Chemosphere 213 (2018) 507–516

Contents lists available at ScienceDirect

Chemosphere

journal homepage: www.elsevier.com/locate/chemosphere

Occurrence of polybrominated diphenyl ethers, perfluorinated compounds, and nonsteroidal anti-inflammatory drugs in freshwater mussels from Latvia

L.E. Ikkere [a, b, *], I. Perkons [a, b], J. Sire [c, b], I. Pugajeva [a], V. Bartkevics [a, b]

[a] *Institute of Food Safety, Animal Health and Environment "BIOR", Lejupes iela 3, Riga LV-1076, Latvia*
[b] *University of Latvia, Jelgavas iela 1, Riga LV 1004, Latvia*
[c] *Latvian Environment, Geology and Meteorology Centre, Maskavas iela 165, Riga LV 1019, Latvia*

HIGHLIGHTS

- Occurrence of PBDEs, PFCs, and NSAIDs in freshwater mussels from Latvia was evaluated.
- The levels of PBDEs in 83% of the samples exceeded the EQS set in the EU.
- The levels of PFCs in Latvian mussels were generally lower than observed elsewhere.
- Ibuprofen was the only NSAID detected in mussels.

GRAPHICAL ABSTRACT

ARTICLE INFO

Article history:
Received 23 July 2018
Received in revised form
4 September 2018
Accepted 5 September 2018
Available online 14 September 2018

Handling Editor: Myrto Petreas

Keywords:
Bioindicators
Freshwater mussels
Nonsteroidal antiinflammatory drugs
Perfluorinated compounds
Polybrominated diphenyl ethers
Principal component analysis

ABSTRACT

The occurrence of polybrominated diphenyl ethers (PBDE), perfluorinated compounds (PFC), and nonsteroidal anti-inflammatory drugs (NSAID) in Latvian freshwater ecosystems was evaluated by using filter-feeding mussels as bioindicators. Twenty four samples of mussels were collected from freshwater bodies throughout the territory of Latvia during the summer of 2017. PBDE contamination was ubiquitous, reaching the highest total concentration of 193.2 pg g^{-1} w.w. BDE-209 was the most abundant compound, followed by penta-BDE components BDE-49, -100, −99, −153, −154, and −47 in decreasing order. The levels of PFCs in Latvian mussels were generally lower than those reported from other regions. Perfluorooctanoic acid (PFOA) was more common in mussels than perfluorooctane sulfonate (PFOS). Ibuprofen was the only NSAID detected in mussels during this study (detection frequency 50%). The observed concentrations of this compound varied between 0.52 and 109 ng g^{-1} w.w., being noticeably higher than reported by other authors. Overall, the results indicate that among the three analysed groups of contaminants, ibuprofen is present in Latvian freshwater environment at relatively high levels and further monitoring should be carried out.

1. Introduction

Several characteristics of freshwater mussels make them suitable as an indicator organism for the occurrence of chemical contamination in the environment (Bedford et al., 1968). They are

* Corresponding author. Institute of Food Safety, Animal Health and Environment "BIOR", Lejupes iela 3, Riga LV-1076, Latvia.
E-mail address: LauraElina.Ikkere@bior.lv (L.E. Ikkere).

https://doi.org/10.1016/j.chemosphere.2018.09.036
0045-6535/

sessile, thus providing location-specific information. Furthermore, mussels are filter-feeders that mainly consume phytoplankton by pumping and filtering large volumes of water. This water filtration behaviour also enables them to effectively accumulate chemical pollutants from water, thereby providing an integrative measure of the concentration and bioavailability of water pollutants. As lower members of the aquatic food chain, they transfer anthropogenic pollutants from the abiotic phase and the primary production level to the higher trophic levels in the food chain, such as mussel-eating invertebrates, birds, and mammals (Beyer et al., 2017). Due to these qualities, bivalve organisms have been used as bioindicators for nearly 50 years (Farrington et al., 2016). The range of contaminants analysed in mussels ranges from "priority pollutants" like heavy metals and halogenated hydrocarbons to chemicals of emerging concern like flame retardants, surfactants, pharmaceuticals, and even drugs of abuse (Beyer et al., 2017; Cunha et al. 2005, 2017; de Solla et al., 2016). In this study, a wide range of contaminants was selected, including brominated flame retardants (PBDEs), surfactants (PFCs) and pharmaceuticals (NSAIDs). To our knowledge, no data on the contamination status of mussels from Baltic inland waters have been published before.

Flame retardants are a group of chemicals that are used to prevent fire incidents. PBDEs were one of the most frequently used groups of flame retardants until the mid-2000s when strict regulations were imposed on the production of these compounds (2003/11/EC, 2002/95/EC, and 2005/717/EC). Due to the high volumes of production, widespread use in the past, as well as their hydrophobicity (lipophilicity) and persistence, PBDEs have become ever-present contaminants in the environment and their occurrence has been confirmed in various environmental media including soil, air, water and sediment samples, as well as humans and biota (Akortia et al., 2016). As a result, their occurrence in various biotic matrices, including mussels, has been studied (Beyer et al., 2017; Vandermeersch et al., 2015). PBDE contamination status in Latvia has been previously reported for freshwater fish samples and significant concentrations were discovered (Zacs et al., 2016). PBDE concentrations in eel samples were above the environmental quality standard (EQS) stated in Directive 2013/39/EU and further studies were recommended.

PFCs are widely used as surfactants in industrial and consumer products and as additives for fluoropolymer production (Ahrens, 2011). PFCs are extremely persistent, bioaccumulative and toxic, and globally distributed in the environment. The best known PFCs are perfluorosulfonates (PFOS) and perfluorocarboxylic acids (PFOA). Both classes of substances are recognised as widespread in the environment (Ahrens, 2011). Despite phasing out the production of long-chain perfluorocarboxylic acids in the United States, Western Europe and Japan, many PFCs are still released into the environment due to continuous production and use in other countries (OECD, 2015). PFCs have been reported in bivalves worldwide (Houde et al., 2006).

Pharmaceuticals are referred to as emerging pollutants, because their occurrence in the environment has been investigated relatively recently and their impact has not yet been fully explored. NSAIDs are some of the most often investigated and detected pharmaceuticals in water samples all over the world (Nödler et al., 2014). They are present in raw and treated wastewater (Nikolaou et al., 2007; Pugajeva et al., 2017), surface water, groundwater (Santos et al., 2010), and in drinking water (Caban et al., 2015). Nevertheless, data on the occurrence of NSAIDs in bivalves are still scarce. Taking into account that the European Commission has recently included diclofenac in the watch list of substances to be monitored in aquatic environments, data on the occurrence of NSAIDs are particularly relevant (2015/495/EU).

This study aims to investigate the contamination levels and spatial distribution of PBDEs, PFCs, and NSAIDs in the Latvian freshwater environment using mussels as bioindicators. The study provides new results on the contamination of mussels in Latvia by compounds of various classes, thus filling the gaps in knowledge about the occurrence of these compounds on a national scale. It also improves the general understanding about the levels and temporal trends of contaminants in Europe.

2. Materials and methods

2.1. Sample collection and storage

Freshwater mussels were collected from July to August 2017 at twenty four sampling sites evenly distributed over the territory of Latvia, as shown in Fig. 1. Batches consisting of three to one hundred and eighty organisms of various species including swollen river mussel (*Unio tumidus*), painter's mussel (*Unio pictorum*), duck mussel (*Anodonta anatina*), swan mussel (*Anodonta cygnea*) and zebra mussel (*Dreissena polymorpha*) were collected at each sampling site. The amount of the specimens of each species is detailed in Table S1. The mussels were kept after collection in water from the respective sampling location for 24 h in order to eliminate particulate matter from the digestive tract. Each specimen was then wrapped individually in aluminium foil, except for zebra mussels that were wrapped in foil in batches because of their small size. Mussels were frozen and stored at −18 °C. Once delivered to the laboratory, shells of the specimens were removed, soft tissue was isolated and homogenised using a food blender (Kenwood FP101T, Kenwood Ltd., UK). The homogenates were packed into polyethylene bags and stored at −18 °C until analysis.

2.2. Chemicals and materials

All of the solvents used in this study were at least of pesticide or HPLC purity grade. Solvents, acids and sorbents were purchased from Sigma−Aldrich (Buchs, Switzerland). Solid phase extraction cartridges were obtained from Phenomenex (Torrance, CA, USA). Deionised water was prepared with a Milli-Q (Millipore, Billerica, MA, USA) water purification system.

The following three groups of anthropogenic pollutants were analysed (the purity of the standards is given in parentheses; for compounds marked with asterisk (*), ^{13}C-labelled or deuterated surrogates were used as internal standards):

1) PFCs: PFOS*(98%) and PFOA*(95.5%)
2) Tri-through deca-PBDEs: IUPAC numbers 28*(99%), 47*(99%), 49 (99%), 99*(99%), 100*(100%), 138*(99%), 153*(99%), 154*(99%), 183*(99%), 209* (99%)
3) NSAIDs: tolfenamic acid*(99.7%), meloxicam*(98%), carprofen*(99.7%), flunixin*(99%), diclofenac*(99.5%), ibuprofen*(99.9%), phenylbutazone*(99%), ketoprofen (99.9%), mefenamic acid (98.5%).

The native standards for compounds listed above were obtained either from Dr. Ehrenstorfer (Augsburg, Germany), Sigma-Aldrich (St. Louis, MO, USA) or Cambridge Isotope Laboratories (Andover, MA, USA). Isotopically labelled standards were supplied either by Cambridge Isotope Laboratories, WITEGA Laboratorien (Berlin, Germany) or CDN Isotopes (Quebec, Canada).

2.3. Sample preparation and analysis

An aliquot of each sample was lyophilized in order to determine the water content. The results are presented in Table S1. Sample preparation and analysis was performed separately for each of the

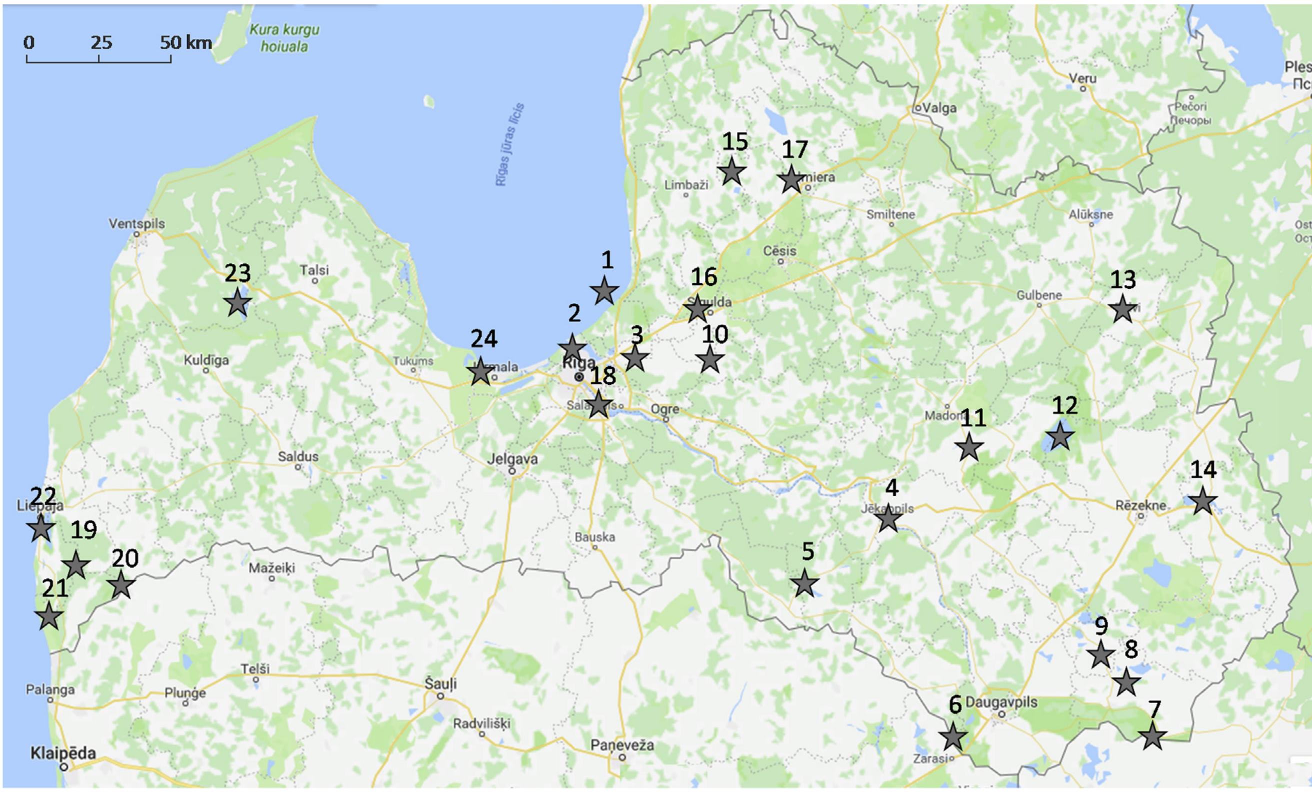

Fig. 1. The distribution of sampling locations throughout Latvia.

three contaminant groups. Detailed description of sample preparation and instrumental methods used in this study is provided in the Supplementary material.

2.3.1. Determination of the compounds of PFC group

The sample preparation procedure included ultrasound-assisted extraction with methanol and sodium hydroxide solution, followed by concentration of the analytes using solid phase extraction on a weak anion exchange cartridge. Instrumental analysis was based on high performance liquid chromatography coupled to Orbitrap high resolution mass spectrometry (HPLC-Orbitrap-HRMS) operated in selected reaction monitoring (SRM) mode, with detection of negative ions. The mass spectrometry conditions are presented in Table S2.

2.3.2. Determination of the compounds of PBDE group

The method for the determination of selected PBDEs was adopted from previously published studies (Zacs et al., 2016). Sample preparation consisted of Soxtec™ automatic extraction of freeze-dried samples with dichloromethane/*n*-hexane (1:1, v/v), cleanup procedure using various sorbents and, finally, treatment with sulfuric acid. Instrumental determination was performed using Agilent 6890N gas chromatograph (Santa Clara, CA, USA) coupled to a Micromass Autospec Premier high resolution mass spectrometer (Milford, MA, USA) by applying electron impact ionisation in positive ion mode (EI+) and selective ion monitoring (SIM) detection mode. Quantification was carried out using isotope dilution method by introducing $^{13}C_{12}$-labelled surrogates as internal standards. Detailed description of the instrumental analysis procedure for PBDEs can be found elsewhere (Zacs et al., 2016).

2.3.3. Determination of the compounds of NSAID group

For the analysis of NSAIDs, homogenised bivalve samples were extracted with acetonitrile and aqueous 0.02 M ascorbic acid solution. Concentration and purification of the analytes was achieved by solid phase extraction with Strata C18 cartridges. Instrumental separation and analysis of compounds was performed by LC-MS/MS using Acquity Ultra Performance liquid chromatography system (Waters, Milford, MA, USA) coupled to a QTrap 5500 (AB Sciex, MA, USA) equipped with an electrospray source operated in MRM mode with negative ionisation. Detailed MS parameters are shown in Table S3.

2.4. Quality assurance/quality control

In the analysis of PBDEs, all stages of the analytical procedure, including the sample extraction, purification, and handling of the final extracts were performed under conditions protected from ultraviolet (UV) radiation (i. e., using amber coloured glassware or wrapping the glassware with aluminium foil).

The quality control criteria for positive identification of the analytes of interest included the retention time of the native compounds within a window of +3 to 0 s compared to the corresponding $^{13}C_{12}$-labelled or deuterated surrogates. The acceptable deviation of the isotopic ratio for the two monitored ions (target/confirmation) was set as ±15% of the theoretical value. Five-point calibration curves were used for the quantification of analyte concentrations in each sample run. Procedural blanks and quality control samples were included in the routine quality control (QC) protocol and were analysed in each sample sequence. The concentrations of contaminants determined in real samples were corrected by taking into account the analyte concentrations found in procedural blanks. The QC samples were in-house reference materials (fortified bivalve homogenates) and the results obtained for QC samples were in a good agreement with the fortification levels (the recovery ranged from 75 to 123%).

2.5. Data analysis

Due to the small sample size and large variability among treatments, we treated observations below method the limit of detection to be zero. Open source software R (http://www.r-project.org/) was used to construct box plots for the data sets. Correlation analysis, principal component analysis (PCA), cluster analysis (CA), and graph construction were performed using Minitab 18 software. CA was applied to cluster observations together based upon similarity. Hierarchical agglomerative CA was performed on the normalised data set using squared Euclidean distances as a measure of similarity. The coordinates of the new cluster were calculated by complete linkage method. CA was performed on standardised experimental datasets in order to avoid misclassification due to wide differences in data dimensionality. PCA was used to interpret the relationship between the contamination of mussel samples and geographical locations. PCA calculates orthogonal linear combinations of the standardised variables of the correlation matrix according to the maximum variance criterion. Such linear combinations are called principal components and the coefficients of the linear combinations are called loadings. When the plot of object is projected onto the first two principal component axes, a linear projection of objects onto the two-dimensional subspace is obtained, saving most of the total variance (Jolliffe, 2002).

3. Results and discussion

Detailed concentration data for the selected compounds in the analysed mussel samples are provided in the Supplementary material, Table S4.

3.1. Levels and profiles of PFCs

In order to assess PFC contamination in the freshwater ecosystem of Latvia, two compounds (PFOS and PFOA) were analysed in mussels. PFOS was detected in 3 out of 24 (13%) samples, with the concentrations ranging from 10 to 21 pg g^{-1} w.w. PFOA, however, was detected more frequently, as 10 out of 24 (42%) samples were above the LOQ, ranging from 13 to 51 pg g^{-1} w.w. These values were two to three orders of magnitude lower than 9100 pg g^{-1} w.w., which is the EQS value for perfluorooctane sulfonic acid and its derivatives in biota stated in the European Commission Directive 2013/39/EC (2013/39/EC). As shown in Table 1, most of the values observed in other studies are significantly higher, with the highest average concentrations of PFOS of 72 000 pg g^{-1} w.w. in north-central Portuguese estuaries, where paper, textile, and leather factories discharge their effluents (Cunha et al., 2005). Similar levels of PFC contamination to ours were observed in coastal waters of Spain – up to 60 and 10 pg g^{-1} w.w for PFOS and PFOA, respectively (Domingo et al., 2012; Gomez et al., 2011). PFCs have already been monitored in Latvian freshwater biota during the summers of 2015 and 2016, when European perch (*Perca fluviatilis*) was used as the indicator organism. The ranges were 0.43–1.97 ng g^{-1} w.w. and n.d.–0.85 ng g^{-1} w.w., respectively (LEGMC, 2016; LEGMC, 2017). The difference in the levels observed in mussels and perch may be explained by accumulation differences. Some studies state that the low accumulation of PFCs in mussels is due to the increased efflux transport activity of proteins belonging to the adenosine triphosphate-binding cassette (ABC) superfamily, which act as a first line of defence of the organism, removing toxic chemicals from the cells (Epel et al., 2008).

Regarding the profiles of PFCs observed in our study, the most abundant compound in mussels was PFOA. PFOA is more water soluble than PFOS, demonstrating low bioconcentration factors (BCFs) at higher trophic levels, whereas the BCFs calculated for mussels are significantly higher (Quinete et al., 2009). It is in good agreement with the data obtained by other authors (Nakata et al., 2006; Quinete et al., 2009), although some studies have demonstrated the opposite trend (Kannan et al., 2005).

3.2. Levels and profiles of PBDEs

PBDEs were found in all of the analysed samples, confirming a wide distribution of these flame retardants in the freshwater environment. The total concentrations of Σ_{PBDE} ranged from 11.3 to 193.2 pg g^{-1} w.w., with the average of 42.1 pg g^{-1} w.w. These levels are lower than those observed in our previous study of European eels (*Anquilla anquilla*) from Latvian lakes, where the sum of PBDEs ranged from 280 to 26 700 pg g^{-1} w.w. (Zacs et al., 2016). Two sampling places overlapped in both studies. Higher contamination levels were observed in the Lake Kisezers – 14 900 pg g^{-1} in eels and 51.68 pg g^{-1} in mussels, whereas in Lake Liepaja the contamination levels were 9910 pg g^{-1} and 23.71 pg g^{-1}, respectively. The concentrations of PBDE observed in eels were more than one order of magnitude higher than those in mussels. This may be partly due to the great differences in lipid content of both organisms. Positive correlation between the lipid content and PBDE concentration has been observed before (Marriusen et al., 2008). Another possible explanation of the great concentration differences would be that eels are at a higher trophic level, and PBDEs are bioaccumulative, hence body burdens are proportional to trophic level. Furthermore, the overall lifespan of the analysed mussel species is shorter than that of eels, which may result in lower accumulation of contaminants in mussels. A comparison with other studies is provided in

Table 1
The concentrations of PFCs (pg g^{-1} w.w.) in mussels from the current study and the data from previous studies (expressed as minimum – maximum (mean)).

Reference	Region	PFOS	PFOA
Present study	Latvia	n.d.–21 (2)	n.d.–51 (9)
Domingo et al., 2012	Spain	n.d.	n.d.
Gomez et al., 2011	Spain	n.d.–60	n.d.–10
Kannan et al., 2005	USA, Great Lakes	n.d.–3100	n.d.
Munschy et al., 2013	France	5–900	–
Cunha et al., 2005	Portugal	36800–125900 (72000)	–
Nania et al., 2009	Mediterranean Sea	n.d.–3000	n.d.–2500
Nakata et al., 2006	Japan	n.d.	3400–8100 (6000)
Quinete et al., 2009	Brazil	n.d.–4700	n.d.–14900
Renzi et al., 2013	Italy	118–228	123–170
Zabaleta et al., 2015	Spain	n.d.–2400	–
So et al., 2006	Japan	109–586	n.d.–661

"n.d." – the value is below the limit of detection.
"-" – not included in the study.

Table 2.

Most of the concentrations observed elsewhere are significantly higher, with only those in mussels from Baiyangdian Lake, China being similar to our study (Hu et al., 2010). Despite the relatively low levels detected in Latvia, the concentration of brominated biphenyl ethers in 83% of the samples exceeded the EQS value in biota (8.5 pg g^{-1} w.w. for the sum of congeners 28, 47, 99, 100, 153, 154), as stated in the European Commission Directive 2013/39/EU. This fact is a source of concern regarding the water quality in Latvia with respect to this group of chemical pollutants.

The congener profile of PBDE (shown in Fig. 2) in most of the samples shows the predominance of tetra- and penta-brominated BDEs, including PBDEs No. 47, 49, 99, and 100. Similar observations have been reported by several other authors (Debruyn et al., 2009; Perez-Fuentetaja et al., 2015; Aznar-Alemany et al., 2017), with the exception of PBDE-49, which is rarely analysed. However, in our study PBDE-49 had the second highest average contribution of 18%. Although this congener was found in small quantities in penta- and octa-bromo technical BDE mixtures, significant amounts have been also observed upon reductive debromination of octa- and deca-brominated mixtures (Gaul et al., 2006). The highest levels were observed in the case of PBDE-209, which is the only deca-brominated BDE. The same results were obtained in the analysis of mussels from the Bohai Sea, China (Wang et al., 2009). This may be the result of several factors: 1) widespread usage of deca-BDE formulation; 2) mussels are known to act as natural water filters and possess limited metabolic capabilities, which leads to the accumulation of pollutants originating from suspended particulate matter, since highly brominated PBDE congeners tend to accumulate in sediments (De Boer et al., 2003); 3) ineffective depuration process. Therefore, the presence of PBDE-209 may result from the presence of particulate matter in the digestive tract of mussels. Some authors have not detected PBDE-209 in raw mussels, however Aznar-Alemany et al., 2017 have observed significant amounts of the congener in mussels after cooking – up to 1870.4 pg g^{-1} w.w. (Van Ael et al., 2012; Aznar-Alemany et al., 2017). The great variance of observed PBDE-209 concentrations could be a result of different usage of deca-BDE formulation across

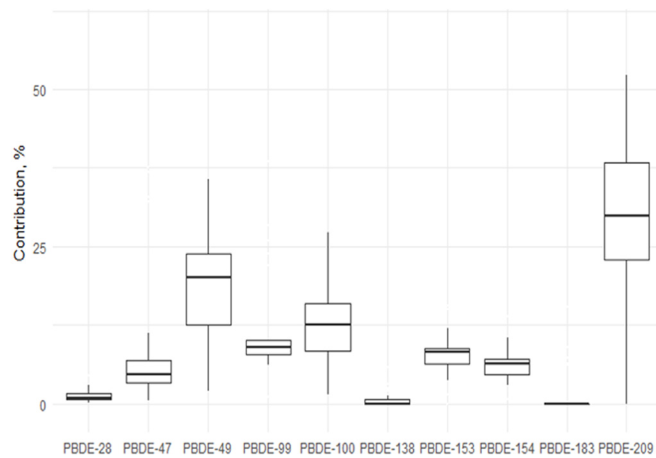

Fig. 2. Box plot of the contributions (%) of selected PBDEs in the analysed mussel samples.

studied regions.

In order to further evaluate the patterns of PBDE contamination and to identify likely sources of PBDE congeners, correlation analysis was performed. The obtained data revealed significant Pearson correlation between the presence of BDE-154 and the PBDE congeners No. 47, 49, 99, 100, and 153 (p-values < 0.01), which all are components of commercial penta-BDE mixture. This mixture was extensively used in the European Union until its phase out in 2004 (2003/11/EC). Strong correlation was observed between BDE-49 and BDE-209 by carrying out Spearman's correlation analysis (Spearman's rho 0.776, p-value < 0.001). This was in a good agreement with the aforementioned observation by other authors that BDE-49 is a degradation product of BDE-209 (Gaul et al., 2006).

3.3. Levels of NSAIDs

Eight of the nine analysed NSAIDs (tolfenamic acid, meloxicam,

Table 2
The concentrations of PBDEs (pg g^{-1} w.w. or pg g^{-1} d.w.) in mussels from the current study and data from previous studies (expressed as minimum – maximum (mean) or mean value ± standard deviation).

Reference	Region		PBDE-28	PBDE-47	PBDE-99	PBDE-100	PBDE-153	PBDE-154	PBDE-183	PBDE-209	Σ_{PBDE}
Present study	Latvia	pg g^{-1}, w.w.	0.1–1.4 (0.5)	0.5–21.5 (3.9)	1.1–29.0 (5.5)	0.9–46.8 (6.3)	0.8–13.4 (3.3)	0.8–5.1 (2.2)	0.9–4.6 (2.0)	3.5–179.0 (17.4)	11.3–193.2 (42.1)
Van Ael et al., 2012	The Netherlands		50–700 (270)	280–5160 (1430)	50–3350 (360)	720–2780 (1530)	50–450 (140)	200–580 (350)	40–270 (90)	n.d.	2090–12400 (3800)
Christensen et al., 2002	Greenland		–	(100)	(20)	–	n.d.	–	–	–	(120)
Perez-Fuentetaja et al., 2015	USA, Great Lakes		(15)	(910)	(1120)	100 ± 10	(80)	50 ± 10	–	(390)	–
Hu et al., 2010	China		2.0–4.1 (3.1)	6.5–9.2 (7.5)	3.9–5.1 (4.4)	1.5–2.4 (1.8)	2.5–5.4 (3.9)	1.8–3.1 (2.6)	0.3–11.6 (5.4)	–	25.4–58.9 (45.2)
Aznar-Alemany et al., 2017	Europe		n.d.-74.2 (27.5)[a]	n.d.-377.7 (123.9)[a]	n.d.-2066.8 (277.0)[a]	n.d.-275.7 (43.6)[a]	n.d.	n.d.	n.d.-2717.8 (292.7)[a]	n.d.	29.3–2989.2 (764.7)[a]
Present study	Latvia	pg g^{-1}, d.w.	1.1–13.2 (4.2)	3.7–183.3 (35.1)	10.0–255.5 (49.1)	7.9–425.4 (54.7)	6.9–121.6 (29.0)	6.9–46.2 (19.8)	7.3–42.2 (18.0)	29.2–1351.3 (143.3)	103.1–1560.1 (362.5)
Debruyn et al., 2009	Canada		–	–	–	–	–	–	–	–	(6710)
Oros et al., 2005	USA, CA		–	17000±700	8000±4000	4000±1000	–	–	–	–	29000±13000
Liu et al., 2005	China		320–25300 (7673)	1420–8560 (3859)	1410–21300 (8266)	n.d.–1270 (677)	n.d.–17400 (6870)	n.d.–1950 (782)	1580–20200 (8019)	n.d.–13900 (4097)	4730–109880 (40243)
Wang et al., 2009	China		20–390 (100)	140–1010 (280)	20–130 (80)	20–110 (30)	10–100 (30)	30–270 (50)	nd–100 (10)	1010 –1801000 (2430)	1250 –1803110 (3010)

"n.d." – the value is below the limit of detection.
"-" – not included in the study.
[a] Values recalculated from ng g^{-1} lipid weight to pg g^{-1} wet weight using data from Aznar-Alemany et al., (2017.

carprofen, flunixin, diclofenac, phenylbutazone, ketoprofen, and mefenamic acid) were not detected in any of the samples. Ibuprofen was present in 50% of the samples, with concentrations ranging from 0.52 to 109 ng g^{-1} w.w. or from 5.1 to 1363 ng g^{-1} d.w. A comparison with levels detected in other studies is shown in Table 3 (compounds that were not detected in this study and were not analysed by other authors are not included in the table). Relatively few studies have been reported so far on the occurrence of NSAIDs in mussels. Only ibuprofen and diclofenac have been detected in mussels and bivalves elsewhere. The levels of ibuprofen measured in Latvian mussels were up to ten times higher than in Taihu Lake, China, where the highest observed value was 93.7 ng g^{-1} d.w. (Xie et al., 2015). Similarly to our study, neither ketoprofen nor mefenamic acid were present in mussels from other regions (Caban et al., 2016; Nunez et al., 2015; Mezzelani et al., 2016; McEneff et al., 2014).

The detectable presence of ibuprofen in mussels corresponds to the statistics of pharmaceutical use in Latvia. The consumption of ibuprofen in 2017 was 23.46 defined daily doses per 1000 inhabitants per day (DID), making it the most consumed medication of NSAID group in Latvia. The consumption of diclofenac was similar to that of ibuprofen–19.73 DID (State Agency of Medicines, 2017). Nevertheless, diclofenac was not detected in any of the mussel samples. This fact can be explained by the rapid photodegradation of diclofenac in open basins (Buser et al., 1998). Furthermore, this trend is confirmed by data obtained in a study of Latvian and Norwegian surface waters, where ibuprofen was detected in 33 and 60% of the samples, whereas diclofenac in only 10 and 20% of samples, respectively (Reinholds et al., 2017). Ibuprofen was also the most common NSAID detected in untreated wastewaters from the Daugavgriva municipal wastewater treatment plant of the Riga city at up to 326 ng L^{-1} (Pugajeva et al., 2017). The primary route for the discharge of ibuprofen into surface waters is through the effluent of wastewater treatment plants. Ibuprofen and its metabolites are excreted into the sewage system along with unused drugs that may be disposed of via drains and toilets (Bound and Voulvoulis, 2006). Taking into account that only 1–8% of the consumed ibuprofen is excreted unchanged (Ternes, 1998), determination of ibuprofen metabolites in mussels should be considered in further studies. Besides that, other studies have shown that ibuprofen and its metabolites could pose ecotoxicological risks (Lienert et al., 2007).

3.4. Distribution patterns of the analysed contaminants

In order to interpret the data reported in Table S4, we focussed on the relationship between the levels of contaminants and sampling locations. The box plots for the total concentrations of each contaminant group are provided in Fig. 3. The samples were grouped by the drainage basin and types of the water bodies – lake, river, river delta or water reservoir. PBDEs were more common in the Daugava and Lielupe basins. The highest variations were observed in the case of ibuprofen, as it was present in the Lielupe and Venta basins at significantly higher concentrations than in the Gauja and Daugava basins. As for the different bodies of water, the only sample from Riga water reservoir contained remarkably high concentrations of PBDEs and ibuprofen. However, geographical variation may not be the only reason for great differences in the concentration of ibuprofen. Xie et al. (2015) have demonstrated drastic contrast in the levels of ibuprofen observed in mussels *Anodonta* and clams *Corbiculidae* – ibuprofen was not detected in mussels, while the concentration in clams reached 93.7 ng g^{-1} d.w. (Xie et al., 2015). This observation suggests that there are major differences in the ability of bivalve species to accumulate ibuprofen. Since the levels of ibuprofen observed in Latvian mussels varied greatly, correlation with mussel species was investigated. Significant correlation was found between the levels of ibuprofen and the contribution of zebra mussels *Dreissena polymorpha* in the sample batch (Pearson correlation 0.6, p-value 0.002 at confidence level 0.95). Nevertheless, no pronounced correlations were observed between the species and the levels of PFCs or PBDEs (p-values > 0.05). This observation should be further investigated in future studies by separately analysing the different mussel species.

We used CA and PCA to further evaluate the extent of contamination at the sampled locations and to identify its sources and distribution patterns. The CA method groups the objects into clusters on the basis of similarity. A dendrogram is presented in Fig. 4a. All 24 samples were grouped into six statistically significant clusters at a similarity level of 0.80. Since three of the clusters consisted of only a single sample each, they were considered as individual samples, rather than clusters. The majority of mussel samples belonged to the cluster 1, which included sampling locations showing low to moderate contamination with the analysed compounds. Cluster 2 (sites 21, 22, and 24) consisted of samples from the Liepaja region and was characterised by the presence of ibuprofen at a concentration of about one order of magnitude higher than those in the rest of the clusters. Cluster 2 samples also contained PFOS, which was not present in the other clusters. This trend may point to the significant anthropogenic impact in this region. Cluster 3 (sites 10, 11, 12, and 13) has the peculiar feature of BDE-47 and BDE-99 present at much higher concentrations than any other brominated compound, and BDE-209 is not present in samples of this cluster at all. The lack of BDE-209 may be due to the lower turbidity of water. The individual sample 8, which did not belong to any cluster, contained the highest concentration of BDE-209. The sampling location was Lake Dridzis – known as the deepest lake in Latvia. This suggests that there might be some relation between the depth of the water body and the

Table 3
The concentrations of NSAIDs (ng g^{-1} d.w.) in bivalves from the current study and previous studies (expressed as minimum – maximum (mean) or mean value ± standard deviation).

Reference	Region	Diclofenac	Ketoprofen	Ibuprofen	Mefenamic acid
Present study	Latvia	n.d.	n.d.	n.d.–1363 (111)	n.d.
Bayen et al., 2016	Singapore	n.d.	–	–	–
Caban et al., 2016	Poland	n.d.	n.d.	n.d.	–
Xie et al., 2015	China	1.41–5.42 (2.59)	–	n.d.–93.7 (41.6)	–
Klosterhaus et al., 2013	USA, CA	–	–	n.d.	–
Nunez et al., 2015	Spain	n.d.	n.d.	n.d.	–
Cunha et al., 2017	Portugal	n.d.–4.5	–	–	–
Mezzelani et al., 2016	Italy	16.11 ± 14.72	n.d.	9.39 ± 0.59	–
McEneff et al., 2014	Ireland	n.d.	–	–	n.d.

"n.d." – the value is below the limit of detection.
"-" – not included in the study.

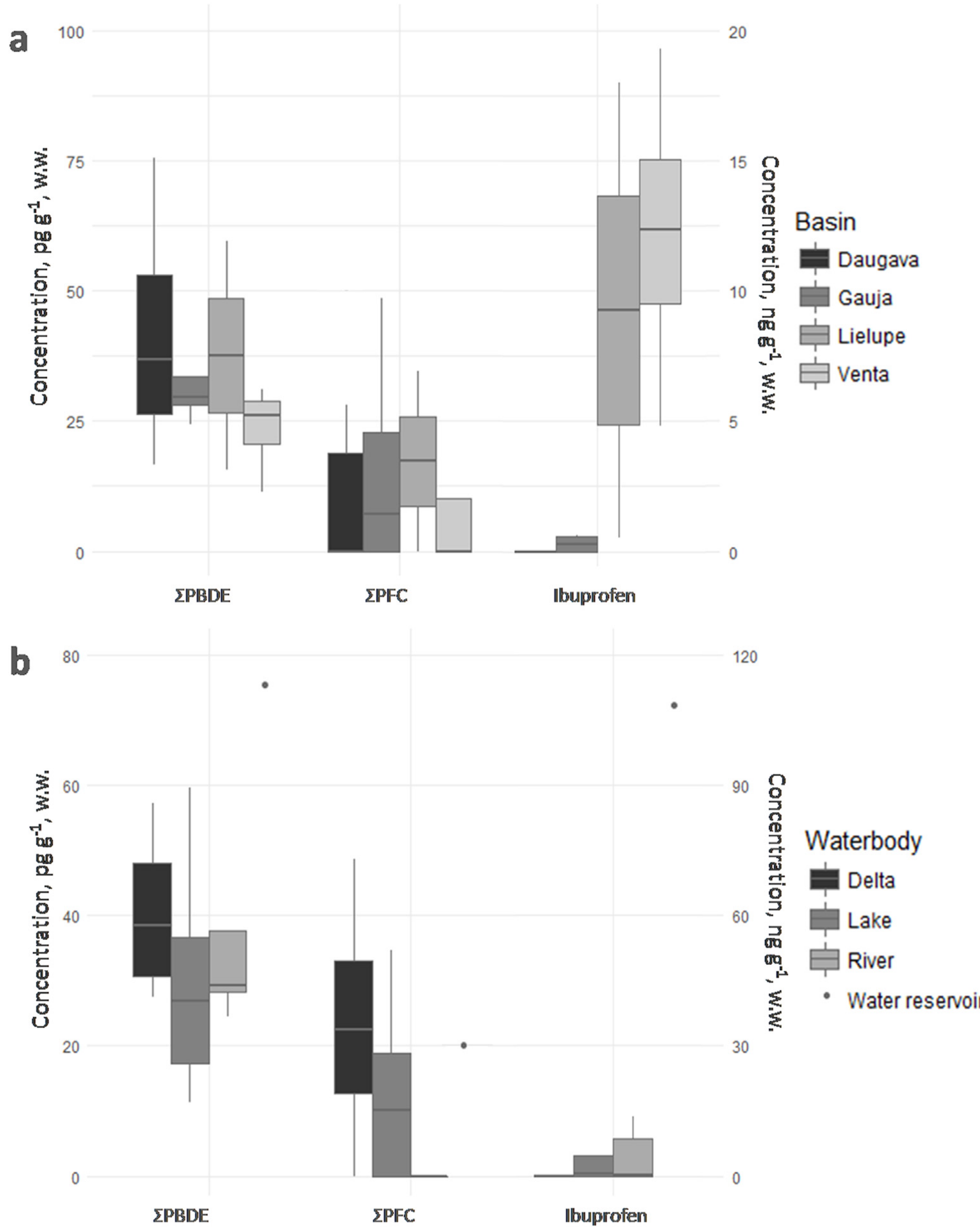

Fig. 3. Box plots of the concentrations of selected contaminants (pg g^{-1} w.w. (ΣPBDE and ΣPFC) or ng g^{-1} w.w. (ibuprofen)), grouped by the drainage basins (a) and types of water bodies (b).

concentration of PBDEs. Sample 18 from the Riga water reservoir had the highest level of ibuprofen. CA confirmed the previously mentioned observation that this sampling site was quite different. Sample 20, collected from the Barta river near the Latvia-Lithuania border had the highest concentrations of tetra-through hexa-BDEs. The source of contamination could be wastewater influx or municipal waste disposal in the surrounding area, since no known PBDE emission sources are located near this sampling site.

PCA was also applied to the data reported in Table S4. Each of the individual contaminant levels were included in the statistical analysis. First, three principal components (PC1, PC2, and PC3) with eigenvalues higher than 1 were extracted. The three principal components together accounted for 67% of the total variation. An exploratory view of the samples/scores plot on the principal components PC1 versus PC2, which accounts for more than 56% of the total variance, is illustrated in Fig. 4b. The principal component PC1 showed positive associations with most of the PBDEs, except for BDE-209, which indicated the possible role of a different source. The PC2 allowed to account for 22% of the total variance and had the highest negative association with BDE-183 and BDE-138. However, with the number of data sets available, it was not possible to identify significant correlation between the 24 sampling locations and the levels of contaminants. All samples in Fig. 4b are grouped in accordance with CA. Cluster 3, as well as the samples 18 and 20 were far different from the other samples, whereas Clusters 1 and 2, as well as the sample 8 were merged on the plot.

4. Conclusions

In order to evaluate the contamination status of Latvian aquatic environment, mussel samples from various freshwater bodies were analysed for the content of ten PBDEs, two PFCs, and nine NSAIDs.

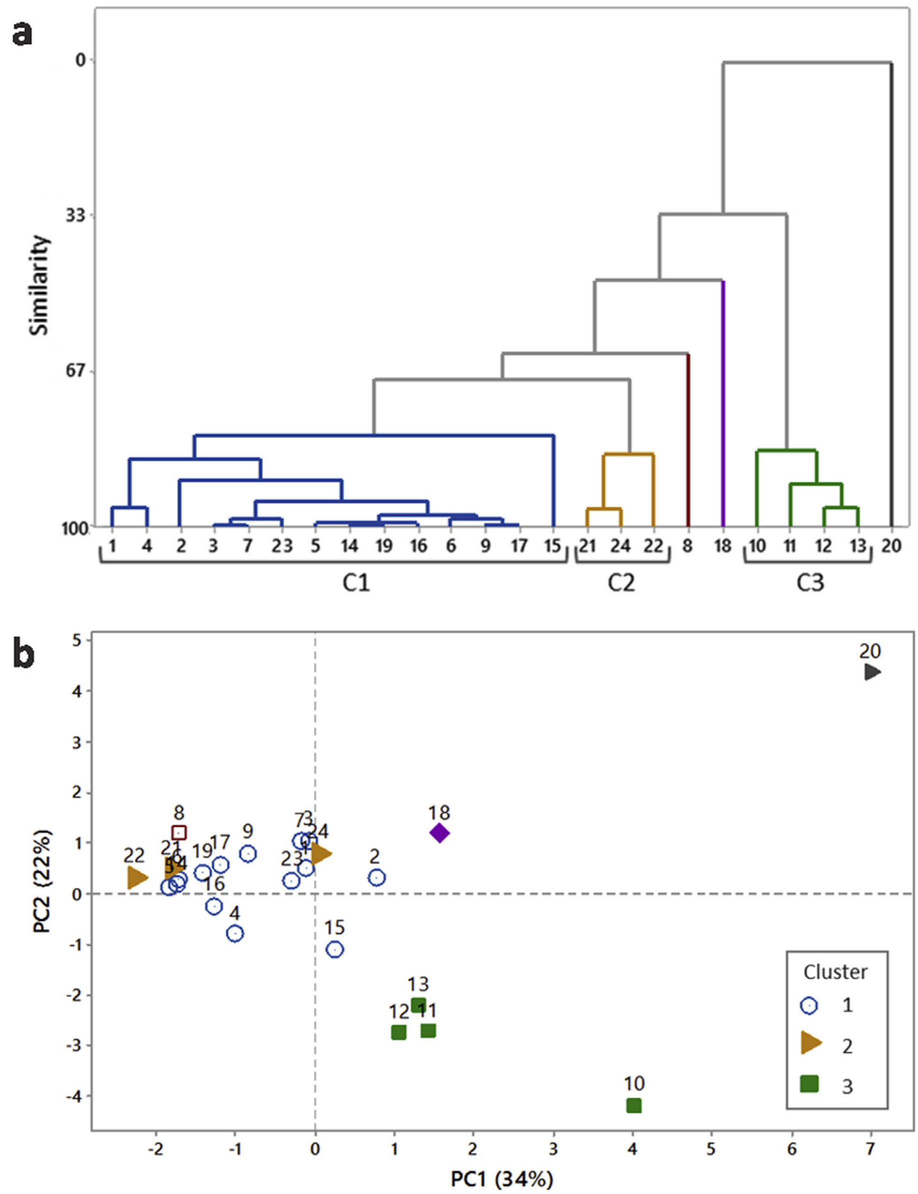

Fig. 4. Hierarchical dendogram and three distinguished clusters of mussel samples by the analysed compounds (a) and plot of the first two principal components after PCA of the analysed compounds in mussels collected from Latvian freshwater sites (b).

For the first time, data on the contamination status of mussels from Latvia are presented. PBDEs were detected in all of the mussel samples, but the concentrations were generally lower than those observed in mussels from other regions. Regardless, 83% of the samples exceeded the EQS threshold for the sum of six PBDEs stated in the Directive 2013/39/EU. The levels of PFCs in mussels were low throughout the territory of Latvia, compared to other regions and did not exceed the EQS criteria. The levels observed for ibuprofen, which was the only detected NSAID in Latvian mussels, were significantly higher than those detected by other authors. It is a source of concern that provides a reason for further monitoring and control of this emerging contaminant, as well as its metabolites.

Declarations of interest

None.

Acknowledgements

This work was funded by the European Regional Development Fund, project No. 1.1.1.1/16/A/258 “Development and the application of innovative instrumental analytical methods for the combined determination of a wide range of chemical and biological contaminants in support of the bio-economy in the priority sectors of economy”.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.chemosphere.2018.09.036.

References

Ahrens, L., 2011. Polyfluoroalkyl compounds in the aquatic environment: a review of their occurrence and fate. J. Environ. Monit. 13, 20–31. https://doi.org/10.

1039/c0em00373e.
Akortia, E., Okonkwo, J.O., Lupankwa, M., Osae, S.D., Adegbenro, P.D., Olukunle, O.I., Chaudhry, A., 2016. A review of sources, levels and toxicity of polybrominated diphenyl ethers (PBDEs) and their transformation and transport in various environmental compartments. Environ. Rev. 24, 253–273. https://doi.org/10.1139/er-2015-0081.
Aznar-Alemany, O., Trabalon, L., Jacobs, S., Liane Barbosa, V., Fernandez Tejedor, M., Granby, K., Kwadijk, C., Cunha, S.C., Ferrari, F., Vandermeersch, G., Sioen, S., Verbeke, W., Vilavert, L., Domingo, J.L., Eljarrat, E., Barcelo, D., 2017. Occurrence of halogenated flame retardants in commercial seafood species available in European markets. Food Chem. Toxicol. 104, 35–47. https://doi.org/10.1016/j.fct.2016.12.034.
Bayen, S., Estrada, E.S., Juhel, G., Kit, L.W., Kelly, B.C., 2016. Pharmaceutically active compounds and endocrine disrupting chemicals in water, sediments and mollusks in mangrove ecosystems from Singapore. Mar. Pollut. Bull. 109, 716–722. https://doi.org/10.1016/j.marpolbul.2016.06.105.
Bedford, J. w., Roelofs, E.W., J, Z.M., 1968. The Freshwater Mussel as Biological Monitor of Pesticide Concentrations in a Lotic Environment, pp. 118–126. https://doi.org/10.4319/lo.1968.13.1.0118.
Beyer, J., Green, N.W., Brooks, S., Allan, I.J., Ruus, A., Gomes, T., Bråte, I.N.L., Schøyen, M., 2017. Blue mussels (*Mytilus edulis* spp.) as sentinel organisms in coastal pollution monitoring: a review. Mar. Environ. Res. 130, 338–365. https://doi.org/10.1016/j.marenvres.2017.07.024.
Bound, J.P., Voulvoulis, N., 2006. Predicted and measured concentrations for selected pharmaceuticals in UK rivers: implications for risk assessment. Water Res. 40, 2885–2892. https://doi.org/10.1016/j.watres.2006.05.036.
Buser, H.R., Poiger, T., Müller, M.D., 1998. Occurrence and fate of the pharmaceutical drug diclofenac in surface waters: rapid photodegradation in a lake. Environ. Sci. Technol. 32, 3449–3456. https://doi.org/10.1021/es980301x.
Caban, M., Lis, E., Kumirska, J., Stepnowski, P., 2015. Determination of pharmaceutical residues in drinking water in Poland using a new SPE-GC-MS(SIM) method based on Speedisk extraction disks and DIMETRIS derivatization. Sci. Total Environ. 538, 402–411. https://doi.org/10.1016/j.scitotenv.2015.08.076.
Caban, M., Szaniawska, A., Stepnowski, P., 2016. Screening of 17α-ethynylestradiol and non-steroidal anti-inflammatory pharmaceuticals accumulation in *Mytilus edulis* trossulus (Gould, 1890) collected from the Gulf of Gdańsk. Oceanol. Hydrobiol. Stud. 45, 605–614. https://doi.org/10.1515/ohs-2016-0050.
Christensen, J.H., Glasius, M., Pécseli, M., Platz, J., Pritzl, G., 2002. Polybrominated diphenyl ethers (PBDEs) in marine fish and blue mussels from southern Greenland. Chemosphere 47, 631–638. https://doi.org/10.1016/S0045-6535(02)00009-7.
Cunha, I., Hoff, P., Van de Vijver, K., Guilhermino, L., Esmans, E., De Coen, W., 2005. Baseline study of perfluorooctane sulfonate occurrence in mussels, *Mytilus galloprovincialis*, from north-central Portuguese estuaries. Mar. Pollut. Bull. 50, 1121–1145. https://doi.org/10.1016/j.marpolbul.2005.06.046.
Cunha, S.C., Pena, A., Fernandes, J.O., 2017. Mussels as bioindicators of diclofenac contamination in coastal environments. Environ. Pollut. 225, 354–360. https://doi.org/10.1016/j.envpol.2017.02.061.
De Boer, J., Wester, P.G., Van Der Horst, A., Leonards, P.E.G., 2003. Polybrominated diphenyl ethers in influents, suspended particulate matter, sediments, sewage treatment plant and effluents and biota from The Netherlands. Environ. Pollut. 122, 63–74. https://doi.org/10.1016/S0269-7491(02)00280-4.
de Solla, S.R., Gilroy, A.M., Klinck, J.S., King, L.E., McInnis, R., Struger, J., Backus, S.M., Gillis, P.L., 2016. Bioaccumulation of pharmaceuticals and personal care products in the unionid mussel *Lasmigona costata* in a river receiving wastewater effluent. Chemosphere 146, 486–496. https://doi.org/10.1016/j.chemosphere.2015.12.022.
Debruyn, A.M.H., Meloche, L.M., Lowe, C.J., 2009. Patterns of bioaccumulation of polybrominated diphenyl ether and polychlorinated biphenyl congeners in marine mussels. Environ. Sci. Technol. 43, 3700–3704. https://doi.org/10.1021/es900472k.
Directive 2003/11/EC of the European Parliament and the Council of 6 February 2003, amending for the 24th time the Council directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (pentabromodiphenyl ether and octabromodiphenyl ether). Offic. J. L 042, 15.02.2003.
Directive 2013/39/EC of the European Parliament and the Council of 12 August 2013, amending Directives 200/60/EC and 2008/105/EC as regards priority substances in the field of water policy. Offic. J. L 226, 24.08.2013.
Domingo, J., Ericson-Jogsten, I., Perello, G., Nadal, M., Bavel, B. Van, Kä, A., 2012. Human exposure to perfluorinated compounds in Catalonia, Spain: contribution of drinking water and fish and shellfish. J. Agric. Food Chem. 60, 4408–4415. https://doi.org/10.1021/jf300355c.
Epel, D., Luckenbach, T., Stevenson, C.N., MacManus-Spencer, L.A., Hamdoun, A., Smital, T., 2008. Efflux transporters: newly appreciated roles in protection against pollutants. Environ. Sci. Technol. 42, 3914–3920. https://doi.org/10.1021/es087187v.
European Commission, 2015. Commission implementing decision (EU) 2015/495 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council (notified under document C(2015) 1756). Offic. J. Euro. Comm. L226, 40–42.
European Court of Justice, 2008. Cases C-14/06 and C-295/06, Judgement of the Court, 1 April 2008. Directive 2002/95/EC and Commission Decision 2005/717/EC.
Farrington, J.W., Tripp, B.W., Tanabe, S., Subramanian, A., Sericano, J.L., Wade, T.L., Knap, A.H., 2016. Edward D. Goldberg's proposal of “the mussel watch”: reflections after 40 years. Mar. Pollut. Bull. 110, 501–510. https://doi.org/10.1016/j.marpolbul.2016.05.074.
Gaul, S., Von Der Recke, R., Tomy, G., Vetter, W., 2006. Anaerobic transformation of a technical brominated diphenyl ether mixture by super-reduced vitamin B_{12} and dicyanocobinamide. Environ. Toxicol. Chem. 25, 1283–1290. https://doi.org/10.1897/05-338R.1.
Gómez, C., Vicente, J., Echavarri-Erasun, B., Porte, C., Lacorte, S., 2011. Occurrence of perfluorinated compounds in water, sediment and mussels from the Cantabrian Sea (North Spain). Mar. Pollut. Bull. 62, 948–955. https://doi.org/10.1016/j.marpolbul.2011.02.049.
Houde, M., Martin, J.W., Letcher, R.J., Solomon, K.R., Muir, D.C.G., 2006. Biological monitoring of polyfluoroalkyl substances: a review. Environ. Sci. Technol. 40, 3463–3473. https://doi.org/10.1021/es052580b.
Hu, G.C., Dai, J.Y., Xu, Z.C., Luo, X.J., Cao, H., Wang, J.S., Mai, B.X., Xu, M.Q., 2010. Bioaccumulation behavior of polybrominated diphenyl ethers (PBDEs) in the freshwater food chain of Baiyangdian Lake, North China. Environ. Int. 36, 309–315. https://doi.org/10.1016/j.envint.2010.01.002.
Jolliffe, I.T., 2002. Principal Component Analysis, second ed. Springer, New York.
Kannan, K., Tao, L., Sinclair, E., Pastva, S.D., Jude, D.J., Giesy, J.P., 2005. Perfluorinated compounds in aquatic organisms at various trophic levels in a Great Lakes food chain. Arch. Environ. Contam. Toxicol. 48, 559–566. https://doi.org/10.1007/s00244-004-0133-x.
Klosterhaus, S.L., Grace, R., Hamilton, M.C., Yee, D., 2013. Method validation and reconnaissance of pharmaceuticals, personal care products, and alkylphenols in surface waters, sediments, and mussels in an urban estuary. Environ. Int. 54, 92–99. https://doi.org/10.1016/j.envint.2013.01.009.
Latvian Environment, Geology and Meteorology Centre, 2016. Pārskats Par Virszemes Un Pazemes Ūdeņu Stāvokli 2015 gadā. [In Latvian]. https://www.meteo.lv/fs/CKFinderJava/userfiles/files/Vide/Udens/stat_apkopojumi/udens_kvalit/VPUK_parskats_2015.pdf. (Accessed 15 June 2018).
Latvian Environment, Geology and Meteorology Centre, 2017. Pārskats Par Virszemes Un Pazemes Ūdeņu Stāvokli 2016 gadā. [In Latvian]. https://www.meteo.lv/fs/CKFinderJava/userfiles/files/Vide/Udens/stat_apkopojumi/udens_kvalit/VPUK_parskats_2016.pdf. (Accessed 15 June 2018).
Lienert, J., Güdel, K., Escher, B.I., 2007. Screening method for ecotoxicological hazard assessment of 42 pharmaceuticals considering human metabolism and excretory routes. Environ. Sci. Technol. 41, 4471–4478. https://doi.org/10.1021/es0627693.
Liu, Y., Zheng, G.J., Yu, H., Martin, M., Richardson, B.J., Lam, M.H.W., Lam, P.K.S., 2005. Polybrominated diphenyl ethers (PBDEs) in sediments and mussel tissues from Hong Kong marine waters. Mar. Pollut. Bull. 50, 1173–1184. https://doi.org/10.1016/j.marpolbul.2005.04.025.
Mariussen, E., Fjeld, E., Breivik, K., Steinnes, E., Borgen, A., Kjellberg, G., Schlabach, M., 2008. Elevated levels of polybrominated diphenyl ethers (PBDEs) in fish from Lake Mjøsa, Norway. Sci. Total Environ. 390, 132–141. https://doi.org/10.1016/j.scitotenv.2007.09.032.
McEneff, G., Barron, L., Kelleher, B., Paull, B., Quinn, B., 2014. A year-long study of the spatial occurrence and relative distribution of pharmaceutical residues in sewage effluent, receiving marine waters and marine bivalves. Sci. Total Environ. 476–477, 317–326. https://doi.org/10.1016/j.scitotenv.2013.12.123.
Mezzelani, M., Gorbi, S., Da Ros, Z., Fattorini, D., d'Errico, G., Milan, M., Bargelloni, L., Regoli, F., 2016. Ecotoxicological potential of non-steroidal anti-inflammatory drugs (NSAIDs) in marine organisms: bioavailability, biomarkers and natural occurrence in *Mytilus galloprovincialis*. Mar. Environ. Res. 121, 31–39. https://doi.org/10.1016/j.marenvres.2016.03.005.
Munschy, C., Marchand, P., Venisseau, A., Veyrand, B., Zendong, Z., 2013. Levels and trends of the emerging contaminants HBCDs (hexabromocyclododecanes) and PFCs (perfluorinated compounds) in marine shellfish along French coasts. Chemosphere 91, 233–240. https://doi.org/10.1016/j.chemosphere.2012.12.063.
Nakata, H., Kannan, K., Nasu, T., Cho, H.S., Sinclair, E., Takemura, A., 2006. Perfluorinated contaminants in sediments and aquatic organisms collected from shallow water and tidal flat areas of the Ariake Sea, Japan: environmental fate of perfluorooctane sulfonate in aquatic ecosystems. Environ. Sci. Technol. 40, 4916–4921. https://doi.org/10.1021/es0603195.
Nania, V., Pellegrini, G.E., Fabrizi, L., Sesta, G., Sanctis, P. De, Lucchetti, D., Di Pasquale, M., Coni, E., 2009. Monitoring of perfluorinated compounds in edible fish from the Mediterranean Sea. Food Chem. 115, 951–957. https://doi.org/10.1016/j.foodchem.2009.01.016.
Nikolaou, A., Meric, S., Fatta, D., 2007. Occurrence patterns of pharmaceuticals in water and wastewater environments. Anal. Bioanal. Chem. 387, 1225–1234. https://doi.org/10.1007/s00216-006-1035-8.
Nödler, K., Voutsa, D., Licha, T., 2014. Polar organic micropollutants in the coastal environment of different marine systems. Mar. Pollut. Bull. 85, 50–59. https://doi.org/10.1016/j.marpolbul.2014.06.024.
Núñez, M., Borrull, F., Pocurull, E., Fontanals, N., 2015. Pressurized liquid extraction followed by liquid chromatography with tandem mass spectrometry to determine pharmaceuticals in Mussels. J. Separ. Sci. 39, 741–747. https://doi.org/10.1002/jssc.201501046.
Organisation for Economic Cooperation and Development, 2015. Working towards a Global Emission Inventory of PFASS: Focus on PFCAS – Status Quo and the Way Forward. Environment, Health and Safety Publications Series on Risk Management No. 30. http://www.oecd.org/chemicalsafety/risk-management/Working%20Towards%20a%20Global%20Emission%20Inventory%20of%20PFASS.pdf.

(Accessed 28 August 2018).
Oros, D.R., Hoover, D., Rodigary, F., Crane, D., Sericano, J., 2005. Levels and distribution of polybrominated diphenyl ethers in water, surface sediments, and bivalves from the san Francisco estuary. Environ. Sci. Technol. 39, 22–41. https://doi.org/10.1021/es048905q.
Pérez-Fuentetaja, A., Mackintosh, S.A., Zimmerman, L.R., Clapsadl, M.D., Alaee, M., Aga, D.S., 2015. Trophic transfer of flame retardants (PBDEs) in the food web of Lake Erie. Can. J. Fish. Aquat. Sci. 72, 1886–1896. https://doi.org/10.1139/cjfas-2015-0088.
Pugajeva, I., Rusko, J., Perkons, I., Lundanes, E., Bartkevics, V., 2017. Determination of pharmaceutical residues in wastewater using high performance liquid chromatography coupled to quadrupole-Orbitrap mass spectrometry. J. Pharmaceut. Biomed. 133, 64–74. https://doi.org/10.1016/j.jpba.2016.11.008.
Quinete, N., Wu, Q., Zhang, T., Yun, S.H., Moreira, I., Kannan, K., 2009. Specific profiles of perfluorinated compounds in surface and drinking waters and accumulation in mussels, fish, and dolphins from southeastern Brazil. Chemosphere 77, 863–869. https://doi.org/10.1016/j.chemosphere.2009.07.079.
Reinholds, I., Pugajeva, I., Zacs, D., Lundanes, E., Rusko, J., Perkons, I., Bartkevics, V., 2017. Determination of acidic non-steroidal anti-inflammatory drugs in aquatic samples by liquid chromatography-triple quadrupole mass spectrometry combined with carbon nanotubes-based solid-phase extraction. Environ. Monit. Assess. 189. https://doi.org/10.1007/s10661-017-6304-9.
Renzi, M., Guerranti, C., Giovani, A., Perra, G., Focardi, S.E., 2013. Perfluorinated compounds: levels, trophic web enrichments and human dietary intakes in transitional water ecosystems. Mar. Pollut. Bull. 76, 146–157. https://doi.org/10.1016/j.marpolbul.2013.09.014.
Santos, L.H.M.L.M., Araújo, A.N., Fachini, A., Pena, A., Delerue-Matos, C., Montenegro, M.C.B.S.M., 2010. Ecotoxicological aspects related to the presence of pharmaceuticals in the aquatic environment. J. Hazard Mater. 175, 45–95. https://doi.org/10.1016/j.jhazmat.2009.10.100.
So, M.K., Taniyasu, S., Lam, P.K.S., Zheng, G.J., Giesy, J.P., Yamashita, N., 2006. Alkaline digestion and solid phase extraction method for perfluorinated compounds in mussels and oysters from south China and Japan. Arch. Environ. Contam. Toxicol. 50, 240–248. https://doi.org/10.1007/s00244-005-7058-x.
State Agency of Medicines, 2017. Statistics on Medicines Consumption. https://www.zva.gov.lv/doc_upl/zva-zstat-2017.pdf?c. (Accessed 15 June 2018).
Ternes, T.A., 1998. Occurrence of drugs in German sewage treatment plants and rivers. Water Res. 32, 3245–3260. https://doi.org/10.1016/S0043-1354(98)00099-2.
Van Ael, E., Covaci, A., Blust, R., Bervoets, L., 2012. Persistent organic pollutants in the Scheldt estuary: environmental distribution and bioaccumulation. Environ. Int. 48, 17–27. https://doi.org/10.1016/j.envint.2012.06.017.
Vandermeersch, G., Lourenço, H.M., Alvarez-Muñoz, D., Cunha, S., Diogène, J., Cano-Sancho, G., Sloth, J.J., Kwadijk, C., Barcelo, D., Allegaert, W., Bekaert, K., Fernandes, J.O., Marques, A., Robbens, J., 2015. Environmental contaminants of emerging concern in seafood - European database on contaminant levels. Environ. Res. 143, 29–45. https://doi.org/10.1016/j.envres.2015.06.011.
Wang, Z., Ma, X., Lin, Z., Na, G., Yao, Z., 2009. Congener specific distributions of polybrominated diphenyl ethers (PBDEs) in sediment and mussel (*Mytilus edulis*) of the Bo Sea, China. Chemosphere 74, 896–901. https://doi.org/10.1016/j.chemosphere.2008.10.064.
Xie, Z., Lu, G., Liu, J., Yan, Z., Ma, B., Zhang, Z., Chen, W., 2015. Occurrence, bioaccumulation, and trophic magnification of pharmaceutically active compounds in Taihu Lake, China. Chemosphere 138, 140–147. https://doi.org/10.1016/j.chemosphere.2015.05.086.
Zabaleta, I., Bizkarguenaga, E., Prieto, A., Ortiz-Zarragoitia, M., Fernandez, L.A., Zuloaga, O., 2015. Simultaneous determination of perfluorinated compounds and their potential precursors in mussel tissue and fish muscle tissue and liver samples by liquid chromatography-electrospray-tandem mass spectrometry. J. Chromatogr. A 1387, 13–23. https://doi.org/10.1016/j.chroma.2015.01.089.
Zacs, D., Rjabova, J., Fernandes, A., Bartkevics, V., 2016. Brominated, chlorinated and mixed brominated/chlorinated persistent organic pollutants in European eels (*Anquilla anquilla*) from Latvian lakes. Food Addit. Contam. A 33, 460–472. https://doi.org/10.1080/19440049.2015.1136436.