were detected, among which HHCB and AHTN with a frequency close to 100%. This is in accordance with the concerns that led them to be included in Environmental Protection Agencies high production list (EPA, 2003). HHCB showed the highest concentrations among all polycyclic musks, reaching 414.4 μg/kg d.w. in plaice/sole, followed by 109.8 μg/kg d.w. in mussels. AHTN showed lower concentrations (up to 14.1 μg/kg d.w. in crabs) than HHCB, probably due to its recent prohibition in cosmetics (2008/105/EC, 2013). HHCB-lactone, which is the main metabolite of HHCB, was also detected in most species, although at lower frequency, at concentrations up to 228.5 μg/kg d.w. in wild mackerel. Despite overall results are in agreement with those reported in literature, some

differences were found. For example, Trabalon et al. (2015) reported similar concentrations of HHCB and HHCB-lactone (from < LOD to 367.3 μg/kg d.w.), but higher concentrations of AHTN (from < LOQ to 31.3 μg/kg d.w.) in sardine. In contrast, Nakata et al. (2012) and Mottaleb et al. (2009) reported higher maximum concentrations for HHCB (3300 μg/kg d.w.) and AHTN (860 μg/kg d.w.) than those of the present study.

DPMI and ATII were detected in two of the assayed species at concentrations ranging from < LOQ to 14.9 μg/kg d.w. in mussels and from < LOQ to 39.6 μg/kg d.w. in crab, respectively. Despite DPMI concentrations are similar to those reported by Trabalon et al. (2015) for several species (hake, sole, cod, shrimp, salmon, mackerel, sardine and mussels) commercialized in Tarragona (Spain), they are slightly lower than those found by Vallecillos et al. (2015) for fish and mussels from Tarragona coast, which ranged between 13 and 34 μg/kg d.w. In contrast, ATII concentrations were slightly higher than those previously reported (Cunha et al., 2015a; Trabalon et al., 2015), whose maximum concentration was 6.1 μg/kg d.w. in hake.

Regarding ADBI and AHMI, they were the polycyclic musks less frequently detected. Only mussels revealed the presence of both compounds at concentrations < LOQ, while monkfish showed the presence of ADBI also at concentration < LOQ, which is in agreement with previous findings (Cunha et al., 2015a; Trabalon et al., 2015).

Wild mackerel showed the highest average total polycyclic musk concentrations (156 μg/kg d.w.), followed by octopus, monkfish, pangasius and shrimp. Trabalon et al. (2015) also reported mackerel and sardine as the most contaminated species by polycyclic musks. In contrast, Sapozhnikova et al. (2010) reported shrimps as being the species attaining higher levels. In this study, monkfish showed the highest number of polycyclic musks (6 out of the 7 studied), whereas canned mackerel and seabream were the species with less number of polycyclic musks.

3.5. UV-filters and musks geographic distribution

The spatial distribution of the UV-Fs and musks is presented in Fig. 1. For each geographic area (Mediterranean, n = 17; North Sea n = 4; North-East Atlantic Ocean, n = 23; and Pacific Ocean n = 4) the UV-Fs total average concentrations were 95.7, 2.5, 146.9 and 36.9 μg/kg d.w., respectively. From the data shown in Fig. 1**A,** it is clear that North-East Atlantic Ocean presented the highest levels of UV-Fs, whereas lower magnitude levels were verified in the other regions. Notwithstanding, most published studies only investigated the presence of UV-Fs in few species and locally, with the total UV-Fs levels in the μg/kg range reported here being similar to those reported in literature for Europe (Gago-Ferrero et al., 2013; Groz et al., 2014; Langford et al., 2015), Asia (Alonso et al., 2015; Tsai et al., 2014) and Oceania (Emnet et al., 2015).

Regarding musks, the overall average values found in each geographic area were 105.8, 41, 99.3, 54.4 and 114.2 μg/kg d.w. for Asia (n = 2), Atlantic southwest (n = 4), Mediterranean (n = 15), North Sea (n = 19) and North-East Atlantic Ocean (n = 2), respectively (Fig. 1**B**). Although North-East Atlantic Ocean also presented the highest levels of total musks, Asia presented similar but slightly lower levels. Moreover, Mediterranean and North Sea presented some less frequent values higher than those corresponding to North-East Atlantic Ocean and Asia. In contrast to UV-Fs, only two musks, HHCB and HHCB-lactone, were the main contributors to the total musk levels. The concentration ratio of HHCB and its main metabolite, HHCB-lactone, varied widely, suggesting differences in biotransformation among species, which is in agreement with other studies (Frewer et al., 2016). Although most of the published studies, as in the case of UV-Fs, focused on the presence of musks in few species from local areas, few studies have focused on their geographical distribution (Nakata et al., 2012) However, number of species and geographical areas here studied are limited.

3.6. Exposure and risk assessment

The possible health risk from exposure to the selected UV-Fs and musks in seafood was assessed using the concentrations of raw samples and based on the overall seafood consumption pattern of adults from Belgium, Ireland, Italy, Portugal and Spain. In general, adults from Portugal and Spain (southern EU countries) showed the highest exposure to these contaminants through their seafood diet, which is in line with their overall higher seafood consumption frequency as compared to the other three countries in the study. The mean and P99 (high seafood consumers) exposure for the UB scenario for the country with the highest exposure are provided in Table 5.

Based on the performed risk assessment it is unlikely that a potential health risk exists when considering these data and the results obtained, as the exposure is substantially lower than the calculated TWI value.

4. Conclusions

This assessment study on the occurrence of PCPs in seafood commercialized in EU represents the largest EU survey on PCPs ever performed. It provides a comprehensive data in PCPs compounds including UV-Fs and musks assessed usually until now on a regional basis. The most relevant UV-Fs found in the fourteen seafood species analysed was 4-MBC with the highest frequency of occurrence close to 100% and OC with the highest average concentration (103.3 μg/kg d.w.). Regarding musks, none of the nitromusks (MX, MM and MK) were detected in seafood samples. In contrast, all polycyclic musks were detected,

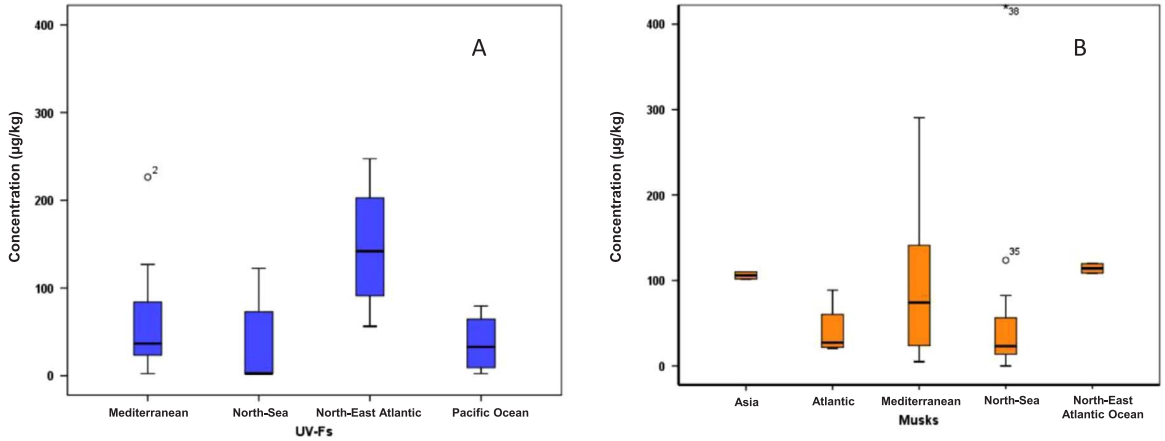

Fig. 1. Box plot of total of UV-Fs (A) and musks (B) from the different geographic region (μg/kg).

Table 5
Results of the exposure assessment for musks and UV-Fs for the country with the highest exposure.

Group	Compound	TWI calculated (μg/kg bw/week)	Mean exposure UB (μg/kg bw/week)	P99 exposure UB (μg/kg bw/week)
Musks	HHCB	3500	0.024	0.052
	AHTN	350	0.013	0.028
UV-Fs	BP1	7000	0.024	0.063
	BP3	14,000	0.016	0.052
	EHS	1750	0.019	0.042
	4-MBC	1750	0.015	0.034
	EHMC	31,500	0.018	0.064
	IMC	31,500	0.015	0.036

although only HHCB and AHTN revealed a frequency of occurrence close to 100%. HHCB presented the highest concentrations, with the highest one in plaice/sole (414.4 μg/kg d.w.), followed by mussels (109.8 μg/kg d.w.). Among seafood species analysed, farmed seabream and wild mackerel showed the highest average concentration of UV-Fs and polycyclic musks, respectively.

Although most PCPs are present in assayed samples, the exposure levels estimated based on the concentration levels for UV-Fs and musks in raw samples were far below the estimated toxicological reference values. These results and conclusions are based on the available data and have to be interpreted with caution as uncertainties and limitations are involved (for details see Jacobs et al., 2017). Especially, the low data availability and the low information available on the toxicology of PCPs are important limitations with regards to the risk assessment for UV-Fs and musks. Moreover, humans can be exposed to these compounds via other routes, such as dermal contact as well as consumption of other foods than seafood. These other exposure routes were however not considered in this study. Finally, even if the sampling was representative of the European seafood consumption, it must be highlighted that these results must be considered as a "first screening". Future research in this specific area is recommended to account for multiple exposure routes, possible synergistic effects with other environmental contaminants, effects of seafood processing and culinary preparation, and to balance eventual exposure risks with benefits from seafood consumption.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2017.11.015.

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