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Review

PBDEs in environmental samples: Sampling and analysis

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ABSTRACT

The paper reviews the subject literature concerning analytical procedures routinely sed for monitoring polybrominated diphenyl ethers (PBDE) in environmental samples.

It describes and summarizes subsequent stages of analytical procedure including sample collection and preparation, extraction, clean-up and final determination. Different approaches with their advantages and limitations are presented. Special attention is drawn to the newly developed, promising extraction techniques, especially: liquid–liquid-microextraction (LLME) with its modifications, cloud point extraction (CPE) and hollow fiber microextraction. The review compares available detection techniques taking into account their usefulness for determining different PBDEs in complex matrix as well as discussing possible limitations that may occur during the analysis. The quality assurance and quality control aspect of analytical procedure is described. Finally special attention is paid to the determination of highly brominated PBDE compounds (e.g. BDE209), which requires implementation of different analytical approach.

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Abbreviations: APCI, atmospheric pressure chemical ionization; APPI, atmospheric pressure photoionization; ASE, accelerated solvent extraction; ASTM, American Society for Testing and Materials; BFR, brominated flame retardants; CPE, cloud point extraction; DCM, dichloromethane; DLLME, dispersive-liquid–liquid-microextraction; ECD, electron capture detector; ECNI, electron capture negative ionization; EIMS, electron impact mass spectrometry; GC, gas chromatography; GFF, glass fiber filter; GPC, gel permeation chromatography; HF-LPM, hollow fiber microporous membrane liquid–liquid extraction; HF-LPME, hollow fiber liquid phase microextraction; HF-MMLLE, hollow fiber micro-porous membrane liquid–liquid extraction; HPLC, high pressurized liquid chromatography; HRMS, high resolution mass spectrometry; ICP-MS, plasma coupled mass spectrometry; IUAPC, The International Union of Pure and Applied Chemistry; IM, ion mobility; LC, liquid chromatography; LLE, liquid–liquid extraction; LLME, liquid–liquid microextraction; LRMS, low resolution mass spectrometry; MAE, microwave assisted extraction; MSD, mass selective detector; MS, mass spectrometry; MWCNTs-SPME, multi walled carbon nanotubes-solid phase microextraction; PBB, polybrominated biphenyls; PBDEs, polybrominated diphenyl ethers; PCBs, polybrominated biphenyls; PCDD/F, polychlorinated dibenzodioxines; POPs, persistent organic pollutants; QA/QC, quality assurance/quality control; PTV, programmed temperature vaporizing injector; PTV-LV, programmed temperature vaporizing large volume injector; QFF, quarto fiber filter; QISTMS, quadrupole ion storage mass spectrometry; QuEChERS, quick easy cheap effective rugged safe; SBSE, stir bar sorptive extraction; SFE, supercrtical fluid extraction; SPE, solid phase extraction; SPE-DLLME, solid phase liquid–liquid-microextraction; SPLE, selective pressurized liquid extraction; SPME, solid phase microextraction; SVOC, semivolatile organic compounds; TOF, time of flight (analyzer); UPLC, ultra performance liquid chromatography; USAE, ultrasound assisted extraction; USAL-DPSE-DLLME, ultrasound-assisted leaching-dispersive solid-phase extraction followed by dispersive liquid–liquid microextraction.

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1. Introduction

1.1. Polybrominated diphenyl ethers; characteristics and distribution

Polybrominated diphenyl ethers (PBDEs) belong to the group of brominated flame retardants (BFRs), introduced in middle of 70s of XX century, in response to the ban of previously used flame retardants, such as polychlorinated biphenyls (PCBs) and polybrominated biphenyls (PBBs) [1]. Since then, the interest in behavior of PBDEs and their distribution into different compartments of environment has systematically increased. This can be reflected in the increasing number of articles published on the issue of chemical analysis of PBDEs during the last 10 years (Fig. 1). According to the ISI Web of Knowledge^{SM}, there have been more than 30 review articles published on the issue of BFRs so far. The most frequently citied review articles, together with their main scientific scopes are listed in Table 1.

According to the scientific papers, 209 congeners are classified as PBDEs, among which all contain diphenyl ether skeleton and all are named according to the number and position of bromine atoms by the IUPAC system [10]. Chemical structure of polybrominated diphenyl ethers (PBDEs) is presented in Fig. 2.

Polybrominated diphenyl ethers are applied as additives to numerous polymers; plastics, textiles, and other materials to prevent or retard the spread of fire. Thus they are present in the wide range of consumer products, such as, furniture electrical or electronic devices and automobile parts [11]. Examples of materials in which different mixtures of PBDEs are present are listed in Table 2. Despite wide range of applications, not all of PBDEs are employed in commercially available mixtures: penta-, octa- and decaBDE. The pentaBDE mixture is mostly applied in furniture, while the two other remaining higher-brominated mixtures (octa- and decaBDE) are employed in hard plastics, house electrical equipment, such as TV sets and computers. PBDEs are easily integrated into polymers during manufacture process, however, due to the lack of binding sites on polymers surface are not chemically bonded to the material. Therefore PBDEs are classified as additive flame retardants and can be easily released into environment by volatilization or dust formation during the use of treated products. According to the reviews published on this issue, PBDEs are distributed into all compartments of environment (Fig. 3) [12,13]. The environmental fate of different congeners depends to a large extent on their chemical properties, such as partitioning coefficients. Therefore pentaBDE is reported to be present mainly in the atmosphere and aqueous media, while higher brominated compounds (e.g. BDE209) tend to accumulate in soil and sediments [6].

Polybrominated diphenyl ethers tend to bioaccumulate, especially in aqueous organisms. Swedes Andersson and Blomkvist were first who in 1981 detected PBDEs congeners in freshwater species collected along the Viskan River in southern Sweden. Then, few years later Jansson confirmed the presence of PBDE in tissues of fish-eating birds and marine mammals living in Baltic

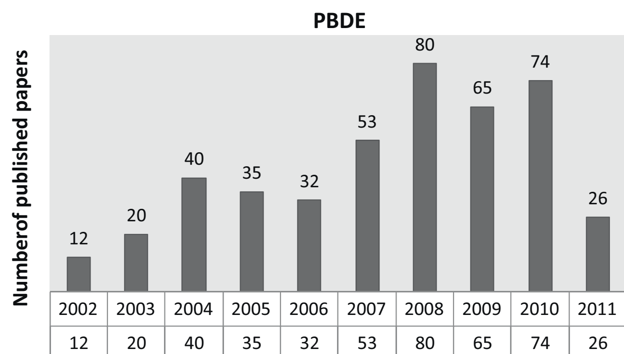

Fig. 1. Number of papers published on PBDEs issue since 2002.

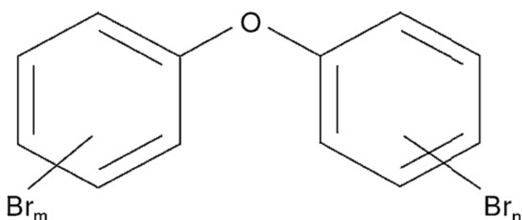

Fig. 2. Chemical structure of polybrominated diphenyl ethers (PBDEs).

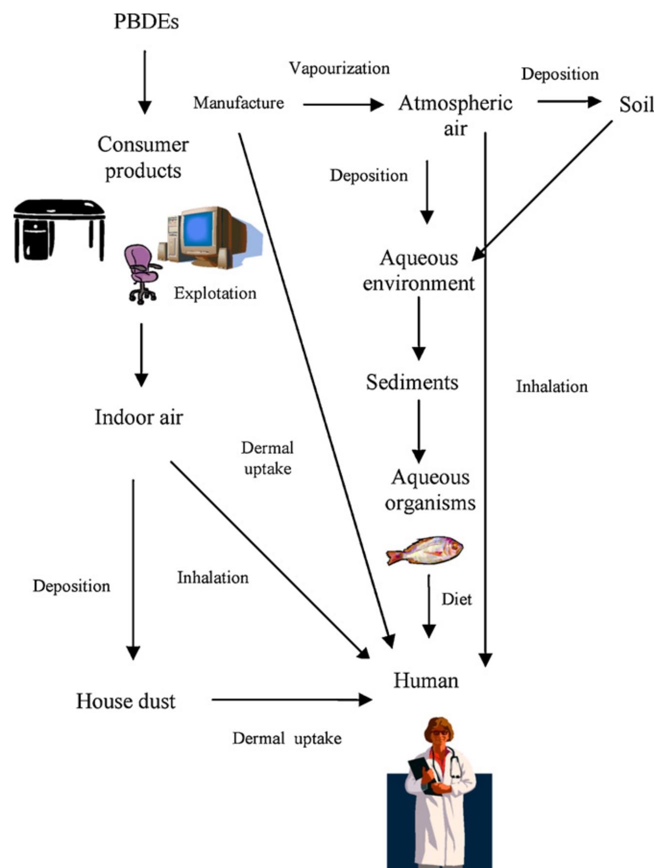

Fig. 3. The scheme of PBDEs circulation and environmental fate.

Table 1
Literature information on the selected review articles published on the issue of BFRs in recent 10 years.

Year of publication	Title	Scope	Reference
2011	"Novel brominated flame retardants: a review of their analysis, environmental fate and behavior"	This review presents information about production, properties, analysis, environmental occurrence, fate, behavior and human exposure to the newly observed BFRs.	[2]
2010	"Application of mass spectrometry in the analysis of PBDEs"	Authors reviews the literature information on novel, promising detection techniques to determine of PBDEs in environmental samples	[3]
2009	"A review of the challenges in the chemical analysis of the polybrominated diphenyl ethers"	Author present literature information on the analysis of PBDE in environmental samples.	[4]
2009	"Environmental analysis of higher brominated diphenyl ethers and decabromodiphenyl ethane"	Authors describes possible limitations that may occur during subsequent stages of analytical procedure for determining decabromodiphenyl ethane and BDE209 in environmental samples	[5]
2009	"Human internal and external exposure to PBDEs – a review of levels and sources"	Authors reviews current literature on the human exposure PBDEs with particular focus on external exposure routes (e.g. dust, diet, and air) and the resulting internal exposure to PBDEs (e.g. breast milk and blood).	[6]
2008	"Polybrominated diphenyl ethers: causes for concern and knowledge gaps regarding environmental distribution, fate and toxicity"	Authors presents literature information on distribution, environmental fate and toxicity of different congeners classified as PBDEs regarding the number of bromine ions in the chemical structure	[7]
2006	"Instrumental methods and challenges in quantifying polybrominated diphenyl ethers in environmental extracts: a review"	Authors reviews current literature on the analysis of BFRs in environmental samples with complex matrix	[8]
2005	"Human exposure to polybrominated diphenyl ethers through the diet"	Article describes the state of the science regarding human exposure to PBDEs through the diet.	[9]

and Northern Sea, as well as in the remote areas of Arctic, thus indicating a widespread environmental fate of PBDEs and their long-range transport [14].

Polybrominated diphenyl ethers (PBDEs) are considered as emerging class of contaminants, therefore some regulations have been adopted by different World and European organizations in order to minimize the use of PBDEs in manufacturing process. The use of commercially available mixtures was banned by European Union (pentaBDE and octaBDE in 2004 and decaBDE in 2008). In certain countries the use of decaBDE has been banned independently, since January of 2007 (e.g. Sweden). Compared to European Union, in U.S. is still in the phase out legislation for PBDEs. So far only California has officially banned the use of PBDEs mixtures (2008), but U.S. producers and the main U.S. importer of the decaBDE committed to end production, import and sales of the chemical for all consumer, transportation, and military uses, by the end of 2013 [15,16].

Detection of brominated flame retardants (BFRs), including PBDEs, in environmental samples has recently spurred scientific investigation. Despite the fact that several studies reported increased concentration levels of PBDEs in human samples (e.g. breast milk), it is remarkable that so far, no standard analytical procedures have been adopted for these analytes. Nevertheless EPA continues to evaluate and assess the risk posed by exposure to PBDEs [16]. So far, the following oral reference doses (RfD) have been accepted for PBDEs:

- 7×10^{-3} mg/kg-day for the decaBDE,
- 3×10^{-3} mg/kg-day for the octaBDE,
- 2×10^{-3} mg/kg-day for the pentaBDE.

1.2. Toxicological properties and human exposure to PBDEs

Although some restrictions have been made in 90s of XX century by European Union on the use of certain PBDEs compounds (penta- and decaBDE), the available evidence for impact of PBDES on human health is still surprisingly limited. Moreover toxicological information is still focused mainly on mixtures – much less information is available on the individual congeners. What has been certainly confirmed is structural similarity of PBDEs to thyroid hormones and polychlorinated biphenyls (PCBs). Available evidence suggests that the majority of congeners easily bioaccumulate in human tissues [6,9]. But what should be mentioned here as well, this is true for all congeners apart from BDE209. The highly brominated deca-BDE congener is poorly absorbed and does not bioaccumulate; it is one of the least bioactive congeners classified in PBDEs group [17].

It has been reported that human exposure to persistent organic compounds (POPs), such as PBDEs (particularly the lower brominated congeners) happens primarily through the diet. This is mainly due to the tendency of POPs to absorb in aquatic organisms. Therefore fish consumption, especially these from contaminated areas is considered major way of human exposure to PBDEs (especially to mid brominated congeners: tetra-to hexaBDE). Recently

Table 2
The content of mixtures of PBDEs in different materials [11].

Material	Mixtures of PBDE	Applications
Epoxy resins	DecaBDE	Adhesive laminates, construction elements for shipbuilding industry, electronic components, etc.
Polymer resins	Penta BDE, decaBDE	Panels, electrical and electronic equipment, military, etc.
Phenolic plastics	Penta BDE, decaBDE	Laminate flooring, automotive interior parts, electrical and electronic devices, etc.
Polyurethane foam	Penta BDE	Upholstery, sound and thermal insulation, automotive seating, furniture coverings, etc.
Polypropylene	DecaBDE	Coatings, automotive interior parts, electrical and electronic devices, etc.
Polystyrene	OktaBDE, decaBDE	Packaging industry, smoke detectors, electrical devices, etc.
Polyamide fibers	OktaBDE, decaBDE	Electronic devices, construction elements for car industry, etc.
Rubber	Penta BDE, decaBDE	Insulation for electrical wiring, etc.
Paints and varnishes	Penta BDE, decaBDE	Shipbuilding industry, protective paints for painting the hulls of ships, etc.
Textiles	Penta BDE, decaBDE	Coverings, furniture, tents, military

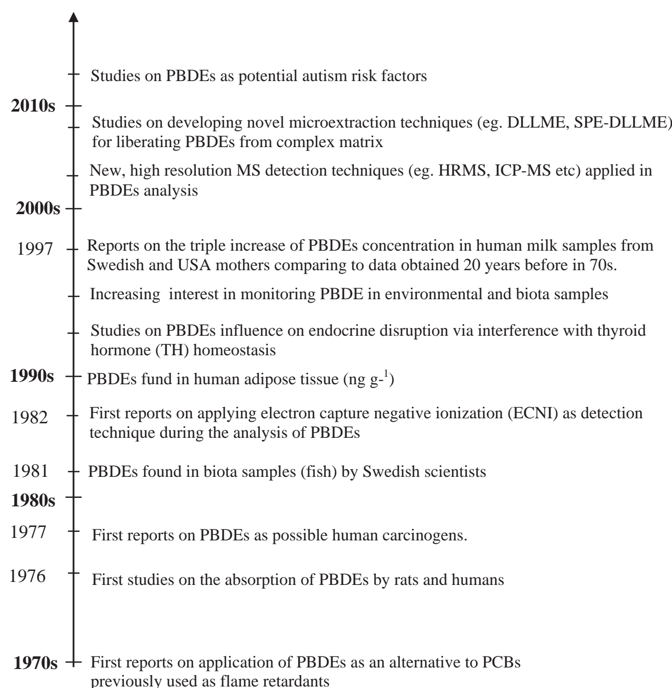

Fig. 4. The milestones in extending of knowledge on the role of PBDEs in environmental chemistry [14,18–22].

there has been much data published on the issue regarding PBDEs concentration levels in different fish species (e.g. salmon, tuna, etc.). But still not much information is available on PBDEs content in other food groups or possible differences that may occur in PBDEs concentration levels between different countries [4,6,9].

Inhalation of air polluted by PBDEs is usually mentioned as an important way of occupational exposure to higher brominated congeners: hepta- to decaBDE.

Increasing concentration levels of PBDEs in human tissues (e.g. blood, serum, breast milk, etc.) have caught worldwide concern due to their potential tendency to disrupt thyroid hormones, neurobehavioral deficits and endocrine effects in laboratory mammals [6]. There are lots of studies currently being carried out considering PBDEs as an autism potential risk factors [9] as well as some other, investigating the possibility of PBDEs to be transferred via placenta and breast milk from the mother to the infant [4,6]. What has been confirmed so far, is the fact that the concentrations of less brominated congeners in human tissues are usually higher than those of their higher brominated counterparts. Vonderheide et al. reported that although the concentration profiles of different PBDE congeners differ depending on the region, in most samples the major congener was BDE47 [4]. In fact it is still unclear whether the presence of PBDEs in human tissues significantly affects human health or not. This indicates the need for more accurate information in that field and calls for more systematical studies to be carried out in the future. The milestones in extending knowledge on PBDEs issue, which have been reported so far are presented in Fig. 4.

2. Determination of PBDEs in environmental and biota samples

Increasing concentration levels of PBDEs observed in indoor environment (house dust), human tissues (breast milk, serum, etc.) as well as environmental samples (water, soil, sediments, biota, etc.) result in significant increase of attention that is now paid to the analysis of PBDEs. One of the main limitations, in case of analysis of SVOC compounds, is still the lack of analytical procedure that would allow the simultaneous analysis of more than one group of SVOC compounds. This results mainly from the fact that most analytical procedures, developed for the determination of PBDEs have to face the problems such as complex composition of matrix that in particular means co-elution of interfering compounds and the need for removal them. Moreover analysis of highly brominated PBDE compounds (e.g. BDE209) usually requires different approach to be adopted to eliminate the risk of lost of analytes (e.g. degradation due to the high temperature).

This paper gives a critical overview of available, commonly used analytical procedures for the determination of PBDEs in environmental (e.g. water, sediment, soil, biota, dust, etc.) and human (blood, milk, tissue) samples. Each of subsequent stages of analytical procedure, which includes: sample collection and preparation, extraction, clean-up and final determination is described separately. Different approaches with their advantages and limitations are presented. Some newly developed solutions or modifications of existing procedures are mentioned as well.

Special attention is paid to the determination of higly brominated PBDE compounds, especially BDE209.

3. Sample collection and preparation

Sample collection and preparation is considered crucial stage in the whole analytical procedure due to the significant risk of committing error. This refers mainly to the possible lost of analytes and contamination of the sample. It is particularly important while only representative and homogeneous samples ensure measurable results to be obtained. Sampling procedures usually differ depending on the properties of the matrix.

3.1. House dust

In case of house dust, sampling procedure is described in detail in method D 5438-00, published by the American Society for Testing and Materials (ASTM) [22]. Normally dust samples are collected during the regular usage (e.g. while cleaning) of indoor environment (e.g. household, laboratory, automobile, etc.) from horizontal, non-electrostatic surfaces, such as floor, carpet, windows or furniture (e.g. bookshelves) [23–25]. The type of analytical information to be obtained affects the choice of sampling sites. Basically there are two types of dust providing different type of information:

- attic dust – lies undisturbed for months or years in inaccessible places such as attics, cellars and the spaces under furniture, on long untouched books, old newspapers. Because of limited access of light the natural degradation of organic compounds in dust is very much slower. This makes it possible to identify compounds that were present in this indoor environment many months or years ago.
- fresh dust – of known age; collection of house dust is done systematically [26,27].

What should be mentioned here, some difficulties may occur at the sampling stage of automobile dust. It usually results from the fact that dust may not originate directly from the vehicle interior components, but from the outside (e.g. atmospheric aerosols, soil from the bottom of occupants shoes, etc.) and may not be representative, in terms of human exposure to vehicle materials of construction [22].

House dust is most often collected using vacuum cleaner but all kinds of brooms, brushes, dustpans or tweezers can be also applied. These have to be previously pre-cleaned in ultrasonic bath with deionized water before sampling can be done. Such treatment allows to eliminate the wall memory effect. After removal of solid

parts, such as hair, dust is sieved using stainless steel sieve (e.g. <150 mesh). In order to remove microorganisms, dust is often sterilized using gamma radiation [23,28].

3.2. Environmental samples (e.g. soil sediments, etc.)

In case of collection of environmental samples, such as soil or sediments, sampling procedure is often similar to this applied to dust samples. Sediments are collected using different stainless steel shovels. It can be done using either grab sampler (e.g. Van Veen grab sampler) [29,30] or, as it has been reported by Zhao et al., by wrapping samples in aluminum foil [31]. Sampling of sediment cores requires gravity corer to be used [32]. After sampling is completed, samples are transported in pre-cleaned, self sealing, aluminum-polyethylene bags to the laboratory [30]. Samples are then stored at low temperatures (<−5 °C), in amber glass bottles covered with solvent-rinsed aluminum foil. This allows to protect them from the access of light. Before further analysis can be done samples are homogenized and wet-sieved using stainless steel sieve (e.g. 2 mm) to remove solid parts. Wet sieving is considered more appropriate than dry sieving mainly due to possible carryover of fine particles that may get into the coarser while dry sieving. Slurries obtained are finally frozen, air-dried, and stored [33,34]. Fractionation of sediments prior to the analysis has been reported by Zhao et al. [30].

3.3. Food and human samples

The collection of food samples (e.g. fish, meat or vegetables) often applies tin foil or normal plastic bag. Collected samples are then cut, homogenized and stored frozen (−20 °C) prior to the following analysis [35]. Depending on the aim of investigation, different parts of collected samples are analyzed. As an example, in case of fish samples, the whole fish (including skin and bones) may be analyzed or if consumption study is to be carried out, only the edible part is analyzed.

Human blood or milk samples are often collected using pre-cleaned amber glass containers equipped with *Teflon* caps [36]. After sampling is done, samples are stored in minus temperature, up to −20 °C prior to the lyophilization and further analysis [28,37]. In case of whole blood samples, an anticoagulant (e.g. heparin) is often used to avoid break down of the sample. Recently, an alternative for the preservation of blood by adding potassium dichromate has been reported. As serum samples are relative homogeneous, in case of milk and whole blood samples special attention should be paid to obtain a homogenous sample for analysis. This can be reached by intensive shaking at room temperature [38]. While analyzing placenta samples, the umbilical cord has to be removed. Placenta samples are often cut into small pieces and homogenized in commercial blender. Then homogenates are freeze-dried in lyophilizer and stored in amber glass bottles in desiccator [39].

3.4. Air samples

Air samples as well as airborne PBDEs are collected using either active or passive sampling technique. Active sampling often implies high volume samplers (4–6 l min^{-1}). Hazrati and Harrad sampled 430 m^3 of air applying polyurethane plugs during the whole sampling campaign of 50 days. In order to minimize the risk of breakthrough, PUF plugs were exchanged at the end of each 10-days sampling period. The total of five PUF plugs were then combined and analyzed as a single sample [40]. The use of active sampling has been more frequently reported in the literature as it is considered less time consuming and offers higher enrichment factor than those obtained using passive sampling. Both active and passive sampling techniques commonly employ polyurethane foam (PUF) as a sorbent medium [41,42]. It is mainly due to its universal properties, which allow to retain wide range of organic compounds. For collecting airborne PBDEs, quartz (QFF) or glass (GFF) fiber filters are successfully used [42]. The use of membrane filter (0.8 μm pore size) was also reported in the literature [40]. Prior to the sampling of PBDEs, PUF plugs are pre-cleaned with water-detergent solution and pre-extracted (applying the same extraction technique and the same organic solvent that are applied during liberating of analytes). QFF and GFF are often activated prior the sampling process using high temperatures [41–43].

4. Extraction techniques

Analysis of complex matrix, such as sediments, biota, house dust, food or human tissues often requires implementation of multistage sample preparation procedure. This, referred as a stage of significant importance in the whole analytical procedure in particular determines the quality of obtained results. Sample preparation, in case of PBDEs analysis, involves extraction, preconcentration (when necessary) and clean up prior to final determination by instrumental techniques (e.g. gas chromatography) [44]. Careful optimization of extraction process requires verification of following parameters influencing extraction efficiency:

- Type of organic solvent, its polarity and density, both of which determinate solvent ability to penetrate the matrix. The main role of extraction solvent is to solubilize analytes of interest as well as to eliminate the co-extraction of other interfering matrix components (according to the published data, DCM and n-hexane, toluene or the mixtures of DCM-n-hexane (1:1) or n-hexane-acetone (1:1), (4:1) [45] are most often applied organic solvents during the extraction of PBDEs).
- Time of extraction process, the number of extraction cycles in case of ASE.
- Temperature of extraction process, efficiency of extraction usually increases with the increase of temperature. This is due to the reduction of solvent viscosity that allows better permeation of solvent into matrix surface. But on the other hand too high temperature of extraction process increases the co-elution of interfering compounds or may lead to the degradation of higher brominated congeners [46].
- Pressure of extraction process in case of ASE [46,47].

Extraction techniques, which are commonly used in liberating PBDEs from environmental, food and human samples together with their advantages and drawbacks are presented in more detail in Fig. 5.

Literature information about the comparison of available extraction techniques together with their applications is listed in Table 3.

All extraction techniques both temperature or pressure enhanced (e.g. ASE or MAE, etc.) are reported to provide better results than traditional Soxhlet or SPE extraction techniques for extracting PBDEs (non-degradable congeners) from solid samples (e.g. house dust, soil, food, etc.) [45–48]. It is due to the increase of analytes solubility in organic solvent that, in turn weakens interaction between analytes and matrix. All extraction techniques mentioned above show significant advantage of reducing extraction time and solvent consumption. But what seems worth noting is the fact that extraction conditions, especially temperature has to be optimized carefully in case of analysis of highly brominated congeners (hex-decaBDE) to avoid debromization and obtain optimum extraction efficiency [46]. The choice of proper organic solvent or mixture of solvents is often a matter of concern. It depends strongly on the extraction technique (e.g. MAE requires polar organic solvent to be applied [45,46]) and matrix characteristics. As an example, soil has high organic carbon content, while high lipid content is

Table 3
Literature information on extraction techniques commonly used in PBDEs analysis in environmental and biota samples.

Extraction technique	Extraction time	Solvent consumption	Extraction temperature	Extraction pressure	Application	Cost
Soxhlet	8–48 h	50–300 ml	Boiling point temperature (BPT) of solvent used for liberating analytes	Atmospheric pressure	Dry and wet sludge, 16 h, 300 ml of hexane-acetone (1:1) [50] Soil, 18 h, hexane-acetone (1:1) [51] Human placenta, 22 h, 150 ml of acetone-hexane-dichloromethane (4.5:4.5:1) [39] House dust, 24 h, acetone-hexane (1:1) [52] Human hair, 24 h, methanol-methylene chloride (1:1) [53] Electronic equipment, 5 h, 60–100 ml of toluene [54] Fish and soil samples, 24 h, 150 ml of hexane-acetone (1:1) [55]	Low
ASE	20–60 min	15–75 ml	Up to 150 °C	Pressurized	Sediments, 100 °C, 6 MPa, dichloromethane-hexane (1:1) [56] Soil, 100 °C, 6 MPa, dichloromethane-hexane (1:1) [57] Fish and soil, 100 ml of hexane-acetone (1:1), 150 °C, 6 MPa [55]	High
UAE	15–60 min	50–150 ml	Up to 80 °C	Atmospheric pressure	Marine foodstuffs, 1 h, hexane-dichloromethane (1:1) [58] Soil samples placed in the glass column, 15 min, 5 ml of ethyl acetate, room temperature [59] Bird eggs, 3 cycles of sonication, dichloromethane-hexane (1:1) followed by standing and decantation [37]	Low
MAE	20–40 min	20–50 ml	Up to 150 °C	Pressurized	Dry and wet sludge, 35 min, 130 °C, 1 MPa [50] Fish and soil, 50 min, 30 ml of hexane-acetone (1:1), 115 °C [55] Electronic equipment, 10 min, 10 ml of hexane, 100 °C [54]	High
SFE	30–60 min	10–50 ml	Up to 150 °C	Pressurized	House dust, supercritical 1,1,2,4 tetrafluoroethane (R134a) 20 ml, 100 °C, 150 °C 200 °C, extraction of dry dust, dry dust dispersed on Ottawa sand, wet dust with dichloromethane [60] Sediment samples, supercritical CO_2, 60 min, 120 °C [61]	High
SPE	30–60 min	Up to 100 ml	–	Atmospheric pressure	Human serum with HLB copolymer with hydrophilic-lypophilic balance, SPE cartridges eluted with 4 ml of toluene [49] Sheep serum, conditioning (5 ml of dichloromethane, followed by 5 ml of 5% methanol in hydrochloric acid), elution with 15 ml of dichloromethane, Snow samples, C18 solid phase disks, pre cleaning with 10 ml of dichloromethane-cyclohexane (1:1), conditioning with 10 ml of methanol, elution with Milli-Q water [62]	Low

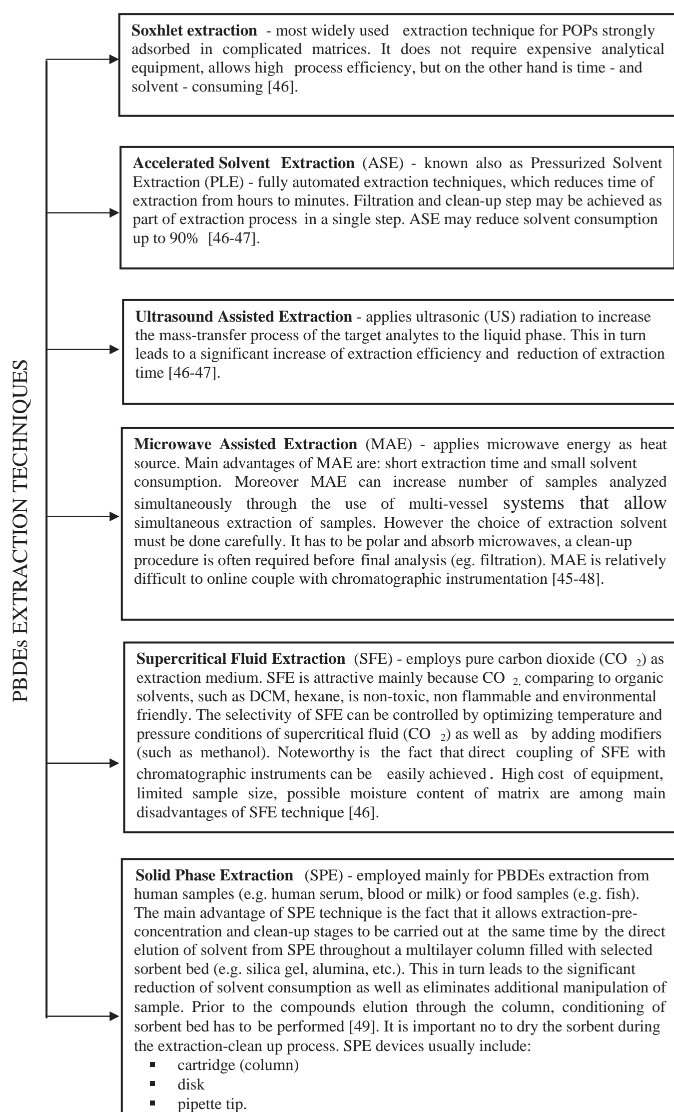

Fig. 5. The characterization of common extraction techniques used for extracting PBDE from environmental and biota samples.

typical for food samples. High protein content is in turn characteristic for human milk samples, which significantly affects extraction efficiency [46–48].

An interesting modification of typically used ASE extraction technique may be pressurized liquid extraction combined with clean-up of the extract also known as *on-line* ASE or selective pressurized liquid extraction (SPLE). SPLE significantly reduces the need for implementation of post-clean-up procedures, such as solid phase extraction (SPE) or gel-permeation chromatography. In recent years, SPLE has been developed for the analysis of wide range of persistent organic pollutants (POPs), including PBDEs in environmental (e.g. house dust, sediments) and food samples [29]. The main impediment at the final determination step regards the simultaneous analysis of more than one group classified as POPs (e.g. PBDEs). Still very few articles have been published on that issue so far [29,63,64].

Recently the modifications of traditional Soxhlet extraction have been reported as well [65]. These refer mainly to the:

- high pressure Soxhlet extraction (6–10 MPa),
- automated Soxhlet extraction (combination of Soxhlet extraction and boiling reflux),
- ultrasound assisted Soxhlet extraction (Soxhlet chamber is placed into thermostatic chamber through which ultrasound is supplied by an ultrasonic probe [65],
- microwave assisted Soxhlet extraction.

All listed modifications of Soxhlet extraction allow to overcome main shortcomings of traditional Soxhlet extraction, so time and solvent consumption. According to the recent data, the most interesting and promising improvement of Soxhlet extraction seems to be microwave assisted Soxhlet extraction that gives the possibility to extract strongly retained analytes from solid matrix. More information on commercially available Soxhlet extractors together with their applications can be found in the review [65]. So far, high pressure solvent extraction has been successfully applied for isolation of POPs from vegetables [53], while automated Soxhlet extraction was reported as useful isolation technique for brominated compounds (BFRs) from human adipose tissue [66].

Limitations, which occur during extracting PBDEs from food samples result in verification of novel approaches. Among such novel approaches is the combination of traditional QuEChERS extraction, followed by liquid–liquid partition and dispersive solid phase extraction [65]. QuEChERS extraction originally developed for the analysis of multiple pesticide residues in high moisture–low fat matrix, has been successfully adopted by Kalachova et al. for determination of PBDEs in shrimps [64]. Compared to traditional QuEChERS extraction, acetonitrile was replaced by ethyl-acetate. Better capability of ethyl-acetate to penetrate into the high moisture matrix (e.g. shrimps) enables (by support of strong shaking) obtaining more effective isolation of non-polar analytes.

Another interesting approach is the combination of pressurized solvent extraction (ASE) and stir bar sorptive extraction (SBSE) [67]. Analytical procedure applied by Camino-Sanchez et al., for extracting PBDEs from sediments provides automatization together with minimal amount of solvent consumption. Additionally, applying SBSE allows pre-concentration of organic compounds in the PDMS layer with a very high enrichment factor [67].

Growing need for developing simple and low-cost extraction-preconcentration technique, providing high extraction efficiency, simultaneously with the possibility to extract wide range of analytes from complex matrix makes ongoing research continue.

As an result novel, alternative extraction techniques are systematically introduced and applied in the analysis of PBDEs.

5. Future trends in extracting PBDEs from complex matrix

From the environmental point of view as well as taking into account the rules of Green Chemistry, it is essential to develop an extraction technique which, in contrast to other commonly used techniques, will not consume large volumes of toxic solvents. Miniaturization of instrumentation, applied during extraction stage is not only considered to simplify analytical procedure but also to minimize the use of organic solvents. Moreover the need for reducing costs, decreasing time of analysis and increasing separation efficiency are main reasons for carrying out research on developing novel microextraction techniques.

Significant advantage of microextraction techniques, compared to other extraction techniques is the aspect of homogeneity and representativeness of small amounts of sample with the respect to the original sample. The interest in microextraction techniques started particularly as a result of introducing SPME technique by Pawliszyn as an alternative to other, solvent consuming extraction techniques, especially LLE. Since then, novel modifications, such as LLME, DLLME, SPE-DLLME as well as new techniques based on the use of solutions of surfactants (CPE) or carbon nanotubes (MWCNTs-SPME) have been systematically introduced into the analysis of PBDEs [68].

A. Liquid–liquid-microextraction
- Dispersive-liquid–liquid-microextraction (DLLME),
- Solid phase liquid–liquid micro extraction (SPE-DLLME) and
- Ultrasound-assisted leaching-dispersive solid-phase extraction followed by dispersive liquid–liquid microextraction (USAL-DPSE-DLLME).

Liquid–Liquid-Microextraction (LLME) was first introduced in the late 90s of XX century. Up to date modifications of LLME, such as dispersive-liquid–liquid-microextraction technique (DLLME) have been reported as promising extraction techniques for PBDEs, mainly from aqueous samples. DLLME employs a mixture of a high-density non-polar water imiscible solvent (extraction solvent) and polar water miscible solvent (disperser solvent). While analyzing water samples, the mixture of extraction solvent and disperser solvent is injected into the constant volume of aqueous sample, which leads to the formation of cloudy solution. Analytes in the sample are extracted into the extraction solvent and then separated usually by centrifugation. Simplicity, rapidity, low sample volumes, low cost and high preconcentration values are among major advantages of DLLME. The application of DLLME to solid samples still has not gained enough attention and only fruit (e.g. watermelon), vegetables (e.g. cucumber) and plant samples have been analyzed so far. One of the main impediments of DLLME extraction technique, in terms of analyzing PBDEs in environmental samples, is low enrichment factor that can be obtained (up to 1000). Moreover DLLME is not considered as a selective extraction technique. It cannot be acceptable, especially in case of trace and ultra trace analysis. The proper solution to this problem may be an inclusion of additional clean up stage before DLLME technique. Combination of SPE-DLLME resulting in significant increase of enrichment factor (up 10,000) and obtaining lower detection limit values can be a good example. However SPE-DLLME extraction technique is still more often applied to the analysis of aqueous samples, research is systematically carried out on the implementation of this technique to the solid samples as well [69].

As modification of SPE-DLLME, the combination of dispersive solid-phase extraction (DSPE) and DLLME has been introduced in the literature as simple and rapid extraction-clean-up technique. It is based on the addition of the sorbent material into the extract to remove the matrix interfering compounds. An interesting and promising analytical procedure – combination of ultrasound assisted leaching – dispersive solid phase liquid–liquid (USAL-DSPE-DLLME) has been also applied as an efficient extraction technique of PBDEs from sediment samples. The combination of USAL-DSPE leads to an increment of selectivity and sensitivity of analytical procedure. Moreover leaching the analytes from the sample provides cleaner extracts as matrix interferences remain in the sediment. The careful optimization of extraction parameters, such as type/volume of leaching solvent, type of sorbent (DSPE), time–temperature of ultrasonication and temperature of leaching is of course required. Especially time of ultrasonication is crucial to achieve an efficient USAL-DSPE extraction values. The US radiation may be applied in two different forms – continuous mode and cycle mode. More detailed information on USAL-DPSE-DLLME procedure for analyzing PBDEs in sediment samples can be found in the article [70].

B. Cloud point extraction (CPE)

Cloud point extraction (CPE) has recently gained broad attention as promising technique for extracting different POPs from aqueous samples. Its advantages, compared to other extraction techniques, include: high extraction efficiency, high enrichment factor and low-cost. One of its main advantages is that CPE employs non-toxic surfactants instead of organic solvents.

The main principle of CPE is based on phase separation tendency, exhibited by aqueous surfactants solutions that show ability to form aggregates-micelles. Surfactant solution is normally added to the aqueous sample containing analytes to be extracted/preconcentrated (PBDEs). When surfactant concentration exceeds its critical micellar concentration (CMC), formation of micelle aggregates commences. Optimizing of extraction conditions, e.g. altering or lowering of temperature and/or proper choice of additives (e.g. salt) allows obtaining proper phase separation. Analytes are then preconcentrated into a small volume of surfactant-rich phase, depending on its density, at the bottom or at the top of solution (Fig. 6). More detailed information regarding CPE technique can be found in the review [45].

As relatively novel approach, CPE technique has not been widely applied as extraction and pre-concentration technique in analysis of environmental samples so far. Up to date CPE has been more frequently applied for extracting compounds from water samples. Analytical procedure presented by Fontana et al. assumes applying CPE technique for extracting PBDEs from both water and soil samples [70]. Due to the high viscosity and low volatility of surfactant phase, sample cannot be injected directly onto GC column. Therefore supplemental stage has to be implemented before injection in order to avoid injector clogging and column deterioration. Ultrasound-assisted back-extraction (UAE) was selected as a suitable approach for coupling CPE to GC–MS [71].

C. Hollow fiber microextraction
- Hollow fiber liquid phase microextraction (HF-LPME),
- Hollow fiber microporous membrane liquid–liquid extraction (HF-MMLE),
- Multi walled carbon nanotubes-solid phase microextraction (MWCNTs-SPME).

The growing need for reduction of organic solvent consumption made the liquid phase microextraction (LPME) technique introduced. Comparing to liquid–liquid extraction (LLE), LPME is simple, rapid and inexpensive. It gives acceptable sensitivity and very good enrichment factor. The use of organic solvent (usually measured in microliters) is significantly reduced, even up to several thousand times [71].

Recently scientists from Denmark have introduced an alternative concept – Hollow Fiber-Liquid Phase Microextraction (HF-LPME) that employs porous, low-cost hollow fibers (usually made of polypropylene) to extract analytes from aqueous samples. More detailed information on extraction process using hollow fibers can be found in the review [71]. HF-LPME technique has been already applied for determining PBDEs congeners in various matrix, such as soil, house dust, human serum, etc. [68]. Comparing to solid phase microextraction (SPME), HF-LPME does not require complicated and expensive equipment that significantly simplifies analytical procedure. The fact that the hollow fiber is disposable eliminates the common problems for SPME technique, such as carryover effects between analyses and limited lifetime of the fiber.

An alternative or modification of HF-LPME extraction technique may be microporous membrane liquid–liquid extraction (HF-MMLLE). It is appropriate mainly for isolation and concentrating PBDEs compounds from aqueous samples [72]. HF-MMLLE is a two-phase (aqueous and organic) membrane extraction technique. The organic phase is supported by a hydrophobic membrane that keeps solvent in right position. The organic phase fills the membrane pores [29,72].

HF-MMLLE extraction technique followed by GC–MS instrumental analysis was reported to achieve good enrichment factors and allow determination of low ng levels of PBDEs [29].

As carbon materials have been successfully employed as adsorbents for separation of wide range of organic compounds from air or aqueous samples, carbon nanotubes (CNTs) are considered as

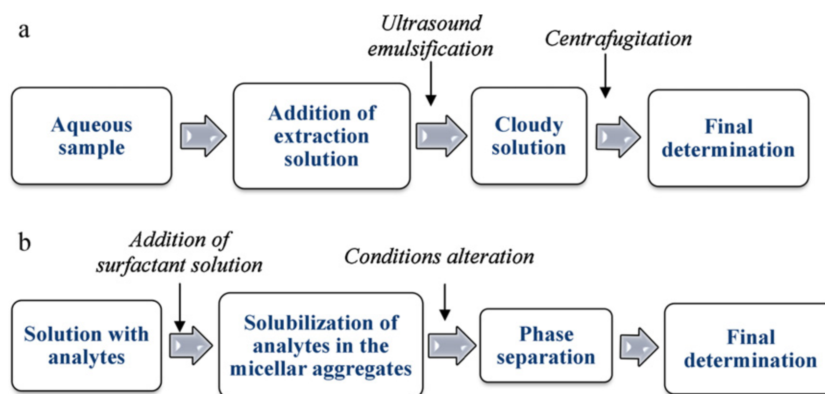

Fig. 6. The principle of (a) USAEME extraction technique, (b) cloud point extraction (CPE) [45].

promising coating material for fibers used for trapping PBDEs. It is mainly due to large adsorption surface and large internal pores volume.

Recently there has been an attempt made by scientists from China to develop new analytical procedure – SPME employing MWCNTs as fiber material for GC-ECD analysis of trace PBDEs in river water and human milk samples. Results of analysis confirmed the possibility to obtain high efficiency and proved that developed method gives promising results in terms of determining trace PBDEs in environmental and biological samples [73].

6. Clean up procedure

Before the last stage of analytical procedure – instrumental analysis follows, appropriate clean-up procedure has to be carried out. This is, very often described as multistage procedure to avoid co-extraction of other compounds, such as PCBs, humic acids or lipids.

As extracts from sediments, sewage sludge or soil samples often contain sulfur or water first step of purification implies treating them with copper powder (sulfur removal) and sodium sulphate (acts like a desiccant). In case of biota extracts, these usually contain high concentrations of lipids, which have to be removed prior to chromatographic analysis. What has been confirmed so far by scientific studies, PBDEs concentrations in food and human samples corresponds to the amount of lipids, so it should be measured gravimetrically prior to the clean-up step. The removal of lipids can be achieved either by destructive or by nondestructive methods. Sulfuric acid as well as silica gel impregnated with potassium hydroxide are among most often applied destructive methods that both may lead to destruction of analyzed compounds. *Alumina* has been reported to offer less harsh lipid removal than sulfuric acid or potassium hydroxide. It is very often used for further clean-up of extracts before the instrumental analysis [61]. The removal of lipids may be also achieved by combing both destructive and nondestructive techniques, first by reducing their solubility in hexane by cooling the extracts in dry ice/acetone and then by treating with the sulfuric acid [5]. Another common approach, which allows selective removal of lipids from biological extracts is gel permeation chromatography (GPC). The separation of interferences is usually done using polystyrene–divinylbenzene column but the combination of silica gel and *Florisil* can be employed as well [61]. GPC is often combined with traditional SPE technique [39].

Solid phase extraction (SPE) has been described as most popular technique for purification of extracts. More detailed information regarding SPE technique is presented in Fig. 5. Crucial task in case of applying SPE for extracts purification is the choice of appropriate sorbent bed and eluent solution. This depends mainly on the chemical properties of studied compounds as well as on the type of matrix. In case of PBDEs, high recoveries (up to 130%) for congeners from triBDE to heptaBDE were reported using both *Florisil* (2–5 g) [29,58,74,75] and *Alumina* (2–5 g) [29,76]. Low recoveries (<40%) were in turn obtained for lowest brominated compounds (mono-diBDE) [29]. It has been reported that recoveries tend to increase with the increase of the sorbent mass [56,49,76]. Good results were also obtained using different combinations of two or more SPE cartridges. As an example, Covaci et al. employed acid silica and acid silica-neutral silica-deactivated alumina column [76], while others used alumina-acid silica combination [42] or two sulfuric acid-silica gel columns [77]. The use of multilayer silica gel columns has been reported in literature [78] as well as silica gel column impregnated with active carbon [76].

In case of analyzing PBDEs in environmental and biological samples, the most important task is to minimize the influence of interfering compounds. It is often achieved by fractionation of extracts applying selective solid-phase extraction technique (SPE, which has particular importance in terms of separating PBDEs from other co-eluting compounds [79]. Silica gel has been found to retain PBDEs more strongly than other compounds (e.g. PCBs) thus allowing the fractionation of extracts upon the polarity of different classes of compounds. While applying n-hexane-DCM solution, almost all PCBs and PCDD/Fs are eluted prior to the PBDEs that are next group to be eluted. Neither *Florisil* nor *Alumin*a columns have the ability to separate PBDEs from PCBs or PCDD/Fs effectively. Moreover some studies report the significant loss of BDE209 congener while applying *Florisil* as sorbent [29,58]. For human blood or milk samples consider to be more complex matrix, multi-layer silica columns (e.g. silica gel–acidic silica gel–silica gel–KOH–silica–silica gel) are successfully employed. The most recent data report that inclusion of silver nitrate ($AgNO_3$) into multi-layer silica column may significantly increase its ability to separate PBDEs from other compounds. According to the scientists from China, good separation ratio of PBDEs from PCBs and PCDD/Fs can be achieved using silica column packed with silica gel including $AgNO_3$–silica [79]. More detailed information on different approaches applied for cleaning-up procedure are listed in Table 4.

7. Final determination step

7.1. Injection

The appropriate method of injecting analytes into the GC column ensures, among other things, the integrity of the sample [5]. According to data published recently, three most commonly used injection systems are often employed for analysis of PBDEs:

Table 4
Literature information on sample pre-treatment, extraction and clean-up procedure applied for PBDEs analysis in environmental and human samples.

Sample type	Pre-treatment	Extraction technique	Clean-up procedure	Detection	Reference
Fish (salmon, tuna, mackerel), vegetables (potatoes carrots), breast milk	Samples homogenized and freezed prior to the analysis.	Organic solvent extraction (toluene – 5 h) under reflux	Multi-layer column Na_2SO_4–10%$AgNO_3$–silica–22%H_2SO_4–silica–44% H_2SO_4–silica–silica–2%KOH–silica	HRMS-EI and LRMS-EI	[80]
Fish (salmon, conger eel, sea bass, green mussel)	Homogenization in a stainless steel blender	MAE extraction with pentane-dichloromethane (1:1)	Acidic silica gel column for lipids removal, GPC	EIMS	[45]
Freshwater fish	Fish samples were thawed, homogenized and stored at −20 °C.	Soxhlet extraction with 180 ml of hexane-DCM (1:1) for 24 h	GPC for lipids removal, glass wool–silica gel–acidic silica–silica gel–anhydrous sulphate column.	EIMS	[81]
Sediments	Surface sediment samples were freeze-dried, ground into powder and sieved (100 mesh)	Soxhlet extraction with 180 ml of hexane-DCM (1:1) for 24 h	GPC for lipids removal, glass wool-silica gel-acidic silica-silica gel-anhydrous sulphate column	EIMS	[81]
Fish	Fish samples collected in tin foil, stored in −20 °C.	Solvent extraction with cyclohexane-DCM	Acid treatment prior SPE (silica–alumina)	HRMS	[82]
Human milk	Milk samples collected in glass containers (50–100 ml), freezed in −20 °C and stored	Solvent extraction with pentane mixed with water, potassium oxalate, ethanol and ether	Acid treatment prior to SPE (silica–alumina column)	HRMS	[82]
Human blood	Blood samples collected in glass containers (50–100 ml), freezed in −20 °C and stored	Solvent extraction with n-hexane and hexane/isopropanol (3:2)	Columns filled with sodium sulphate–silica–sulfuric acid on silica–potassium silicate and alumina	HRMS	[82]
Human milk	Samples thawed and homogenized	Solvent extraction hexane-acetone (1:1)	Acid treatment, silica gel column	ECD	[83]
Human adipose tissue	Samples homogenized and stored at −20 °C	Soxhlet extraction (hexane-diethyl ether)	GPC for lipid removal, silica gel column	MSD	[67]
Human liver and adipose tissue	Samples collected in hexane-pre-washed polyethylene recipients, frozen and stored at −20 °C.	Soxhlet extraction (hexane-acetone 3:1)	Acidic silica gel column	EIMS	[84]
Human serum	No data available Plasma and serum samples were diluted	SPE extraction SPE extraction (cross linked polystyrene–divinylbenzene). The lipids were removed using sulfuric acid added directly on the SPE column	Multilayer column filled with silica gel–acidic silica gel–anhydrous sodium sulphate. Acidic silica gel column	ITD MS-MS EIHRMS ECNIMS	[81][85]
Human hair	Hair samples washed with deionized water mixed with shampoo, dried with paper towel, and cut into small pieces (<1 cm), and stored at 4 °C. Hydrochloric acid was added to each hair sample (200 mg). Glass tubes with hair samples were then incubated over night at 40 °C.	Solvent extraction with hexane (4 ml × 2 ml) with agitation using mixer	Extract was purified in a glass chromatographic column (5 cm × 10 mm) with a Teflon frit at the end, packed with 2 g Florisil and 1 g of anhydrous sodium sulphate (Na_2SO_4) on the top.	EIMS	[53]
Waste streams	Samples were homogenized and sieved (2 mm sieve)	MAE extraction with DCM-acetone	Silica and alumina column	ECD	[86]
Marine sediments	Surface marine sediments were collected using a box-corer. Samples were then wrapped in clean aluminum foil and stored frozen at −20 °C.	Soxhlet extraction with acetone (200 ml) for 24 h	Multi-layer silica gel Na_2SO_4, 10% $AgNO_3$–silica gel, silica, 22% H_2SO_4–silica gel, 44% H_2SO_4–silica gel, silica–2% KOH–silica	HRMS	[33]
Soil	Samples were collected, air-dried, sieved (2 mm) and wrapped in aluminum foil	Soxhlet extraction with n-hexane-acetone (1:1) for 48 h	Multi-layer silica gel column	ECD	[87]
Plants	Samples rinsed with distilled water, freezed-dried at −50 °C for 48 h in lyophilizer	Soxhlet extraction with n-hexane-acetone (1:1) for 48 h	Multi-layer silica gel column	ECD	[87]
House dust	Samples sieved using stainless steel sieve (100 mesh), solid parts (e.g. hair) were removed using clean tweezers. To prevent cross-contamination, paint brushes, sieves and tweezers were cleaned in ultrasonic bath for 5 min and air dried.	No data available	No data available	ECNIMS	[88]

Table 4 (*Continued*)

Sample type	Pre-treatment	Extraction technique	Clean-up procedure	Detection	Reference
Air	QFF and PUF were pre-cleaned with hexane-acetone solution. Active sampling high volume samplers 8 h (145–215 m^3)	Soxhlet extraction with hexane-acetone (1:1) for 72 h	Acid basic multilayer silica gel column	No data available	[41][41][43]
	QFF and PUF pre-cleaned with DCM-hexane solution Active sampling high volume samplers	Soxhlet extraction with DCM-hexane	No data available	MSD	
	QFF and PUF plugs were pre-cleaned with water-detergent solution, pre-extracted (ASE) with DCM-hexane (1:1), dried and stored at 18 °C. Passive sampling low volume air passive samplers (PUF)	ASE extraction with DCM-hexane (1:1)	Silica gel-acid silica gel (40%) column, after solvent exchange to hexane activated silica gel column	EIMS	
	Active sampling Active air sampler (PUF) (10 l min^{-1})				

- splitless/pulsed splitless
- on-column,
- PTV.

While employing splitless injection, transfer of analytes depends on type of solvent used, volume of liner and injected volume. Too small volume of liner may lead to the memory effects, while very large liner volumes cause a poor transfer of early eluting compounds [5].

Parameter of high importance, in terms of chromatographic analysis of PBDEs, is injection port temperature (usually between 250 and 300 °C). If too high or if the residence time of PBDEs in the liner is too long, degradation of highly brominated congeners (octa- to decaBDE) occurs. According to data published on this issue, the small volume that can be injected (1–3 μl) using split/splitless injection is considered the main limitation of presented injection technique [5,8,89]. Although this shortcoming can be eliminated with pulsed splitless injector that significantly improves the injection performance by injecting larger volumes (up to 5 μl). This, in turn allows to obtain lower detection limits.

On-column injection technique is considered suitable injection technique especially for VOC but has recently gained popularity also in case of analysis of PBDEs. In on-line injection extract is introduced directly into the GC column or into a glass insert fitted into injector and kept at low temperature. It requires only clean extracts to be injected, as otherwise GC column may quickly deteriorate. On-line injection has been successfully applied for the accurate introduction of PBDEs into GC column by Swedish scientists. No significant degradation of higher brominated PBDEs including BDE209 was observed [89].

An interesting alternative, especially if matrix effects cannot be eliminated altogether, may be either the programmed temperature vaporizing injector (PTV) or (PTV-LVI) that both permit larger volumes to be injected (up to 125 μl) [8]. In general injection of large volumes enables determination of low concentration levels of PBDEs, especially in biota samples (e.g. human serum). Moreover the combination of cool injection with a controlled vaporization eliminates a huge disadvantages common for conventional hot inlets – significantly reduces the risk of discrimination of less volatile compounds.

The main principle of PTV injection technique is often described as three steps as follows: injection, solvent venting, splitless transfer of analytes. During the first two steps the split exit is open and the temperature of injection port does not exceed 50 °C. The solvent is removed via split exit and analytes, first retained in the liner, are then transferred to the GC column. This requires the split exit to be closed. The PTV injection technique is considered suitable especially for less volatile compounds (e.g. PBDEs), as in case of VOC, the significant loss of analytes may be observed [90]. The special attention should be paid while injecting aqueous samples, since the analytes may be removed during the solvent venting stage. In order to prevent the loss of analytes, the careful optimization of injection step should be made. This involves inter alia applying the “rapid injection mode”. More details on this issue are given in the review, where the PTV injection technique was described in detail [90].

Apart from the possibility to inject large volumes, the huge advantage of PTVE injection technique may be the fact that it can be, if necessary, transferred into on-column injector by applying on-column insert. The PTV injector (20 μl) has been successfully applied for the determination of PBDEs in human adipose tissue [76].

7.2. Chromatographic analysis

According to scientific articles published recently, gas chromatography (GC) is most often applied separation technique during PBDEs analysis [50–56]. It is mainly because of PBDEs vapor pressure and polarity. The crucial step in case of analysis using GC is selection of an appropriate column. This allows proper resolution as well as discrimination of compounds. In the past years packed columns were successfully applied, but nowadays the majority of studies is done on capillary columns [61]. PBDEs are separated mainly using non-polar stationary phases (e.g. DB-5). Best separation efficiency is reported to be achieved using 30–50 m non-polar or semi polar, capillary columns with diameters <0.25 mm. Good resolution may also be obtained with narrow bore columns – internal diameter – 0.1 mm [8,76,89].

Analysis of highly brominated congeners BDE209 often requires special conditions due to the possible thermal degradation that may happen during injection as well as due to long retention time in chromatographic column. Therefore GC column for highly brominated PBDEs analysis should have higher temperature limits and should be relatively short 10–15 m (while compared to traditional 30–60 m) to reduce the resistance time of compounds in chromatographic column. It has been reported, that the film thickness of such column should be between 0.1 and 0.2 mm [5,8,61,89]. Good results were also shown using narrow bore columns, already mentioned in this review. The proper choice of stationary phase is considered very important in case of analysis of higher brominated congeners. Very often columns recommend for analysis of lower brominated compounds may be highly discriminating against BDE209 (e.g. DB-XLB). Moreover Kierkegaard et al. reported on possible differences in response of BDE209 that may occur between non-polar and semi-polar columns (e.g. DB-1 HP-1, VF-1) from different manufacturers. These are not observed in case of analysis of lower brominated compounds [60].

Some attention has been recently paid to the application of comprehensive two-dimensional gas chromatography (GC–GC) for analysis of PBDEs. This is mainly due to its high resolving power that increases with the use of two columns with different separation properties. So far GC–GC has been successfully applied inter alia for the analysis of polyhalogenated micro-contaminates [90]. GC–GC coupled with MS-TOF has been reported to overcome all co-elution limitations in terms of analysis of PBDE congeners [3]. Unfortunately GC–GC separation technique is still considered very expensive alternative to traditional GC, therefore available literature information on this issue is limited.

Literature information on the GC conditions during the analysis of PBDEs in different samples is listed in Table 5.

The risk of thermal degradation of less stable, highly brominated congeners while operating GC can be avoided applying liquid chromatography (LC) [91–95]. Among stationary phases, commonly employed in LC analysis of PBDEs, biphenyl and Ultra Aqueous C18 have been reported to give the most complete chromatographic separation, while co-elutions of isobaric compounds are observed when applying pentafluorophenylpropyl stationary phase [93]. As a confirmation to this statement, the Ultra C18 stationary phase has been successfully used for chromatographic separation of PBDEs in fish samples [91]. Most commonly reported mobile phase in LC analysis of PBDEs refers to methanol–water solution, usually in 85:15 ratio [91,95] but acetonitrile-water solution has also been mentioned in literature [94]. More detailed information on LC separation of PBDEs is listed in Table 5.

Two-dimensional separation is considered advantageous over its one-dimensional counterpart. This is because of excellent selectivity it demonstrated as well as extended peak and higher resolution capacity [94]. A comprehensive two-dimensional system coupling ultra-performance liquid chromatography (UPLC) has been applied for the separation and analysis of 23 metabolites of PBDEs, hydroxylated polybrominated diphenyl ethers (OH-PBDEs based). The separation was done due to hydrophobicity difference and mobility disparity of investigated compounds [94]. Still, not enough information is available on the use of high performance liquid chromatography (HPLC) in analysis of lower PBDEs [96], but according to the most recent data, HPLC may be also considered as an alternative for GC analysis of higher brominated congeners, especially in water and sediment samples [5].

7.3. Detection technique

Reported concentrations of PBDEs are often lower than those reported for other SVOCs (e.g. PCBs). It is particularly important in analysis of humans samples. Therefore instrumental analysis using highly sensitive systems should be carried out. Mass spectrometry (MS) is considered most suitable and most often applied detection technique for GC and LC analysis of PBDEs in environmental and food samples.

In case of GC analysis, according to most recent data for identification and quantification of PBDEs, electron capture negative ionization (ECNI) with mass spectrometry (LRMS) is most often applied. Ions formed then are bromine isotopes m/z 79 and 81. Mass spectra obtained for different PBDEs using ECNI are available elsewhere in literature. ECNI-LRMS offers high sensitivity and lower cost than other (high resolution) alternatives, such as electron impact high-resolution mass spectrometry (EI-HRMS). However, the mentioned technique ensures higher selectivity than ECNI-LRMS, as the accurate mass of the fragment ion for each level of bromination is recorded. While operating in electron impact ionization (EI), ions formed – $[M^+]$ and $[M–Br_2]^+$ are considered as identification ions. Furthermore, operating in EI allows the use of ^{13}C-labeled standards (as internal standards) that makes the quantification procedure more accurate. When isotope dilution technique is applied, samples are treated prior to sample preparation with isotopically labeled standard solution. The knowledge of the isotope ratio allows the calculation of the sample concentration by measuring the isotope ratio of the sample together with the isotope addition [4,80,99].

The use of electron impact low-resolution mass spectrometry (EI-LRMS) has also been mentioned in the literature. It is considered useful especially due to an easy and low-cost maintenance of the instrumentation. So far EI-LRMS has been successfully applied for determination of PBDEs in different environmental samples. But what has to be mentioned, EI-LRMS ensures good result for samples with relatively high content of PBDEs. Applying low resolution instrument to the analysis of human samples, where PBDEs are often present at very low concentration levels (pg g^{-1}) may lead to problems caused by the co-elution of same mass interferents (e.g. the nominal mass of the $[M–Br^2]^+$ ion for the tetra-BDEs is the same as that for the hepta-PCB) [3,99]. As an alternative to mass spectrometer (MS), described as most often applied detection technique during the chromatographic analysis of PBDEs, electron capture detector (ECD) can be pointed out. Taking into account relatively low sensivity and selectivity obtained while working with ECD it cannot be matched to any of MS techniques. But it can be applied to the analysis of samples where PBDEs are present at high concentration levels (ng g^{-1}). Normally it does not refer to the analysis of human tissues, but combined with double capillary column, electron capture detectors have been successfully employed to the analysis of PBDEs in human milk samples. This was mainly because of the fact that the use of two capillary columns of different polarity may significantly decrease co-elution effect [83]. Recently good results for analysis of BDE209 in dust samples have been reported using ECD detector with optimum conditions: 90 °C (initial temperature), 300–310 °C (final oven temperature),

Table 5
Literature information on GC and LC conditions applied during final determination stage of PBDEs analysis in complex matrix.

Sample	Injection	Column	Dimensions	Detection technique	Separation technique	Reference
Fish, human blood, human milk	Splitless (1 μl) 290 °C	DB-5	30 m × 0.25 mm film thickness 0.1 μm	HRMS	GC	[82]
Human serum	Programmable temperature vaporizing injector (PTV) in hot splitless mode (4μ)	VF-5MS	55 m × 0.25 mm film thickness 0.25 μm	ITD MS/MS	GC	[33]
Human adipose tissue	No data available	DB-1	30 m × 0.25 mm film thickness 0.25 μm 15 m × 0.25 mm film thickness 0.1 μm	EI-MSD	GC	[47]
Human liver	No data available	DB-1 AT-5	30 m × 0.25 mm film thickness 0,25 μm 12 m × 0.18 mm film thickness 0.2 μm	EIMS	GC	[48]
Human hair	Pulsed splitless mode 300 °C	ZB-5MS	15 mm × 0.25 mm film thickness 0.1 μm	EI-MSD	GC	[49]
Sewage sludge	Pulsed splitless mode 300 °C	DB-5MS	25 m × 0.25 mm film thickness 0.25 μm 20 m × 0.25 mm film thickness 0.25 μm	ECNIMS	GC	[50]
Soil	Splitless (1 μl)	DB-5MS	60 m × 0.25 mm film thickness 0.25 m 30 m × 0.25 mm film thickness 0.1 μm	HRMS	GC	[97]
Sediments	No data available	DB-1	30 m × 0.25 mm film thickness 0.25 μm	MS/MS	GC	[98]
Dust	Injection volume 2 μl 250 °C	DB-5HT	15 m × 0.25 mm film thickness 0.1 μm	MS (ion trap)	GC	[97]
	No data available	DB-XLD CP-Sil13CP	30 m × 0.25 mm film thickness 0.25 μm 12.5 m × 0.25 m film thickness 0.25 μm	ECNI-MS	GC	[88]
Air	On-column injector	DB-5MS	15 m × 0.25 mm film thickness 0.1 μm	EIMS	GC	[43]
Fish Wastewater	Injection volume (2 μl)	Ultra II C18	100 mm × 2.1 mm, film thickness 2.2 μm	APPI MS/MS APCI MS/MS	LC LC	[91] [93]
No data available	No data available	Nucleodur 100-C8 Ultrabase RP18	250 mm·4 mm, film thickness 5 μm 250 mm·2 mm, film thickness 5 μm	APPI MS/MS	LC	[95]
Human liver	No data available	C-18 BetaBasic	100 mm × 2.1 mm, film thickness 3 μm	IT-APCIMS	HPLC	[101]
No data available	No data available	sub-2 μm BEH C18	150 mm × 2.1 mm, film thickness 1.7 μm	IM-TOFMS	UPLC	[94]

290 °C (injection temperature) and 2.5 ml min^{-1} (flow rate for 15 m column). Authors reported no degradation of BDE209, which is considered most significant drawback in case of analysis of highly brominated congeners [82].

Some new and attractive detection techniques for GC analysis of PBDE have been introduced as well. First, coupled plasma mass spectrometry (ICP-MS) that compared to other detection techniques, such as ECD and MS offers better sensitivity and selectivity. It is mainly due to the fact that in ICP-MS bromine ions are detected what in the same time eliminates interferences resulting from the presence of chlorinated compounds. Another promising option can be quadrupole ion storage mass spectrometry (QISTMS) operating in tandem mode. It is confirmed to be some low-cost alternative to high-resolution devices for analysis of complicated matrices. So far (GC-QISTMS) has been successfully applied for analyzing low concentrations (ng g^{-1}) of mono to heptaBDEs in environmental samples (e.g. sewage sludge). Obtained chromatograms showed no significant matrix effects, neither problems with co-eluting interfering compounds. Further research for developing GS-QISTMC methodology for analysis of octa-decaBDE congeners is planned in the future [58].

High mass resolution instruments (e.g. HRMS spectrometer), compared to traditionally applied mass spectrometers, offer greater sensitivity (EI) and selectivity (ECNI) for complex matrices analysis, applying GC or LC technique. Moreover, such instruments allow more extensive data collection program. Detection limits, which can be obtained operating with HR instruments (usually pg g^{-1}) may differ depending on the type of analyzer applied in mass spectrometer [82]. Comparative study carried out for determining PBDEs in human milk samples showed that detection limits obtained by high-resolution TOF analyzer were one order of magnitude lower than those obtained with traditional quadrupole analyzer [99]. Time of flight analyzer (TOF) mass spectrometer operated in high resolution mode combined with mass-defect-based digital noise filtering technique was also successfully applied to facilitate the observation of bromine-containing compounds [82]. Promising results have been obtained using HRGC-HRMS technique for analyzing PBDEs in biota samples. HRGC-HRMS is reported to be reliable and sensitive method (apparently three–five times more sensitive than HRGC-LRMS [82] for determination of PBDEs however, what should be clearly mentioned, the cost together with maintenance of such equipment is few times higher than those of conventional low resolutions MS techniques [82]. Application of tandem mass spectrometry (MS/MS) has been reported in the literature, especially in case of LC analysis of PBDEs [100] and their metabolites [101,102]. In case of sensitivity, LC–ESI-MS/MS can be considered competitive with GC–EI-MS/MS, with limits of detection in ppt range [95].

Implementation of LC coupled with MS technique into PBDEs analysis requires appropriate ionization techniques to be applied. Although electrospray (ESI) and atmospheric ionization techniques are considered most popular ionization techniques for LC, PBDEs do not ionize well with two mentioned techniques. This limitation can be overcome using atmospheric pressure photoionization (APPI), reported as complementary ionization technique for most PBDEs. It is performed either in positive ion (PI) mode for less brominated, mono- to tetra-BDE congeners or in negative ion (NI) mode for highly brominated, penta- to deca-BDE congeners [3]. The APPI ionization technique has been successfully applied for analysis of PBDE in fish [78,91] and water samples [79,92], while liquid chromatography atmospheric pressure chemical ionization (APCI) has been used for analysis of PBDEs in wastewater samples [93]. Compared to APPI, APCI does not require UV lamp and dopant reagent to assist atmospheric pressure ionization. Applying APCI technique ensures three main advantages: simplicity, rapidity, and high sensitivity [93].

The comparison of detection techniques, which are most frequently applied during the chromatographic analysis of PBDEs, together with their advantages and drawbacks is presented in Table 6.

8. Quality control and quality assurance

The assessment of quality control and quality assurance is considered very important part of analytical procedure. According to Paepke et al., it covers about 30% of total analytical concept [103]. QA/QC measures include inter alia:

- analysis of chemical and glassware blanks (this is mainly due to the possible contamination of solvents, sorbents, etc.) [37,58,59,76],
- instrumental blanks [58,104],
- identification based on retention time criteria as well as on internal and external standards [23],
- quantification based on the isotope dilution method with the use of internal and external standards [23,82],
- establishing of calibration curve with the use of matrix matched standards, prepared independently from each other [76],
- analysis of duplicate samples [37,58,59,74,104],
- careful check of method performance by analyzing control samples (of known concentrations),
- certified reference material
- inter-laboratory studies [89].

The reliability of analytical results has significantly increased with the use of (^{13}C) labeled standards. According to the most recent data, the majority of PBDE congeners (more than 150 from 209) standards are now commercially available. Accustandard, Cambridge Isotope Laboratories or Wellington Laboratories are among most popular suppliers of PBDE standards. (^{13}C) labeled PBDE standards are applied during the quality and quantity analysis [80,103]. As definition of internal standard refers to the compound that has similar properties and behaves in a similar way to studied analytes, the use of ^{13}C labeled PBB and PCB has been also reported in literature. Recently Chiron Co. introduced fluorinated (F-PBDE) standards as an alternative to the traditional ^{13}C labeled PBDE standards [105]. They have several advantages:

- give one single isotope, as F has only ion isotope
- can be used with ECD detection without co-elution that was observed with ^{13}C labeled standards,
- useful with both EI- and ECNIMS detection techniques, while ^{13}C labeled cannot be used while operating with ECNIMS technique,
- considered cost-efficient, cheaper than traditional ^{13}C labeled standards [105].

In order to verify the trueness of developed analytical procedure, the certified reference material, is often applied (if available). In case of house dust, reference material (often 50–80 g) is commercially available. The same situation occurs with marine sediment reference material [106]. In response of the growing need for measuring organic compounds in human body fluids, the National Institute of Standards and Technology (NIST) introduced in 2009 standard materials for human milk and human serum [107]. In case of lack of respective reference material, other approaches, such as the addition of standard have been reported in the literature [103].

Inter-laboratory studies are also considered important tool for validation of analytical procedures. They are reported to significantly improve the quality of analysis, which is mainly due to the advice given by the organizers [103]. Since 1999 several inter-laboratory studies have been organized on BFRs issue, inter alia

Table 6
Comparison of available detection techniques applied during the chromatographic (GC, LC) analysis of PBDEs and their metabolites [3,83,89,95].

Detection technique	Identification ion	Selectivity	Sensitivity	Advantages	Limitations	Cost
ECD	Molecular ion	+	+	Cost effective, easy to operate and maintain, provides good results with the use of dual capillary column with different polarity that decreases the risk of co-elutions	Can be applied for samples with higher concentrations of PBDEs. The use of ^{13}C labeled standards is impossible due to the co-elutions with the native compounds	Low
ECNI-MS	Bromide ion	+++	++	Eliminates interferences orgining from co-elution of chlorinated compounds	The use of isotope-labeled standards for lower brominated compounds is impossible	Medium
EI-MS	Extract ion	++	++	Gives better structural information, allows the use of an isotope dilution method for quantification that is more reliable at trace analysis	Interferences especially from PCB compounds, higher LOD values especially for higher brominated compounds	Medium
EI-HRMS	Extract ion	+++	+++	High sensitivity especially for higher brominated compounds (hepta-decaBDE)	Need for personel with high qualities, sample fragmentation is required	High
QITMS	Extract ion	+++	+++	Allows quantification with isotopic dilution, eliminates matrix effects	Possible co-elutions other compounds, requires optimization	High
ICP-MS	Extract ion	+++	+++	Eliminates interferences orgining from both S-and Cl compounds	Cannot eliminate interferences origining from other brominated compounds, still requires research to be carried out before will be used as a routine detection technique	High
TOF-MS	Extract ion	+++	+++	Short time of analysis (milliseconds), almost no co-elutions, does not require complex extract clean up and fractionation procedure to be implemented	Limited linear range, still not used as routine detection technique	High
EI-MS/MS	Extract ion	+++	+++	Applicable for wide range of compounds in environmental samples, reduces or even eliminates matrix effect despite the type of sample, provides excellent sensitivity and selectivity	High cost	High
APCI-MS/MS	Extract ion	+++	+++	No need for UV lamp and dopant reagent application to assist atmospheric pressure ionization., short time of analysis (14 min), applicable for analysis of BFRs compounds, which are not amenable to GC–MS	Applicable mainly for TBBP-A and HBCDs analysis, not efficient ionization technique for PBDEs compounds	High
APPI-MS/MS	Extract ion	+++	+++	Reported as the preferred ionization method for the determination of PBDEs, good ionization efficiency, gives the possibility for simultaneous analysis of wide range of compounds, the use of pre-heated dopant decreases the level of background noise, which enhanced sensitivity.	Susceptibility regarding solvent composition during gradient elution, which is significant limitation in case of simultaneous determination of several compounds without the use of several internal standards	High
IT-MS/MS	Extract ion	+++	+++	Applicable for both PBDEs and their metabolites (MeO-PBDE) in a single run, an excellent alternative to HRMS instruments for determination of PBDEs in environmental samples, low limits of detection	High cost	High
IM-MS	Extract ion	++++	+++	As a second-dimensional post-ionization separation technique IM-MS gives an additional rapid separation for metabolites of PBDEs (OH-PBDEs) according to their relative mobility. Unique selectivity and improved peak capacity.	Expensive, better performance is observed when coupled to UPLC rather than to traditional LC	High

by the Netherlands Institute for Fisheries Research (RIVO) and Bromine Science and Environmental Forum (BSEF). In case of PBDEs, different matrices have been analyzed (e.g. soil, sediment, fish, etc.). Good agreement has been obtained for lower brominated congeners. The different situation was observed for higher brominated congeners, (e.g. BDE209). Some results supplied by the participants were significantly outside the range of values reported by the majority of laboratories. This calls for more inter-laboratory studies to be carried out in the future [89].

The issue of inter-laboratory studies was accurately covered by Covaci et al. in the review [89].

9. Conclusions

The presence of PBDEs in the environment has recently gained much attention among numerous scientific groups. This is mainly due to the growing social awareness of possible hazardous effect that may result from long-time exposure to SVOC compounds. Due to the widespread use, flame retardants PBDEs are considered as ubiquitous in the environment. This, in turn makes them become the issue of particular concern. Taking into account data published recently, there is still lack of information on potential impact of PBDEs on human health. Therefore monitoring studies should continue in order to obtain more reliable results regarding human exposure to PBDEs. As human intake of PBDEs happens mainly through the diet, there is still not much information available on PBDEs concentration levels in different food groups (apart from aquatic organism). Studies regarding occupation exposure to PBDEs (e.g. via furnishing materials or electronic equipment) need to be carried out as well.

From the analytical point of view, analysis of SVOCs faces impediments resulting from their low concentration levels (e.g. PBDEs in human samples – $pg\,g^{-1}$) as well as from the composition of matrix (the presence of interfering compounds such as lipids, solid parts, etc.). Co-elution of different groups of analytes often requires high resolution instrumentation (HRMS) to be applied. This provides high selectivity and low detection limits but is considered few times more expensive than traditional low resolution techniques.

In case of trace analysis, quality assurance and quality control is consider very important part of analytical concept. This includes analysis of blanks, duplicate samples and implementation of labeled standard solutions, etc. In order to verify the trueness of newly developed analytical procedure, analysis of certified reference material is also advised. Inter-laboratory studies are believed to be the good way to improve the quality of analysis of PBDEs as well. It is particularly important in case of analysis of higher brominated compounds (e.g. BDE209) where problems tend to occur more often than in case of analysis of lower brominated congeners.

However, broad attention paid to the analysis of PBDEs, together with numerous reports that are systematically published around the world suggest that further research on developing rapid and simple analytical procedure, allowing simultaneous analysis of more than one group of SVOCs will be carried out successfully.

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