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Microwave-assisted extraction: Application to the determination of emerging pollutants in solid samples

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ABSTRACT

Flame retardants, surfactants, pharmaceutical and personal care products, among other compounds, have been the object of numerous environmental studies. In this chapter, the application of microwave-assisted extraction (MAE) in the development of analytical methods for several groups of organic compounds with growing concern as emerging pollutants has been considered. Compared to other extraction techniques, optimization of MAE experimental conditions is rather easy owing to the low number of influential parameters (i.e. matrix moisture, nature of the solvent, time, power, and temperature in closed vessels). The great reduction in the extraction time and solvent consumption, as well as the possibility of performing multiple extractions, increasing the sample throughput, can also be highlighted among MAE advantages. In summary, the study of several applications of MAE to environmental problems demonstrates that this technique constitutes a good alternative for the determination of organic compounds in environmental samples. It can be used as a rapid screening tool, and also to obtain detailed information on the sources, behaviour and fate of emerging pollutants in environmental matrices.

1. Introduction

Emerging pollutants are defined as compounds that are not currently covered by existing water-quality regulations, have not been studied before, and are thought to be potential threats to environmental ecosystems and human health and safety [1,2]. They encompass a diverse group of compounds, including pharmaceuticals, drugs of abuse, personal care products (PCPs), steroids and hormones, surfactants, perfluorinated compounds, flame retardants, industrial additives and agents, and gasoline additives, as well as their transformation products [1,3–5]. The way that organic compounds enter the environment depends on their pattern of usage and mode of application (e.g. disposal of municipal, industrial and agricultural wastes, excretion of pharmaceuticals and accidental spills). Once in the environment, they can be widely distributed at any time between the moment of their production through to use and disposal. Because most emerging pollutants are from human use, their emissions are an issue for some wastewater processes, so the study of the fate of the emerging pollutants in wastewater treatment plants (WWTP) is of most importance. Once released into the environment, emerging pollutants are subject to processes (e.g. biodegradation, and chemical and photochemical degradation) that contribute to their elimination. Depending on the compartment in which synthetic chemicals are present in the environment (e.g. groundwater, surface water and sediment) or in the technosphere (e.g. WWTPs and drinking-water facilities), different transformations can take place, sometimes forming products that can differ in their environmental behaviour and ecotoxicological profile.

The analysis of micropollutants in the environment constitutes a difficult task, first, because of the complexity of the matrices, and second, because of the normally very low concentrations of the target compounds. Essentially, in most of the cases of interest, substantial analyte enrichment is necessary to isolate the target compounds from the matrix and to achieve the limits of detection (LODs) required. According to the kinetic model of Pawliszyn [6] (established for supercritical fluid extraction, SFE), the compounds, fixed to the surface of core, are extracted in several steps: desorption from the matrix surface, diffusion in the porous organic layer up to the solvent and solubilization in the solvent. The extraction recovery can be limited by one or several steps. The solubility is rarely the limiting factor if the solvent is well chosen. Desorption is the most important factor to consider. A quantitative extraction must overcome interactions between analytes and matrix. These interactions depend partly on the composition of the matrix. A typical analytical procedure includes various sample preparation steps, such as extraction, filtration, purification, and evaporation; and, if the final determination is performed by bioassays or gas chromatography–mass spectrometry (GC–MS), liquid chromatography–mass spectrom-

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etry (LC–MS); hydrolysis and derivatization are also frequently necessary [7]. Therefore, sample preparation plays an essential role in analytical methodology. Most analytical instruments are unable to handle matrices directly and some forms of pre-treatment are required to extract and to isolate the analytes [8]. Trends in analyte isolation include: less solvent consumption; improved extraction throughput (in some instances linked to automation); higher recoveries; and, better reproducibility. Sample preparation is considered to be potentially the most polluting step of analysis since it usually requires the use of organic solvents. Application of traditional solvent extraction for this purpose may cause significant pollution by releasing solvents into the environment. Some green solvent extraction techniques have been developed, among them microwave-assisted extraction (MAE) or, also called, microwave-assisted solvent extraction (MASE). The use of microwave energy in sample preparation first emerged in the early 1970s [9]. Specifically, the extraction of organic compounds by microwave irradiation appeared with the work of Ganzler et al. [10] in 1986. Since then, the technique has attracted growing interest, and it has been widely used in analytical chemistry. Because of its advantages, the use of microwave energy for the extraction of analytes in various matrices has become very popular in the last 15 years or so. This technology has been used in related analytical determinative protocols in addition to being applied to more recalcitrant matrices such as drugs and contaminants in animal and human tissues, and to matrices found at contaminated sites where screening or characterization is required for the purpose of subsequent or on-going remediation work [11]. The main advantages of MAE from the point of view of green chemistry are: significant reduction of solvent required, which reduces waste generation, shortens extraction times, and reduces the amount of sample required and correspondingly reduces energy input and cost [12,13]. One of the main advantages using MAE is the reduction of extraction time when applying microwaves. This can mainly be attributed to the difference in heating performance employed by the microwave technique and conventional heating. In conventional heating a finite period of time is needed to heat the vessel before the heat is transferred to the solution, while microwaves heat the solution directly. This keeps the temperature gradient to a minimum and accelerates the speed of heating. Additionally MAE allows for a significant reduction in organic solvent consumption as well as the possibility of running multiple samples simultaneously. These are of course minimum criteria for modern sample preparation techniques and are all fulfilled to a great extent by MAE. Consequently MAE is an attractive alternative to conventional techniques [14].

2. Principles of microwave-assisted extraction

In MAE, microwave energy is used to heat solvents in contact with solid samples or liquid samples and to promote partition of the analytes from sample matrix into the solvent (the extractant). Microwave energy is a non-ionizing radiation (frequency 300–300,000 MHz) that causes molecular motion by migration of ions and rotation of dipoles. Microwaves are electromagnetic waves made up of two oscillating perpendicular fields: electrical field and magnetic field. Microwaves are used as information carriers or as energy vectors. This second application is the direct action of waves on material which is able to absorb a part of electromagnetic energy and to transform it into heat [12,15]. Thus, the principle of MAE is based on the direct effect of microwaves on molecules of the extraction system caused by two mechanisms, ionic conduction and, dipole rotation [16,17]. The ionic conduction generates heat due to the resistance of medium to ion flow. The migration of dissolved ions causes collisions between molecules because the direction of ions changes as many times as the field changes sign. The dipole rotation is related to alternative movement of polar molecules which try to line up with the electric field. Multiple collisions from this agitation of molecules generate energy release and therefore a temperature increase [18].

It should be noted that, unlike usual conventional forms of heating (convection and conduction), microwaves heat the extracted system directly, leading to very short extraction times. Heat generation in the sample in the microwave field requires the presence of a dielectric compound. The greater the dielectric constant, the more thermal energy is released and the more rapid is the heating for a given frequency. In fact, the heat generation in a sample depends in part of the dissipation factor ($\tan\delta$), which is the ratio of the sample's dielectric loss (i.e. the loss factor ε'') to its dielectric constant (ε'). Indeed, the dielectric constant is a measure of the sample's ability to absorb microwave energy, and the loss factor its ability to dissipate the absorbed energy. Consequently, the effect of microwave energy is strongly dependent on the nature of both the solvent and the matrix. Most of the time, the solvent chosen has a high dielectric constant, so that it strongly absorbs the microwave energy. However, in some cases, only the sample matrix may be heated, so that the solutes are released in a cold solvent (this is particularly useful for thermolabile components, to prevent their degradation) [17]. The compounds which have high dielectric losses are principally polar compounds. One characteristic of microwave heating is therefore the selectivity. The second specificity is that the temperature gradient is reversed compared to conventional heating and the heating is volumic [12]. In MAE processes, analytes can be extracted into a single solvent or mixture of solvents that absorb microwave energy strongly, into a solvents mixture of high and low dielectric losses solvents; and also into a microwave transparent solvent from a sample of high dielectric losses [16].

The technical application of microwave energy to the samples may be performed using either closed vessels (under controlled pressure and temperature), or open vessels (at atmospheric pressure). These two technologies are commonly named pressurized MAE (PMAE) or focused MAE (FMAE), respectively. Both systems are shown in Fig. 1. Whereas in open vessels the temperature is limited by the boiling point of the solvent at atmospheric pressure, in closed vessels the temperature may be elevated by simply applying the adequate pressure.

3. Influential parameters on MAE performance

The main parameters influencing MAE performance include: nature of the solvent and the matrix; solvent volume; microwave power; exposure time; and, temperature [16,17,19].

In the extraction of organic compounds, the selection of the organic solvents should account for three facts:

1. The microwave-absorbing properties of the solvent (and the ability of the solvent to convert this energy into heat). As microwave absorption occurs owing to the reorientation of permanent dipoles by the electric field, the amount of energy absorbed is proportional to the dielectric constant (ε') of the solvent. In practice, most of the time, the absorption is also proportional to the solvent polarity. Apart from absorbing the energy, the solvent must be able to convert this energy into heat, so the efficiency of the conversion process is dependent on the dielectric factor loss (ε''). The overall efficiency of heating is then expressed by the dissipation factor ($\tan\delta$).
2. Preferably the solvent should have a high selectivity towards the analyte of interest excluding unwanted matrix components.

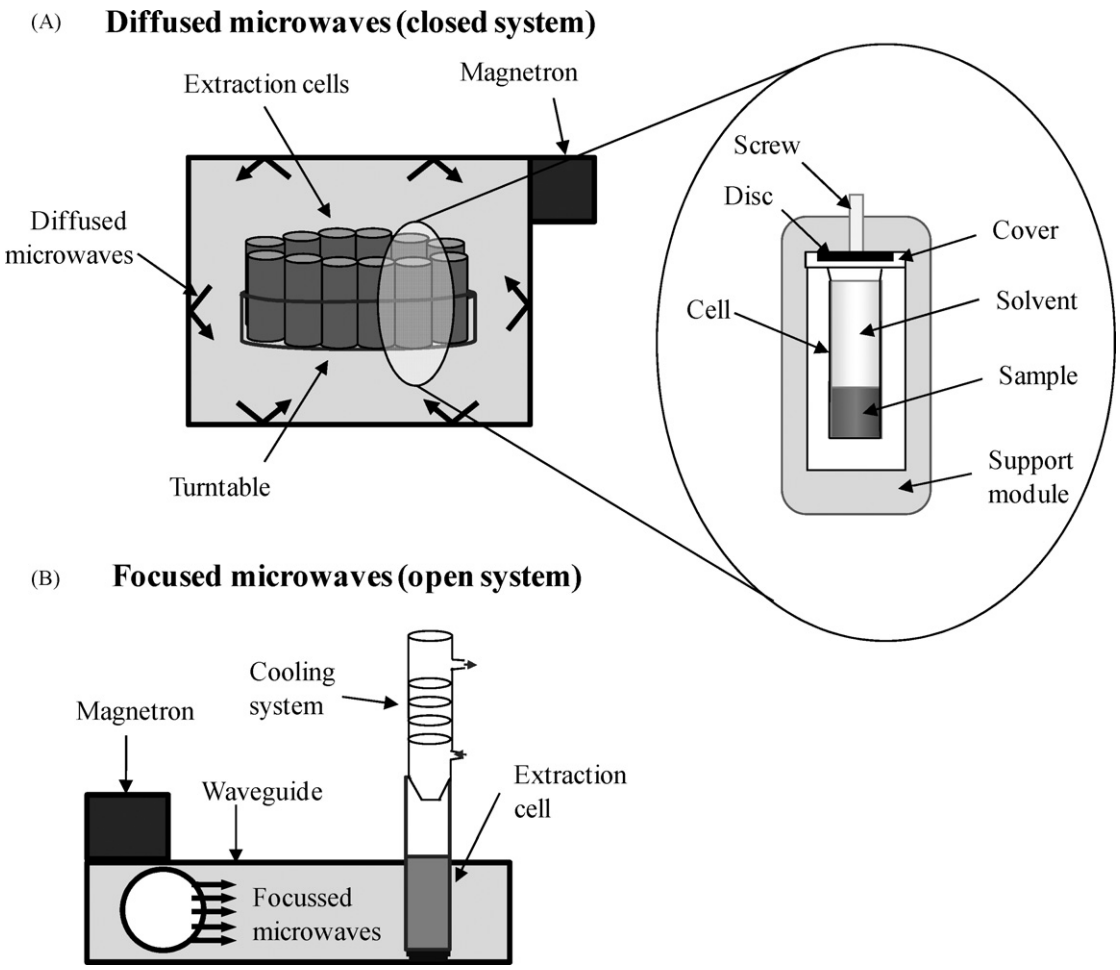

Fig. 1. Schematic view of devices for (A) pressurized MAE (PMAE) and (B) focused MAE (FMAE). Redrawn from Ref. [19].

3. The interaction of the solvent with the matrix.

The dielectric properties of several solvents used for MAE are presented in Table 1.

The extraction heating process may occur by a number of mechanisms [20]:

A. Mechanism I: the sample could be immersed in a single solvent or mixture of solvents that absorb microwave energy strongly.
B. Mechanism II: the sample could be extracted in a combined solvent containing solvents with both high and low dielectric losses mixed in various proportions.
C. Mechanism III: samples that have a high dielectric loss (i.e. samples with high water content) can be extracted with a microwave transparent solvent.

Table 1
Dielectric properties of several solvents used in MAE.

	ε'	ε''	$\tan\delta$ ($\times 10^4$)
Hexane[a]	1.89	0.00019	0.10
Ethyl acetate[a]	6.02	3.2	5312
Acetone[a]	21.1	11.5	5555
Methanol[b]	23.9	15.3	6400
Ethanol[b]	24.3	6.1	2500
Acetonitrile[b]	37.5	2.3	620
Water[b]	76.7	12.0	1570

[a] Data from [15].
[b] Data from [12].

Most MAE applications involved mixtures of non-polar solvent and water, including the humidity of biological matrices themselves (following the third extraction mechanism).

Generally, in conventional extractions a higher volume of solvent will increase the recovery of the analyte but, in MAE, the same approach may lead to lower recoveries, probably due to inadequate mixing of the solvent with the matrix by the microwaves. The selection of solvent volume depends on the type and the size of sample, but, on average, the amounts of solvent may be about 10-fold lower than those used in classical extractions, always considering that the solvent volume must be sufficient to ensure that the whole sample is immersed [17].

Regarding the nature of the matrix, its water content is a key factor, because of the high dipole moment of the water molecules which leads to high efficiency in heating the sample. The inconvenience is the requirement of controlling the matrix water content to obtain reproducible results. Other possible components of the matrix (such as ferrous material) can cause arching due to the absorption of microwave energy. The organic carbon content of the matrix is known to hinder the extraction, owing to strong analyte–matrix interactions that are difficult to disrupt.

The selection of microwave power and the corresponding irradiation time depend on the type of sample and solvent used. In theory, the use of high-power microwaves should allow to reduce the exposure time. However, in some cases, a very high-power microwaves decreases the extraction efficiency through degrading the sample or rapidly boiling the solvent in open-vessel systems, which hinders contact with the sample. Generally, extraction times in MAE

are much shorter than those of classical extraction techniques. Usually, increasing extraction times above the optimal range does not improve extraction efficiency, and, in some cases, may even decrease analyte recoveries (e.g. thermolabile compounds).

In most cases, elevated temperatures result in improved extraction efficiency as a result of an increased diffusivity of the solvent into the internal parts of the matrix, and the enhanced desorption of the component from the active sites of the matrix. In closed systems, pressure is also an important variable (directly depending on the temperature). Particular consideration should be given to applications dealing with thermolabile substances, which may be decomposed at high temperatures.

4. Application of MAE to environmental analysis

The use of MAE for the extraction of pollutants from environmental matrices has attracted considerable interest in the past few years. The first applications were related to the determination of polycyclic aromatic hydrocarbons (PAHs) [21,22] and polychlorinated biphenyls (PCBs) [23–25] from soils and sediments. Since then, numerous other compounds have been extracted efficiently—such as pesticides, phenols and organometallic components [10,26–28]. Matrix effects due to strong adsorption of the solutes onto the matrix are particularly crucial for environmental matrices.

In the last years, flame retardants, surfactants, pharmaceutical and personal care products (the so-called PPCPs), among other compounds, have been the object of numerous environmental studies. In this section, the application of MAE to develop analytical procedures for several groups of compounds with growing concern as emerging pollutants is being considered.

4.1. Flame retardants

Flame retardants are chemicals that are added to polymers which are used in plastics, paints, textiles, electronic circuitry and other materials to prevent fires [29]. Brominated flame retardants (BFRs) such as polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane (HBCD), tetrabromobisphenol-A (TBBPA) and polybrominated biphenyls (PBBs), are among the most used flame retardants and have attracted enormous attention over the past decade [30]. Other less known BFRs like bis(2,4,6-tribromophenoxy)ethane and decabromodiphenyl ethane (DeBDethane) have an increasing interest due to their emerging use as substitutes of octaBDE and decaBDE commercial mixtures, respectively [31]. From the materials they are added and because of their widespread use and waste, flame retardants are easily released into the surrounding environment. The water solubility and vapour pressure of PBDEs and PBBs are very low, so that, when released to the environment, these compounds are quickly adsorbed onto solid particles of sediment and soil. All these BFRs, with the exception of TBBPA, appear to be lipophilic and bioaccumulate in biota and humans.

Analytical methods based on MAE developed for flame retardants are summarized in Table 2. Bayen et al. [32] presented the first validated method for the quantification of major PBDE congeners (BDE 47, BDE 99 and BDE 100) in marine biological tissues (muscle, liver, soft tissues) using MAE. The accuracy and precision of the proposed method, together with the effective removal of matrix interference, make possible the accurate quantitative analysis of three different PBDEs in marine biological tissues, reaching LODs in the low nanogram per gram. Meng et al. [33] used a MAE method to determine and compare fourteen PBDE congeners levels among regionally abundant pinniped species; examine the influence of gender and age; and evaluate for temporal trends in levels during the period ranged from 1994 to 2006. Tapie et al. [34] tested four extraction protocols for the determination of PCBs and PBDEs in biological matrices such as trout and eels muscle. The first protocol used MAE combined with two purification steps. The second one was similar, excepting that MAE was replaced by pressurized liquid extraction (PLE; also known under the trade name ASE, accelerated solvent extraction; PSE, pressurized solvent extraction; or PFE, pressurized fluid extraction). The third one combined extraction/purification by PLE with final purification on a silica gel column. The last one combined MAE with purification on an acidic silica gel column. All of the protocols produced good performance in terms of recovery and reproducibility. The two last protocols showed promising results in terms of applicability to natural matrices, as they required a minimum of sample handling and minimal amounts of solvent and time.

Another important issue is the presence of PBDEs in aquaculture samples. Feeds for aquaculture consist mainly of products and by-products of the cereal and fishing industries together with various additives. European Union food safety legislation includes measures guarding against the possibility that these feeds and the fish they nourish contain pollutants constituting a risk to consumers' health. Of particular concern are organochlorine pesticides applied to cereal crops, and a variety of chemicals that can be present in packaging, such as PCBs, PBBs and PBDEs. In this way, Carro et al. [35] applied MAE with a simple solid phase extraction (SPE) cleanup step, followed by headspace solid phase microextraction (HSSPME) and GC–MS/MS quantification, for the simultaneous ultratrace-level determination of PBBs and PBDEs (among other contaminants, i.e. organochlorine pesticides and PCBs) in aquaculture feeds and products. The initial MAE stage, carried out at 85 °C, required less than 1.5 g of raw sample, being fast (15 min) and sparing in its use of solvent (14 mL of 1:1 hexane/dichloromethane). Subsequent SPE on acidic silica gel reduces lipid content to less than 0.05%, and further cleanup by HSSPME (60 min at 75 °C with a 100-μm polydimethylsiloxane-coated fused silica fibre) required no additional solvent. In real-life samples, inclusion of the HSSPME stage allowed detection and quantification of analytes that were not detected without this stage, improving limits of quantification (LOQs) up to 21-fold. Fajar et al. [36] described, and compared with MAE, the efficiency of MAE with saponification (MAES) for the determination of seven PBBs and PBDEs in aquaculture samples (feed for turbot and trout and samples of scallop, clamp and mussel). Their results showed that MAES does not need additional cleanup steps because the lipid content of the extracts is lowered by a factor of 26 as compared with MAE. The LOQs for the analytes were 40–750 pg g^{-1} (except for BB-15, which was 1.43 ng g^{-1}) using MAES–GC–μECD (μ-Electron capture detector). Precision was significantly better (relative standard deviation (RSD) < 13%) than for MAE–GC–μECD (RSD < 23%). The accuracy of both optimized methods was satisfactorily demonstrated by analysis of a certified reference material.

The presence of PBDEs in human tissues has also been studied. Li et al. [37] reported a method based on MAE, in conjunction with GC–MS analysis, to determine the concentration level of five PBDE congeners in maternal adipose tissue, showing a dominance of BDE 47 (values ranged from 0.50 to 9.01 ng g^{-1}, all the samples were positives) over the other congeners (BDE 100 was detected in six samples over sixteen at concentrations below 3.29 ng g^{-1}; and BDE 99, BDE 153 and BDE 154 were not detected or positives values were below the LODs of the method), which indicates that BDE 47 is readily bioaccumulated in human adipose tissues. The same authors found important levels of PBDEs in thirty-six human adipose tissues and eight human muscle tissues [38].

Yusà et al. [39] used the statistical design of experiments for the optimization of a MAE-large volume injection (LVI)–GC–MS/MS method for the identification and quantification of PBDEs, and PBBs

Table 2
Flame retardants.

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
BDE 47 BDE 99 BDE 100	Marine biological tissues (2–4 g)	1. Blended. 2. Surrogate addition PCB 55 and PCB 61. 3. Ground with 5 g Na_2SO_4 per gram of sample.	40 mL pentane: dichloromethane (1:1, v/v), 115 °C, 25 min	1. 10 g acid silica gel column. 2. GPC [116].	GC–MS (EI)	89–95	<0.1 ng g^{-1}	6.8–13.2		[32]
14 PBDEs	Blubber samples from pinnipeds (1 g)	1. Grounded. 2. Addition of Na_2SO_4.	25 mL dichloromethane, 100 °C, 15 min, 1500 psi	1. Addition of surrogates BDE 71 and 172. 2. Concentration. 3. 10 mm i.d. glass column packed neutral alumina and silica gel, elution 50 mL dichloromethane: hexane (3:7, v/v). 4. Solvent reduction to 1 mL.	GC–MS	93–115	1.0 ng g^{-1} w.w.; 2.3 ng g^{-1} w.w. (BDE 47)	<11	Up to 33.7 μg g^{-1} (w.w.)	[33]
BDE 47 BDE 99 BDE 119 BDE 153 among other compounds (PCBs)	Biological tissues (trout and eels muscle and pooled mysids) (0.5 g)	1. Surrogate addition SRM 2262. 2. Homogenized. 3. Freeze-dried.	30 W, 10 min, 30 mL dichloromethane, 115 °C	1. Filtrated. 2. Concentrated to 300 μL isooctane. 3. Purified with acidic silica gel column (2 g), eluted with 3× 5 mL pentane: dichloromethane (90:10, v/v). 3. Concentrated and transferred to isooctane.	GC–ECD	>80	1.1–2.6 ng g^{-1}	Average about 10	BDE 47 (6–44 ng g^{-1}) BDE 99 (4 ng g^{-1})	[34]
BDE 47 BDE 99 BDE 100 BB 15 BB 49	Aquaculture samples: feed and products (0.5–1.5 g)	1. Homogenized. 2. Spiked with ^{13}C-labelled PCBs and BDE 99 as IS.	Central composite design: 14 mL hexane: dichloromethane (1:1), 80 °C, 15 min	1. Centrifugation. 2. SPE, 3 g of acid silica gel, elution with 3× 3 mL hexane. 3. Concentration to dryness. 4a. Reconstitution with 200 μL hexane. 4b. HS-SPME (60 min, 70 °C)	GC–MS/MS		1.94–580 pg g^{-1}	<14.1	N.D.	[35]
BDE 47 BDE 99 BDE 100 BDE 153 BDE 154; BB 15 BB 49	Aquaculture samples (Feed for turbot and trout; samples of scallop, clam and mussel) (1 g)	1. Triturated and homogenized.	Central composite design: 200 W, stirring MAE: 15 mL hexane, 1 mL of water, 75 °C, 9 min. MAES: 15 mL hexane, 9 mL of 2 M KOH in methanol, 65 °C, 3 min.	1. Centrifuged 5 min, 3000 rpm. 2. SPE column with 3 g acid silica gel. 3. Elution with 15 mL hexane. 4. Concentration to dryness. 5. Reconstitution with 200 μL hexane.	GC–μECD	78.3–102.0 (MAES) 60.1–116.6 (MAE)	0.01–0.4 ng g^{-1}	<13.1 (MAES) <23.1 (MAE)	BB 49 (1.23 and 1.48 ng g^{-1}), BDE 47 (1.57 ng g^{-1})	[36]

BDE 47 BDE 99 BDE 100 BDE 153 BDE 154	Maternal adipose tissue (0.5 g)	1. Surrogate addition ^{13}C-labelled PBDE congeners.	15 mL hexane: dichloromethane (1:1), 3 g Na_2SO_4, 115 °C, 25 min	1. SPE cleanup: 20 g acid silica gel, elution with 100 mL hexane and 50 mL hexane: dichloromethane (1:1). 2. Concentration to dryness. 3. Addition of ^{13}C-labelled PCB 208. 4. Reconstitution with 25 μL dodecane.	GC–MS (EI)	70–130	0.5–1.2 ng g^{-1}	<13	0.50–9.01 ng g^{-1} (BDE 47) 1.20–3.29 ng g^{-1} (BDE 100)	[37]
PBDEs among other compounds	Human adipose and muscle tissues (0.5 g)	1. Surrogate addition ^{13}C-labelled PBDE congeners.	15 mL hexane:dichloromethane (1:1), 3 g Na_2SO_4, 115 °C, 25 min	1. SPE cleanup: 20 g acid silica gel, elution with 100 mL hexane and 50 mL hexane: dichloromethane (1:1). 2. Concentration to dryness. 3. Addition of ^{13}C-labelled PCB 208. 4. Reconstitution with 25 μL dodecane.	GC–MS (EI)	70–130	0.5–1.2 ng g^{-1}	<13		[38]
PBDEs, PBBs and PCNs	Sediments (5 g)	1. Freeze-dried, pulverized and sieved.	Plackett–Burman design: 48 mL hexane:acetone (1:1, v/v), 152 °C, 24 min	1. GPC: dichloromethane 5 mL min^{-1}. 2. Evaporation to dryness. 3. Reconstitution with 200 μL isooctane solution of IS.	PTV–LVI–GC–MS/MS	85–95	4–20 pg g^{-1}	4–13	0.22 and 0.32 ng g^{-1} (BDE 47)	[39]
BDE 47 BDE 99 BDE 100 BDE 138 BDE 153 BDE 154 BDE 183 BDE 209	Sewage sludge (0.25–0.5 g d.w.)	1. Homogenized. 2. Mixed with 15 g anhydrous Na_2SO_4 and 100 ng of surrogate BDE 77.	30 mL hexane:acetone (3:1, v/v), 130 °C, 35 min	1. Mixed with 5 mL H_2SO_4/waster (1:1, v/v). 2. Transfer solvent layer to 5 cm anhydrous Na_2SO_4 column. 3. Hexane added to acid layer to extract remaining PBDEs. 4. Concentration <1 mL. 5. Silica gel column cleanup.	GC–MS (NCI)	80–110	1–7 ng g^{-1}	<10	Most abundant: BDE 47 (250–700 ng g^{-1}), BDE 99 (300–800 ng g^{-1}), BDE 209 (200–500 ng g^{-1})	[40]

Table 2 (*Continued*)

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
BDE 47 BDE 85 BDE 99 BDE 100 BDE 153 BDE 154	House dust (0.8 g)	1. Surrogate addition 20 ng ^{13}C-labelled-BDE 99	Mixed level factorial design: 8 mL hexane, 4 mL 10% NaOH aqueous solution, 80 °C, 15 min	1. Dried with Na_2SO_4. 2. Cleanup with Florisil. 3. Filtration. 4. Concentration to 0.2 mL.	GC–MS/MS	92–114	0.29–0.55 ng g^{-1}	11–16	8.1–59.2 (BDE 47), 9.4–64.2 (BDE 99), 2.7–19.6 (BDE 100), 1.3–1.4 (BDE 85), 1.6–4.6 (BDE 154), 2.7–3.4 (BDE 153) ng g^{-1}	[41]
PentaBDE, OctaBDE mixtures, and decaBDE	House dust (0.8 g)	1. Surrogate addition 30 ng PCB 30	Mixed level factorial design: 8 mL hexane, 4 mL 10% NaOH aqueous solution, 80 °C, 15 min	1. Dried with Na_2SO_4. 2. Cleanup with Florisil. 3. Filtration. 4. Concentration to 0.2 mL.	GC–μECD	90–108	0.044–1.44 ng g^{-1}	4–13	6.9–69.5 (BDE 47), 6.2–60.0 (BDE 99), 1.0–18.2 (BDE 100), 0.286–1.62 (BDE 85), 0.98–9.07 (BDE 153), 0.685–9.69 (BDE 154), 4.55–142 (BDE 183), 1.13–5.51 (BDE 190), 3.73–58.5 (BDE 197), 3.71–16.3 (BDE 203), 3.20–15.7 (BDE 196), 14.9–172.9 (BDE 207), 58.4–1615 (BDE 209) ng g^{-1}	[42]
BDE 28 BDE 47 BDE 99 BDE 100 BDE 153 BDE 154 BDE 183 BDE 209	House dust (0.2 g)		25 mL hexane: dichloromethane (1:1, v/v), 2 g of Na_2SO_4, 115 °C, 15 min	1. Acid silica gel column, elution with 100 mL hexane, and 50 mL of hexane: dichloromethane (1:1, v/v). 2. GPC. 3. Concentration to 25 μL dodecane containing the IS.	GC–MS (NCI)	71–130	0.02–40 ng g^{-1}	<26; 32 for BDE 209	Most abundant congeners: BDE 47 (5.1–1500 ng g^{-1}), BDE 99 (4.4–6300 ng g^{-1}), BDE 209 (68–13,000 ng g^{-1})	[43]
TBP, TiBP, TCEP, TDCP, TBEP, TEHP, TPP, TPPO, TCPP	House dust (0.5 g)		Factorial design: 10 mL acetone, 130 °C, 30 min	1. Dilution 500 mL of water. 2. Concentration OASIS HLB sorbent. 3. Elution with 2 mL ethyl acetate. 4. Purification with silica.	GC–NPD	85–104	0.04 μg g^{-1} (TiBP, TBP, TCEP, TCPP); 0.05 μg g^{-1} (for the rest)	<11	Average concentration ranged between 0.09 and 3.9 μg g^{-1}	[46]

TPrP, TiBP, TBP, TCEP, TDCP, TBEP, TPP, TEHP, TPPO, TCPP	River sediment (0.5 g)	1. Dried. 2. Sieved (<300 μm particle size)	Factorial design: 5 mL solvent in two sequential steps of 15 min, the first using acetone and the second acetonitrile, 150 °C	1. The extracts were combined and centrifuged (4000 rpm, 4 min). 2. Addition 1 mL ethyl acetate. 3. Evaporation to 0.5 mL. 4. Purification with 50 mg silica cartridges, elution with 1 mL ethyl acetate. 5. Addition IS: TPeP. 6. Concentration to 0.2 mL.	GC–ICP-MS	78–105	20 ng g^{-1} (TCPP), 10 ng g^{-1} (the rest)	<12	Most abundant species: TBP (2.8–8 ng g^{-1}), TCPP (4–10 ng g^{-1})	[47]
BPA, among others	Liver and muscle tissue of fish (1.0 g)		20 mL dichloromethane: methanol (2:1), 25 min, 20% of power	1. Filtration. 2. Addition of 0.9% KCl solution. 3. 10 min centrifugation. 4. Evaporation, and reconstitution with 1 mL of cyclohexane or methanol:cyclohexane (1:20). 5. SPE, elution with 4 mL methanol. 6. Evaporation.	LC–MS	49 (liver) 79 (muscle)	50 ng g^{-1}	<10 (liver) <8.7 (muscle)		[49]
BPA, among others	Sediment (5 g dry mass)	1. Addition of copper granules	Methanol, 110 °C, 15 min	1. Washing and rotary evaporation to 1 mL. 2. Silica gel column cleanup, elution with 20 mL ethyl acetate:hexane (4:6). 3. Evaporation to dryness. 4. Derivatization.	GC–MS	80.2–103	1.0 ng g^{-1}	<24.3	5–9 ng g^{-1}	[50]
BPA, among others	River sediment (3 g)	1. Lyophilized. 2. Sieved through a 0.5-mm screen. 3. Addition of 2 g copper granules.	25 mL methanol, 110 °C, 15 min, 200 psi	1. Solvent reduction to 1 mL. 2. Addition of 500 mL of water. 3. SPE through Water Oasis HLB cartridges, elution with 15 mL ethyl acetate. 4. Solvent reduction to 0.5 mL. 5. Derivatization.	GC–MS/MS	100	0.13 ng g^{-1}	1.23	7.7–56.1 ng g^{-1}	[51]

Table 2 (*Continued*)

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
BPA, among others	Marine sediments (1 g)	1. Lyophilized. 2. Sieved through a 0.5-mm screen.	FMASE, 100 W, 5 cycles, 120 s, 35 mL dichloromethane	1. Dichloromethane extracts: evaporation to dryness, reconstitution ethyl acetate. 2. Water extracts: LLE with hexane and 500 mg NaCl, evaporation to dryness, reconstitution ethyl acetate.	GC–MS/MS	97	0.4–4.0 pg g^{-1}	3	9.3 μg kg^{-1}	[52]
BPA, among others	Marine samples (1 g)		20 mL dichlormethane: methanol (2:1), 25 min, 30% power	1. Filtered followed by addition of 4 mL of aqueous 0.9% KCl solution. 2. Centrifuged and evaporated to dryness. 3. Dissolved with 0.5 mL methanol and diluted to 100 mL water with 0.5 g of NaCl. 4. SPE, elution with acetone, evaporation and reconstitution in 0.5 mL acetone. 5. For GC analysis, derivatization with a 0.5-M methanolic solution of phenyltrimethylam-moniun hydroxide.	GC–MS, LC–UV, LC–MS	60–95	GC–MS: 0.004 ng LC–UV: 1.6 ng LC–MS: 1.0 ng		1.5–5.0 ng g^{-1} (sediments); 5.0–13 ng g^{-1} (plankton); 28.3 ng g^{-1} (clam gills)	[53]

HBCDs	Marine sediments (5 g)	1. Dried and homogenized.	40 mL acetone:hexane (1:3, v/v), 12 min, 90 °C; 800 W.	1. Filtration through 0.45 μm PTFE filter. 2. Concentration to ca. 1 mL (rotary vacuum evaporator). 3. Addition of TBA-S reagent (1 mL) and 2-propanol (2 mL), shake (1 min). 4. Addition of deionized water (5 mL), shake (1 min), centrifuged (5 min, 3000 rpm). 5. Addition hexane (7 mL) and 50% H_2SO_4 (c) (4 mL), and shake (2 min). 6. Centrifugation (10 min, 4000 rpm), solvent reduction to ca. 1 mL. 7. Anhydrous sodium sulfate/acidified silica column (10 cm × 0.5 cm i.d.), elution 20 mL of hexane. 8. Evaporation to dryness, and redissolved in 100 μL of methanol with 100 ng/mL of $^{13}C_{12}$-γ-HBCD as an IS.	HPLC–ESI–ITMS	68–91	5–10 pg g^{-1}	<11	[57]

BB: brominated biphenyl; BDE: brominated diphenyl ether; EI: electron impact ionization; GPC: gel permeation chromatography; HSSPME: headspace solid phase microextraction; IS: internal standard; N.D.: not detected; PBDEs: polybrominated diphenyl ethers; SPE: solid phase extraction; w.w.: wet weight; d.w.: dry weight; LVI: large volume injection; PBBs: polybrominated biphenyls; PCB: polychlorinated biphenyl; PCNs: polychlorinated naphthalenes; PTV: programmable temperature vaporizer; NCI: negative chemical ionization; NPD: nitrogen–phosphorous detector; TBEP: tris(butoxyethyl) phosphate; TBP: tributyl phosphate; TCEP: tris(2-chloroethyl) phosphate; TCPP: tris(chloropropyl) phosphate; TDCP: tris(2-chloro-,1-chloromethylethyl) phosphate; TEHP: tris(2-ethylhexyl) phosphate; TiBP: triisobutyl phosphate; TPP: triphenyl phosphate; TPPO: triphenyl phosphine oxide; BPA: bisphenol A; LLE: liquid–liquid extraction; TPeP: tripentyl phosphate; TPrP: tripropyl phosphate; ESI: electrospray ionization; HBCD: hexabromocyclododecane; ITMS: ion trap mass spectrometer; TBA-S: tetrabutylammonium sulphite.

(polychlorinated naphthalenes were also included in this work) in sediments at low levels (LODs ranged between 4 and 20 pg g^{-1} when 5 g of sediment were analyzed). BDE 47 was detected in two of the three samples collected in the harbour of Valencia at concentration levels of 0.22 and 0.32 ng g^{-1}. The same samples were analyzed using Soxhlet extraction finding out no significant differences between both methods results, but MAE allowed reduction of both, extraction time (24 min vs 2 h) and organic solvent consumption (48 mL vs 75 mL), and increased sample throughput.

It is generally accepted that PBDEs tend to concentrate in sewage sludge because of their hydrophobic properties and resistance to biodegradation during sewage sludge treatment processes. An efficient MAE-based method of analysis was developed and evaluated for the quantification of eight major PBDEs including BDE 209 in sewage sludge [40]. The method exhibited recoveries of >80% for the studied PBDEs when extracted from wet and dry sludge. The extraction efficiency for BDE 209 was higher than using conventional Soxhlet extraction, allowing the analysis of the PBDE congeners in a single run. BDEs 47, 99 and 209 were the most abundant congeners found in different sewage treatment plant (STP) sludge samples.

As PBDEs are widely added to materials that are predominantly used indoors, the presence of these compounds in the indoor environment cannot be neglected. Since people spend most of their time indoors, the indoor environment is a particularly important source of human exposure. For this reason, a rapid and simple method for the analysis of tetra to hexaBDEs in house dust samples based on MAE and GC–MS/MS has been developed by Regueiro et al. [41]. Extraction conditions were optimized using a multifactorial experimental design approach. An aqueous NaOH phase in combination with a non-polar organic phase (hexane) allowed an efficient extraction of the target analytes from dust and reduced chromatographic background. The final hexane extracts were analyzed after a simple one-step cleanup procedure using Florisil. The LODs ranged from 0.29 to 0.55 ng g^{-1} for all compounds. PBDEs were found in real dust samples collected in urban and rural houses of Northwestern Spain in concentrations ranging from 1.31 to 64.2 ng g^{-1}. In addition, the same authors [42] attempted to achieve better control of gas chromatographic analysis of PBDEs, not only for decaBDE (compound with tendency to show up high variability in analysis) but for all the other congeners also, especially the highly brominated octa and nonabrominated compounds. A narrow-bore column was used to achieve good and rapid separation of the analytes. The gas chromatographic conditions were optimized by means of a multifactor experimental design approach to obtain both good sensitivity and adequate precision. The results obtained were then used to develop a method for the simultaneous determination of tetra to decaBDEs in domestic dust. PBDEs were isolated by MAE. Quantitative recovery and good precision were obtained for all the PBDEs. LODs ranged from 0.0439 to 1.44 ng g^{-1}. Accuracy was tested by the analysis of the standard reference material SRM 2585. PBDEs were detected in all samples of house dust analyzed. Although decaBDE was the predominant congener, components of octa and pentaBDE commercial mixtures were present in all samples. Tan et al. [43] applied the MAE method developed by Bayen et al. [32] to ascertain prevailing of PBDEs in residential house dust. They determined the concentrations and profiles of PBDE in such environment in order to assess human exposure of these contaminants via dust ingestion and inhalation. Recoveries of the method applied to house dust ranged from 71 to 130%, whereas LODs varied from sample to sample depending on sampling size, and ranged from 0.02 to 40 ng g^{-1} (dust weight).

Several esters of phosphoric acid (organophosphate compounds, OPhs) are also extensively employed as plasticizers and flame retardant additives in textiles, wallpapers, varnishes and polymeric materials [44]. In most cases, and as PBDEs, these species are not chemically bounded to host materials; therefore, they can be easily emitted to the surrounding areas. As a result, nowadays, OPhs are ubiquitous pollutants in sewage water and indoor atmospheres. Although the toxicity of OPhs is relatively low, at least in comparison to the BFRs, their increasing use and some negative effects reported for the chlorinated OPhs, have increased the concern about possible long-term effects associated to a chronic exposure to these species [45]. Garcia et al. [46] presented an analytical procedure for the determination of several OPhs in bulk dust samples from indoor environments based on MAE and cleanup of extracts using normal and reversed-phase SPE sorbents. The extraction efficiency of this technique (85–104% recoveries) was similar to that achieved using Soxhlet, with the advantage of a reduced consumption of organic solvent and the possibility of processing up to 12 samples simultaneously. Data obtained for non-spiked samples revealed the ubiquitous presence of most of the selected OPhs in house dust. These authors also developed a procedure to extract a group of 10 OPhs from sediment samples [47]. MAE was the technique of choice and gas chromatography–inductively coupled plasma–mass spectrometry (GC–ICP-MS) was used for determination purposes. Several variables affecting the extraction efficiency were evaluated in detail and ICP-MS parameters were optimized. Finally, the performance of the method was demonstrated with real-life polluted sediments.

Bisphenol A (BPA) is used in the production of flame retardants, for this reason it is often included in the studies of BFRs, although BPA is part of the fabrication of many other products, as polycarbonate and epoxy resins. Although BPA has low acute toxicity, it behaves as an endocrine disruptor compound (EDC). EDCs are defined as exogenous substances which alter the functions of the endocrine system and consequently cause adverse health effects in an intact organism, or its progeny. EDCs are of global concern due to their widespread occurrence, persistence, bioaccumulation and potential adverse effects on ecosystem functioning and human health [48]. BPA has been detected at considerable concentrations in marine and freshwater habitats around the world.

Different analytical strategies have been developed for the selective and accurate determination of BPA in environmental matrices. Pedersen and Lindholst [49] developed a selective and sensitive method, based on MAE followed by SPE and LC–MS equipped with an atmospheric pressure chemical ionization interface for the determination of BPA, together with other EDCs, in water, and in liver and muscle tissue of fish species. The combined methods for tissue extraction allowed the use of small sample amounts of liver or muscle (typically 1 g), low volumes of solvent (20 mL), and short extraction times (25 min). LOQs of BPA were approximately 50 ng g^{-1} in both muscle and liver tissue (based on 1 g of fresh tissue). A MAE method followed by GC–MS analysis has been successfully developed by Liu et al. [50] for the simultaneous extraction and determination of EDCs including BPA in river sediments. Reasonably low LOD values (1 ng g^{-1} for BPA) were made possible by an effective cleanup step with silica gel. The levels of BPA found in different sediment samples ranged between 5 and 9 ng g^{-1}. River sediments were also the object of Hibberd et al. [51], who developed a method based on MAE for the simultaneous determination of a wide group of EDCs (BPA among them) from sediments, obtaining good recovery (100% for BPA) and reproducibility (RSD, 1.23%) as well as low LODs (0.13 ng g^{-1}). Levels of BPA found in samples ranged from 7.7 to 56.1 ng g^{-1}. Morales-Muñoz et al. [52] have investigated the extraction of BPA, together with other contaminants, from marine sediments using a sequential automated focused microwave-assisted Soxhlet extraction (FMASE) reaching LODs in the low picogram per gram levels. The total time required for quantitative extraction of the target compounds was 75 min, a short time as compared with the 24 h Soxhlet extraction. Stuart et al. [53] carried out analyses of

marine bottom sediment samples collected by a remotely operated submersible vehicle, and zooplankton samples. Careful sample pre-treatment involving enhanced organic solvent extraction by microwave heating, followed by an effective SPE cleanup and preconcentration allowed for the detection by either GC–MS or LC–MS. Four different analysis methods were compared, i.e. GC–MS (non-derivatized), GC–MS (derivatized), LC–UV (non-derivatized) and LC–MS (non-derivatized) in terms of their method detection limits for the four phenolic compounds: BPA, 4-cumylphenol, OP and NP. Pre-derivatization of the phenols followed by GC–MS provided for the highest sensitivity of the four analytical methods used. Their analyses of the bottom sediment, plankton and clam extracts taken from the same eight sites showed that primarily BPA was present at concentration levels of 1–30 ng g^{-1}.

HBCDs are non-aromatic brominated cyclic alkanes that are used widely as additive BFRs in buildings, in upholstery textiles and in electronic devices as the thermal insulation. The commercially used HBCD comprises three diastereoisomers: α-, β- and γ-HBCD [54]. The physical and chemical properties of HBCDs are similar to those of many persistent organic pollutants: persistency, bioaccumulation, long-range transport and toxicity. They have been detected worldwide in variety of environmental samples, including air, fresh water, sediments, aquatic biota, indoor air and dust, and even in human blood and breast milk [54,55]. Soxhlet has been used for the determination of HBCDs in soils and sediments [56]. Wu et al. [57] evaluated an efficient MAE procedure coupled with high performance liquid chromatography–electrospray-ion-trap mass spectrometry (HPLC–ESI-ITMS) to determine HBCDs diastereoisomers (α-, β- and γ-HBCD) in marine sediments. They also compared the extraction efficiency of the MAE technique with Soxhlet extraction and PLE. They found recoveries for these three methods not different statistically. The MAE and PLE methods were more effective in extracting the HBCD residues from the sediment samples in terms of their significant savings of time and solvent. Moreover, relative to PLE, the MAE approach provides a higher throughput for sample preparation (the entire MAE process took ca. 35 min and up to 6 samples could be extracted simultaneously). The LOQs ranged from 25 to 40 pg g^{-1} (dry weight) in 5 g of the sediment samples. The recoveries of the HBCDs in spiked sediment samples ranged from 68 to 91% (RSD: 2–11%).

4.2. Surfactants

Surfactants are key components of detergent formulations due to their surface activity. They are among the most widely used chemicals in the world, and coastal ecosystems receive large quantities of these compounds. The two major groups of surfactants, classified according to the charge on the hydrophilic moiety, are anionic and non-ionic. Their main components are linear alkylbenzene sulfonates (LAS) for the anionic and alkylphenol polyethoxylates (APEOs) for the non-ionic.

4.2.1. Linear alkylbenzene sulfonates

LAS are the most important anionic surfactants used in household laundry (powder and liquid); dishwashing detergents (>80% of LAS European consumption is in household detergency); and all purpose cleaners. LAS (the 20% remaining of European consumption) are also used on the textile processing as wetting; cosmetic, food and leather industries; as dispersing and cleaning agents; in industrial processes as emulsifiers; and for the polymerization in the formulation of crop protection agents [58]. The presence of LAS in many commonly used household detergents gives rise to a variety of possible consumer contact scenarios including direct and indirect skin contact, inhalation, and oral ingestion derived either from residues deposited on dishes, from accidental product ingestion, or indirectly from drinking water. LAS on the European market is a specific and rather constant mixture of closely related isomers and homologues generated in the manufacture of the raw material linear alkyl benzene, the LAS precursor, each containing an aromatic ring sulphonated at the *para* position and attached to a linear alkyl chain at any position except the terminal carbons. This commercial LAS consists of more than 20 individual components. The ratio of the various homologues and isomers, representing different alkyl chain lengths and aromatic ring positions along the linear alkyl chains, is relatively constant across the various household applications. After use and disposal, LAS are usually discharged through the sewage infrastructure to municipal WWTPs where are subjected to physical and biological treatments. In the STPs, LAS break down only partly and, consequently, some of them remain in the effluent and other fraction is adsorbed in sewage solid, in which they constitute the major synthetic compounds in quantities between 2 and 5 g kg^{-1}. Through waterways and sewage sludge disposal, LAS are discharged into the environment [59].

During recent decades a variety of procedures have been used to extract LAS from solid samples. Soxhlet and ultrasonic methods using methanol as extraction solvent are mainly employed. Some attempts performed in order to reduce both the volume of organic solvents used and the time needed for the complete extraction have been based on SFE [60] and PLE [61]. The application of MAE is presented in Table 3.

Morales-Muñoz et al. [62] studied the application of a FMASE coupled to a preconcentration/derivatization/detection system for a fully automated screening method for LAS in sediment samples. The proposed approach provided not only better efficiencies than conventional Soxhlet (with both water and methanol) but also a drastic reduction of extraction time (∼2 h vs >24 h). Villar et al. [63,64] proposed a new method for the extraction and determination of LAS from sewage sludge based on microwaves extraction, and three different separation-detection systems, i.e. high performance liquid chromatography with diode array detection (HPLC–DAD); capillary electrophoresis with diode array detection (CE–DAD) and fluorescence detection (CE–FL). Advantages of the developed method included a short extraction time (10 min) for C_{10}–C_{13} homologues, no special equipment was required, and extractions were not dependent on the LAS alkyl chain length. These characteristics compare favourably with those of the classical extraction of LAS from solid samples (Soxhlet extraction) where high volumes of methanol and sample treatment of 10–12 h are required. In addition, the purification of MAE extracts prior to the final chromatographic determination was not required. Recovery values obtained using MAE were comparable with those determined by Soxhlet extraction. Therefore MAE was proved to constitute reliable, efficient and reproducible method for the extraction of LAS in sewage sludge and sediments. In this way, MAE should be preferred to Soxhlet because it requires less time and solvent. Pakou et al. [65] used MAE to assess the potential efficiency of composting as an aerobic thermophilic process allowing for removal or, at least, reduction of LAS, nonylphenol ethoxylates (NPEO) and diethylhexyl phthalate concentrations present in primary and secondary sludge.

4.2.2. Alkylphenol ethoxylates

APEOs are one of the most widely used classes of surfactants and, particularly, octylphenol ethoxylates (OPEOs) and NPEOs are two of the most common non-ionic surfactants in the marketplace. They have been used commercially as emulsifiers and solubilizers in pharmaceutical and agrochemical formulations, in cosmetics, as well as in various biotechnological processes, because of their favourable physicochemical characteristics. Furthermore, they are used in the industrial production of cleaning products, textiles, petroleum, pulp and paper and pesticides formulation [66]. APEOs are discharged to wastewater treatment facilities or

Table 3
Surfactants.

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
LAS	Sediment	1. Dried.	FMASE, 200 W, 200 s, 120 s delay time, 9 cycles	1. Preconcentration (C18-Hydra), elution with water:methanol, 1:1, v/v. 2. Derivatization.	HPLC–FL	95–102	4.4 $\mu g\,g^{-1}$	4.3		[62]
LAS	Sewage sludge (CS and DS) (0.5 g)	1. Dried 40 °C. 2. Grounded agate mortar and sieved (<1 mm).	5 mL methanol, 250 W power, 10 min	1. Filtration through glass wool.	HPLC–FL HPLC–DAD	83–102	0.33–1.83 mg kg^{-1} (FL) 0.25–2.50 mg kg^{-1} (DAD)	<5.42 (FL) <5.18 (DAD)	Most abundant: 4700 mg kg^{-1} (LAS C-12, DS) and 945 mg kg^{-1} (LAS C-12, CS)	[63]
LAS	Sewage sludge (CS and DS) (0.5 g)	1. Dried 40 °C. 2. Grounded agate mortar and sieved (<1 mm).	5 mL methanol, 250 W, 10 min	1. Filtration through glass wool	HPLC–FL CE–DAD	>85	3.03 mg kg^{-1} (HPLC) 21.0 mg kg^{-1} (CE)	2.98 (CE)	≈5000 mg kg^{-1} (DS) ≈2700 mg kg^{-1} (CS)	[64]
LAS, among others	Compost samples (0.2 0.3 g)	1. Dried.	20 mL methanol, 100 °C, 600 W, 15 min	1. Concentration. 2. Reconstitution with 10 mL methanol/water (1:1), 1% HCHO and 0.05 M SDS.	HPLC–FL	>92.3	46–194 $\mu g\,L^{-1}$	<22.5	30.9 g kg^{-1} (sludge), 1.49 g kg^{-1} (compost)	[65]
OP, among others	Liver and muscle tissue of fish (1 g)		20 mL dichloromethane: methanol (2:1), 25 min, 20% of power	1. Filtration. 2. Addition of 0.9% KCl solution. 3. 10 min centrifugation, evaporation. 4. Reconstitution with 1 mL of cyclohexane or methanol:cyclohexane (1:20). 5. SPE, 4 mL methanol, evaporation.	LC–MS	60 (liver) 78 (muscle)	OP: 10 ng g^{-1} (muscle), 50 ng g^{-1} (liver)	<8.8 (liver) <10.9 (muscle)		[49]
NP, NP1EO, NP2EO	River sediments	1. Freeze-dried.	40 mL methanol, 120 °C, 20 min	1. Concentration to 1–2 mL. 2. Cleaned-up with deactivated neutral alumina column and eluted with 15 mL 10% acetic acid in methanol. 3. Concentration to 0.5 mL and filtration.	HPLC–FL		0.1–0.3 $\mu g\,g^{-1}$ (LOQ)	10–30		[73]
NP, OP, among others	River sediments (5 g dry mass)	1. Addition of copper granules.	25 mL methanol, 110 °C, 15 min	1. Washing, rotary evaporation to 1 mL. 2. Silica gel column cleanup, elution with 20 mL ethyl acetate:hexane (4:6, v/v). 3. Concentration to 0.5 mL and IS addition (BPA-d16). 4. Evaporation dryness. 5. Derivatization with pyridine and BSTFA (30 min, 60–70 °C).	GC–MS	61.5–133	0.5 ng g^{-1} dry mass	<18.3	2–12 ng g^{-1} d.w.	[50]
NP, among others	Sediment (2 g)	1. Lyophilized. 2. Grinded. 3. Addition of 2 g of activated copper.	Experimental design optimization: 15 mL methanol, 159 kPa, 15 min, 80% power	1. Filtered and concentrated to dryness. 2. Redissolved in 0.5 mL methanol. 3. Cleaned-up on 200 mg Lichrolut®, elution 1 mL of the extract, 1 mL of methanol:water (3:1), elution 5 mL ethyl acetate. 4. Blown down to dryness, and redissolved in 1 mL methanol after IS addition.	GC–MS HPLC–DAD–UV–FL		0.1 mg kg^{-1}	7–30	Up to 1.10 mg kg^{-1} (NP) and 1.51 mg kg^{-1} (NPEO)	[74]

NP, among others	Sediment (1.0 g)	1. Lyophilized. 2. Grinded. 3. Addition of 1 g of activated copper.	15 mL acetone, 145 kPa (full power) and then 15 min constant at 80% MW power	1. Filtration, concentration to 0.5 mL. 2. Addition of 1 mL isooctane. 3. Fractionated in two groups using Florisil: elution of PAH and PCBs with 12 mL of hexane:toluene (4:1), and PE and NPs with 5 mL ethyl acetate. 4. Concentration to dryness and redissolved with isooctane.	GC–MS		100 ng	7–30	0.14–1.10 mg kg^{-1} (NP) and <0.1–1.51 mg kg^{-1} (NPEO)	[75]
OP, among others	Marine sediments (1 g)	1. Lyophilized. 2. Sieved through a 0.5-mm screen	FMASE, 100 W, 5 cycles, 120 s, 35 mL dichloromethane	Dichloromethane extracts: 1. Evaporation to dryness. 2. Reconstitution ethyl acetate. Water extracts: 1. LLE with hexane and 500 mg NaCl, 2. Evaporation to dryness. 3. Reconstitution ethyl acetate.	GC–MS/MS	~100	0.4–4.0 pg g^{-1}	<10		[52]
NP, OP, among others	Sediment (3 g)	1. Lyophilization. 2. Ground and sieved to <500 μm	25 mL methanol, 2 g copper granules, 110 °C, 15 min, 7 min ramp, at 200 psi	1. Rinsed with 3× 15 mL methanol. 2. Volume reduction to 1 mL. 3. Addition of 500 mL water. 4. SPE (Oasis HLB, 15 mL ethyl acetate, solvent evaporation to dryness. 5. Derivatization with BSTFA and pyridine.	GC–MS/MS	86–114	0.08–0.14 ng g^{-1}	<20	4.7–31.3 ng g^{-1} (OP) <11.2 ng g^{-1} (NP)	[51]
NP	Sewage sludge (0.03–0.3 g)	1. 1% formaldehyde. 2. Grinded	20 mL hexane:acetone (1:1), 1 mL water, 17 min, ramp to 120 °C in 2 min and hold for 15 min, 1200 W	1. Concentration 1 mL. 2. Redissolved in 10 mL acetonitrile. 3. Filtration.	HPLC–FL	61.4 (NPEO)–91.4 (NP)	1.82 μg g^{-1} d.w. (NPEO)–2.86 μg g^{-1} d.w. (NP)	3.62 (NPEO)–4.69 (NP)	Up to 233.5 mg kg^{-1} (NPEO) and 93 mg kg^{-1} (NP)	[68]
CP, OP, NP, among others	Marine samples (1 g)		20 mL dichloromethane: methanol (2:1), 25 min, 30% power	1. Filtered followed by addition of 4 mL of aqueous 0.9% KCl solution. 2. Centrifuged and evaporated to dryness. 3. Dissolved with 0.5 mL methanol and diluted to 100 mL water with 0.5 g of NaCl. 4. SPE, elution with acetone, evaporation and reconstitution in 0.5 mL acetone. 5. For GC analysis: derivatization with a 0.5-M methanolic solution of phenyltrimethylammoniun hydroxide.	GC–MS LC–UV LC–MS	60–95	GC–MS: 0.010 ng LC–UV: 3.4–4.7 ng LC–MS: 1.3–2.4 ng		11.4–12.5 ng g^{-1} OP, 22.9 ng g^{-1} NP (sediments); 3.7 ng g^{-1} Cumylphenol (plankton)	[53]
NP, NPEO, among others	Compost samples (0.2–0.3 g)	1. Dried	20 mL methanol, 100 °C, 600 W, 15 min	1. Concentration. 2. Reconstitution with 10 mL methanol/water (1:1), 1% HCHO and 0.05 M SDS	HPLC–FL	>92.3	33.0 μg L^{-1} (NPEO), 52.1 μg L^{-1} (NP)	<22.5	NPEO: 4.39 g kg^{-1} (sludge), 197 g kg^{-1} (compost) NP: 0.0872 g kg^{-1} (sludge), 3.73 g kg^{-1} (compost)	[65]

BPA: bisphenol A; BSTFA: bis(trimethylsilyl)trifluoroacetamide; CS: compost Sludge: obtained by exhibition to the sun, with a process of natural fermentation that takes place helped by ventilation; CE: capillary electrophoresis; DAD: diode array detector; DS: digestive sludge: primary sludge undergoes a process of digestion; d.w.: dry weight; FL: fluorescence detector; FMASE: focused microwave-assisted Soxhlet extraction; LAS: linear alkylbenzene sulfonates; NP: 4-Nonylphenol; NPEO: nonylphenol ethoxylates; OP: 4-*tert*-Octylphenol; SDS: sodium dodecyl sulphate; SPE: solid phase extraction; IS: internal standard; LLE: liquid–liquid extraction; PAHs: polycyclic aromatic hydrocarbons; PCBs: polychlorinated biphenyls; PE: phthalate esters; CP: cumylphenol.

directly released into the environment. During biological wastewater treatment they are partially converted to more persistent and toxic metabolites (nonylphenol mono- or di-ethoxylates, NPEO1,2 or nonylphenol, NP) [67]. NP and short chain NPEOs are lipophilic compounds with $\log K_{OW}$ of around 4.2–4.5, so they partition preferentially to the organic fraction of sediments and show considerable potential to bioaccumulate in aquatic organisms. Studies have found that these APEO metabolites are more toxic than the parent substances and possess the ability to mimic natural hormones by interacting with the estrogen receptor, inducing endocrine disruption of aquatic organisms. Additionally, NP is a raw material for the production of NPEO as well as other chemicals such as phosphate antioxidants, modified phenolic resins, additives to machine oils and metallurgical oils [68]. The levels of these APEO metabolites present in the environment may be well above the threshold necessary to induce endocrine disruption in wildlife. These findings have raised public concern over their environmental and human health effects [69].

For these reasons, the use of NPEO is being restricted in some countries. In fact, NP is considered as a toxic xenobiotic compound [70] and is classified as a 'priority hazardous substance' in Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy (amended by the Directive 2008/105/EC) [71]. Moreover, the Directive 2003/53/EC [72] establishes that NP and NPEO may not be placed on the market or used as a substance or constituent of preparations in concentrations equal or higher than 0.1% by mass for industrial and institutional cleaning (with some exceptions), domestic cleaning, textiles and leather processing (except processing with no release into waste water, systems with special treatment where the process water is pre-treated); emulsifier in agricultural teat dips; metal working; manufacturing of pulp and paper; cosmetic products; other PCPs; and co-formulants in pesticides and biocides.

A summary of methodologies based on application of microwaves to the analysis of alkylphenol ethoxylates can be found in Table 3. Pedersen and Lindholst [49] developed a selective and sensitive method based on MAE followed by SPE and GC–MS analysis, for the determination of octylphenol (OP), among other EDCs in fish tissues. The combined methods for tissue extraction allowed the use of small sample amounts of liver or muscle (typically 1 g), low volumes of solvent (20 ml), and short extraction times (25 min). LOQs of OP in tissue samples were found to be approximately 10 ng g^{-1} in muscle and 50 ng g^{-1} in liver (both based on 1 g of fresh tissue).

Croce et al. [73] evaluated five different extraction techniques (i.e. Soxhlet and automated Randall extraction; PLE; MASE; and extraction with a surfactant (Tween 80)) for the determination of NP and NPEO in river sediments. All the techniques were applied to the same three samples collected from northern Italian rivers. Recovery and reproducibility of the different extraction techniques were comparable but the small amount of solvent consumed, the reduced extraction time, and a real improvement in operator safety, were the most important advantages of methods based on PLE and MAE.

A MAE method also followed by GC–MS analysis has been developed for the simultaneous extraction and determination of EDCs including NP, OP, in river sediments by Liu et al. [50]. The best extraction conditions involved methanol as solvent, using an extraction temperature of 110 °C during 15 min. Low LOD values were made possible by an effective cleanup step with silica gel. The method developed coupling MAE and GC–MS technique provided means for the quantitative analysis of EDCs from river sediments down to 0.5 ng g^{-1}. Cortazar et al. [74] followed two approaches in their work to evaluate the extraction process of NPs and phthalate esters also in sediment samples. In the first one, a MAE method was studied, and once this process was optimized the recoveries obtained were compared to those obtained with a different extraction technique, i.e. PLE. In the second approach, the sediments were extracted two times in order to assure the completeness of the extractions. The cleanup of the extracts was also optimized in get the highest recoveries. Exhaustive extraction of the analytes occurred and the RSD values were comparable to those obtained in other works. They concluded that the capability of the microwave-oven to handle 12 samples simultaneously is very helpful in monitoring programs where a large number of samples are handled. In case of the detection, comparable results were obtained by GC–MS and HPLC–DAD–UV–FL. By using a closed-vessel extraction, Bartolomé et al. [75] dealt with the simultaneous extraction of PAHs, PCBs, phthalate esters, and NPs in sediments using acetone as solvent. A cleanup and fractionation step was also optimized using Florisil cartridges and (4:1) *n*-hexane:toluene and ethyl acetate as eluents. The method proved to be good for monitoring programs, as it was rugged and could accommodate the treatment of a large number of samples (12 in this case) simultaneously. Morales-Muñoz et al. [52] have investigated the extraction of OP, together with other contaminants, from marine sediments using a sequential automated FMASE reaching LODs in the low picogram per gram levels. Exhaustive extraction of the analytes occurred and the RSD values were lower than 10%. Hibberd et al. [51] described an improved method for the extraction and analysis of seven EDCs with wide-ranging polarities from water and sediments using gas chromatography–tandem mass spectrometry (GC–MS/MS). The analytes included OP and NP. Extraction from sediment samples by MAE, with cleanup of sediment extracts by SPE, enhanced the recovery (86–114%) while reduced matrix interference and sample drying time. Final sample extracts were derivatized using *N*,*O*-bis(trimethylsilyl)trifluoroacetamide and pyridine, and the derivatized extracts were reconstituted in hexane to improve their stability. The optimized GC–MS/MS method allowed high selectivity and sensitivity, with LODs ranging from 0.08 to 0.14 ng g^{-1} in sediment.

MAE has been shown as a good extraction technique for the analysis of sludge and sediments from sewage treatment plants. Fountoulakis et al. [68] developed and optimized a MAE-based method for the extraction of NP and NPEOs from sewage sludge. The developed method was compared with other more traditional methods such as Soxhlet extraction and ultrasonication demonstrating that MAE was a suitable alternative for the analysis of NP and NPEO in sewage sludge. Then, it was used to monitor the presence of NP and NPEO in sludge samples collected from different sewage treatment plants and to evaluate the fate of these compounds at different stages in a particular STP of the city of Patras (Greece), and the removal efficiency of the treatment applied. The NPEO highest concentrations were determined in the primary sludge from the STP of Heraklion (Greece) (233.5 mg kg^{-1}) and the lowest in the secondary sludge at the STP of Patras (12.8 mg kg^{-1}). NP, the main degradation product of NPEO, was detected in all samples at concentrations ranging from 3.6 mg kg^{-1} in the secondary sludge from Patras to 93 mg kg^{-1} in the primary sludge from Heraklion. Pakou et al. [65] used MAE to investigate the fate of LAS, NPEOs and DEHP in municipal sewage sludge during composting. This was the first report on the application of MAE on the extraction of the LAS, NPEO, NP and DEHP from compost samples.

In their previously commented article, Stuart et al. [53] analyzed different marine samples finding levels of OP in sediments of 11.4 and 12.5 ng g^{-1}, and 22.9 ng g^{-1} of NP.

4.3. Personal care products

Characterized as emerging organic pollutants, PCPs have been the focus of global environmental research attention since the late

Table 4
Personal care products.

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
Polycyclic musks and NMs	Sewage sludge (1–2.5 g)	1. Addition of 10 g anhydrous sodium sulphate.	30 mL 1:1 (v/v) acetone:hexane, 35 min: 15 min ramp with a 20-min hold at 110 °C	1. Evaporated. 2. Cleaned-up on a silica gel column.	GC–MS	80–105	27–41 ng g^{-1} polycyclic musks, 4 ng g^{-1} NMs			[81]
Polycyclic musks and NMs	Sewage sludge, biosolids (1–2.5 g)	1. Addition of 10 g anhydrous sodium sulphate. 2. Centrifugation and filtration.	30 mL 1:1 (v/v) acetone:hexane, 35 min: 15 min ramp with a 20-min hold at 110 °C	1. Evaporated. 2. Cleaned-up on a silica gel column.	GC–MS	60–123	27–41 ng g^{-1} polycyclic musks, 3–4 ng g^{-1} NMs	11	The highest concentration HHCB 36,500 ng g^{-1}. MX was not detected but the other studied musks were always detected.	[82]
MK among others	Soil and sediment (3 g)	1. Dried. 2. Homogenized.	800 W, dichloromethane: methanol (2:1)	1. Concentration. 2. Derivatization (pyridine:BSTFA, 2:1). 3. Silica micro-column cleanup, evaporation, reconstitution hexane.	GC–MS	89.6			N.D.	[83]
NMs, among others	Indoor dust (0.8 g)	1. Sieving.	Factorial design optimization: 80 °C, 10 min, 8 mL hexane, 4 mL sulphuric acid solution 1 M, with ascorbic acid 0.10% (w/w)	1. Centrifugation (3000 rpm, 5 min). 2. Dried with anhydrous sodium sulphate. 3. Addition of Florisil 100 mg mL^{-1}, shaken for 2 min, and filtration.	GC–μECD	88–97	1.03–3.26 ng g^{-1}	<8.5	691.6 ng g^{-1} MX 14.94 ng g^{-1} MM 2303 ng g^{-1} MK	[84]
TRC among others	Marine sediments (1 g)	1. Lyophilized. 2. Sieved through a 0.5-mm screen.	FMASE, 100 W, 5 cycles, 120 s, 35 mL dichloromethane	Dichloromethane extracts: 1. Evaporation to dryness. 2. Reconstitution with 200 μL of ethyl acetate. Water extracts: 1. LLE with hexane and 500 mg NaCl. 2. Evaporation to dryness. 3. Reconstitution with 200 μL of ethyl acetate.	GC–MS/MS	96	0.4–4.0 pg g^{-1}	9	9.5 μg kg^{-1}	[52]
TRC among others	Soil and sediment (3 g)	1. Dried. 2. Homogenized.	800 W, dichloromethane: methanol (2:1)	1. Centrifugation (1000 rpm, 5 min). 2. Concentrated, fractionated. 3. Derivatization (pyridine:BSTFA, 2:1). 4. Silica micro-column cleanup, evaporation, reconstitution hexane.	GC–MS	89.6			N.D.	[83]
TRC among others	Sludge (0.5 g) and sediments (1 g)	1. Lyophilized. 2. Sieved.	30 mL 1:1 acetone:methanol, 130 °C, 20 min	1. Centrifugation. 2. Addition of 100 mL NaOH 0.2 M. 3. Washed with 2× 15 mL hexane. 4. pH readjusted. 5. SPE, 60 mg OASIS HLB. 6. Silica cleanup, elution with 5 mL ethyl acetate and evaporation to 2 mL. 7. Derivatization with MTBSTFA.	GC–MS/MS	82.2–99.7	0.4 ng g^{-1} (sediments) 0.8 ng g^{-1} (sludge)	<11.5	River sediment: 35.7 ng g^{-1} PS: 2696 ng g^{-1} BS: 5400 ng g^{-1} DiS: 1508 ng g^{-1} S: 1474 ng g^{-1}	[87]

BSTFA: bis(trimethylsilyl)trifluoroacetamide; FMASE: focused microwave-assisted Soxhlet extraction; HHCB: 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-γ-2-benzopyran (Galaxolide); LLE: liquid–liquid extraction; MK: musks ketone; MM: musk moskene; MX: musk xylene; N.D.: not detected; NM: nitromusks; TRC: triclosan; BS: biological sludge; DiS: disinfected sludge; MTBSTFA: N-(butyl-dimethyl-silyl)-2,2,2-trifluoro-N-methyl-acetamide; PS: primary sludge; S: sludge; SPE: solid phase extraction.

1990s. PCPs have caused widespread concerns due to their extensive human consumption. Their entry into the environment takes place through effluents of WWTPs, as well as surface-water runoffs and soil leaching after agricultural applications of manure or treated sludge. Concern about the environmental fate and potential effects of synthetic organic chemicals used in soaps, lotions, toothpaste, and other PCPs continues to increase. Their relatively low environmental concentrations, high polarity, and thermal lability of PCPs, together with their interaction with a host of complex environmental matrices, make their analysis challenging. Sample preparation followed by GC or HPLC separation, and qualitative and quantitative analysis using various detectors has become the standard approach [76]. Of particular concern are compounds that are used in large volumes, persist in the environment, bioaccumulate, or have a designed bioactivity [77] such as synthetic musk fragrances and antimicrobials. Table 4 summarizes the application of MAE-based methodology for the determination of synthetic fragrance components and triclosan in environmental samples.

4.3.1. Synthetic musk fragrances

Synthetic fragrances are added to toiletries, cosmetics, household products and a wide variety of consumer products. In addition, the use of products to scent the environment, such as air fresheners and scented candles, is also very popular. There is exposure from flavours in foods and beverages as well. It is because of this immense popularity of scented products that problems have surfaced. Concerns relate to direct effects on the health, to the bioaccumulation of fragrance chemicals in human tissue and the long-term impact, and to the environmental impacts [78]. There are two types of synthetic musk fragrances: nitro musk fragrances and polycyclic musk fragrances. The nitro musk fragrances were the first to be produced and include musk xylene (MX), musk ketone (MK), musk ambrette (MA), musk moskene (MM), and musk tibetene (MT). In the environment, the nitro substituents can be reduced to form amino metabolites of these compounds and possibly these transformation products are even more problematic that the parent compounds. MX and MK are two of the most widely used nitromusks and they are found in detergents and cosmetics. The polycyclic musk fragrances include 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-γ-2-benzopyrane (HHCB), 7-acetyl-1,1,3,4,4,6-hexamethyl-1,2,3,4-tetrahydronaphthalene (AHTN), 4-acetyl-1,1-dimethyl-6-*tert*-butylindane (ADBI), 6-acetyl-1,1,2,3,3,5-hexamethylindane (AHMI), 5-acetyl-1,1,2,6-tetramethyl-3-iso-propylindane (ATII), and 6,7-dihydro-1,1,2,3,3-pentamethyl-4(5H)-indanone (DPMI). The polycyclic musk fragrances are used in higher quantities than the nitro musk fragrances. HHCB and AHTN are used in the highest quantities and HHCB is on the US Environmental Protection Agency (EPA) High Production Volume (HPV) list (its use and production in the United States is greater than 450,000 kg per year) [79] and the Organization for Economic Co-operation and Development (OECD) list which includes chemicals which have annual production volumes greater than one thousand metric tonnes per year in at least one Member country or in the European Union region [80].

They have been analyzed in sewage sludge to study the efficiency of sewage treatments to remove synthetic musks. Extraction of musks from activated and digested sludge [77] has been accomplished by PLE, SFE, Soxhlet extraction, SPME, liquid–liquid extraction (LLE) and MAE. Synthetic musk fragrances have been Soxhlet-extracted from suspended sediments. In addition to MAE, dispersion extraction, PLE, simultaneous steam-distillation/solvent extraction (SDE) [77] were also applied for the analysis of these kind of compounds in sediments. MAE afforded several advantages over classical techniques (Soxhlet extraction and LLE), as lower solvent consumption, speed, and the potential to recover tightly bound residues not easily released by conventional techniques. The drawbacks of the more recent techniques comparing with MAE are possible losses of the analytes upon trapping or difficulty of releasing them from the matrix, larger number of parameters to be optimized, high cost of equipments, problems for matrices with high water content, and co-extraction of matrix materials.

The presence of polycyclic and nitromusks in sewage sludge was checked by Svoboda et al. [81] using MAE and a silica gel column for the cleaning up of the extracts obtaining recovery values ranged from 80 to 105%. The LODs ranged from 27 to 41 ng g^{-1} for the polycyclic musks and 4 ng g^{-1} for the nitromusks. Smyth et al. [82] presented the equivalence of two extraction methods: SFE vs MAE, in the analysis of polycyclic and nitromusks in sludge samples. They found out no significant differences between SFE and MAE extraction methods. Nevertheless, the air-drying sample preparation step for SFE has the potential to allow degradation and/or volatilization of the polycyclic and nitromusks. Moreover, MAE of centrifuged or filtered sludge resulted in recoveries that compare well with literature reports. Regarding the application of MAE for the detection and quantification of musks compounds in soil and sediments, Rice and Mitra [83] developed a time and cost-effective MASE-based method for the simultaneous analysis of eight structurally diverse PPCPs, MK among them, in these matrixes. The method consisted of optimizing the following variables: derivatization of the polar target analytes, silica gel open column cleanup, and GC–MS analysis of sample extracts for analysis and detection of the target compounds The final multi-residue PPCP method was applied to both standard-amended soil samples and to natural sediment samples collected directly outside a WWTP effluent pipe. Good recovery ($89.6 \pm 2.89\%$) was achieved for MK.

The occurrence of hazardous chemicals in the outdoor environment has been the subject of many studies. Nevertheless, investigation of chemical exposure inside the homes and offices where people spend the majority of their lives has only recently begun. Related with this, Regueiro et al. [84] developed a high-throughput method for the determination of nitromusks (together with organochlorinated compounds and pyrethroid insecticides) in indoor dust. House dust is a complex matrix characterized by a high organic carbon content derived from the presence of skin tissues, hair fibres and mites [85], which makes difficult the extraction and further determination of target compounds. In fact, only a few methods have been proposed for the analysis of organic compounds in house dust samples. In most cases, analytes are extracted by Soxhlet. However, other extraction techniques such as PLE, ultrasound-assisted extraction and matrix solid-phase dispersion have been recently applied for the extraction of polar organic contaminants in house dust. MAE has been proposed as the extraction technique in this work in which several cleanup procedures were tested. An on-batch cleanup step, avoiding other more complex multi-step cleanup procedures reduced sample manipulation while increased the throughput of the analysis. LODs were at the low nanogram per gram level for most of compounds. The proposed method was then applied to the analysis of real house dust samples where nitromusks were found in most of them at concentrations between 14.94 and 2303 ng g^{-1}. Therefore, the presence of high concentrations of several groups of pollutants in house dust was demonstrated in this study, which confirms the necessity of paying more attention to indoor pollution.

4.3.2. Triclosan

Triclosan (2,4,4′-trichloro-2′-hydroxydiphenyl ether) is a broad-spectrum bactericide used throughout North America and Europe for a variety of antimicrobial functions [86]. Approximately 96% of the uses of triclosan are in consumer products that are disposed of down residential drains. These include soaps, detergents, surface cleansers, disinfectants, cosmetics and other topical PCPs, pharmaceuticals, and oral hygiene products. The remaining uses involve

impregnation of domestic surfaces, including food wrappers, chopping boards, and refrigerator linings. In the case of liquid waste, community wastewater treatment systems will remove a significant proportion of the triclosan and the resultant sewage sludge may be spread on agricultural and other lands.

Triclosan was detected in marine sediments by Morales-Muñoz et al. [52] using FMASE and GC–MS/MS. Their proposed method using sequential extractions with dichloromethane and water as extractants, allowed the simultaneous removal of compounds with different polarity in sediments: an organic solvent was used for the extraction of non-polar compounds; however, medium polar and polar compounds were extracted in the aqueous phase. Rice and Mitra [83] developed a method for isolating a number of PPCP compounds in natural solid samples (soil and sediment) based on MAE followed by derivatization and GC–MS analysis. Triclosan exhibited high extraction efficiency (higher than 80%) and it was not detected in the natural sediments analyzed.

Triclosan was also detected in river sediments by Morales et al. [87]. They developed a procedure for the determination of triclosan, 2,4-dichlorophenol (2,4-DCP) and 2,4,6-trichlorophenol (2,4,6-TCP) in sludge from urban STP and sediments. MAE was chosen as the extraction technique and the analytes were isolated from co-extracted compounds in function of their acid-base properties and polarity. Compounds were silylated and selectively determined by GC–MS/MS. Only low levels of triclosan were detected in some of the sediments; however, the recorded values found in sludge were ranged from 418 to 5400 ng g^{-1}.

4.4. Pharmaceutical compounds

Human and veterinary drugs are continually being released to the environment mainly as a result of manufacturing processes, improper disposal or metabolic excretion [88]. Fig. 2 shows the spreading and fate of pharmaceutical compounds in the environment. A huge diversity of veterinary pharmaceutical compounds is employed in food-animal agriculture worldwide for the purposes of treating or preventing infectious and non-infectious diseases, managing reproductive processes and promoting growth. Used compounds belong to a variety of therapeutic classes, including antimicrobials, anti-inflammatory drugs, parasiticides, anaesthetics, sex hormones, antiseptics, bronchodilators and anti-fungal [89]. Moreover, residues of pharmaceutical compounds end up in the environment due to the common practices to improve the state of health of humans. New emerging compounds, such as modern

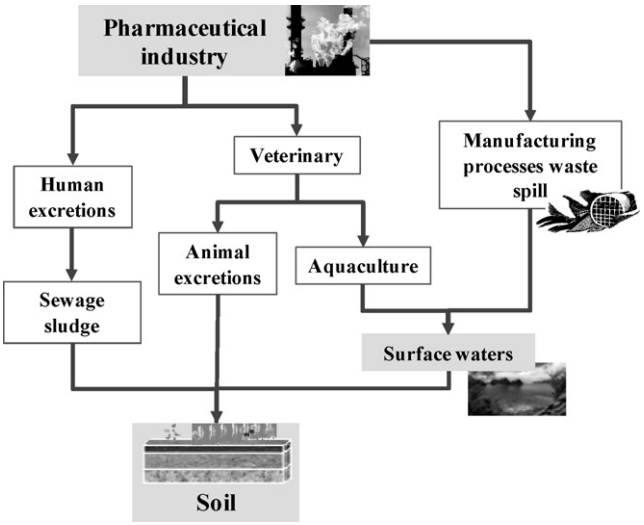

Fig. 2. Pathways of pharmaceuticals pollution of the environment.

pharmaceuticals which are not targeted in the usual conventional wastewater treatment processes, often reach the environment in concentrations causing noticeable effect [90–92].

The occurrence and the fate of pharmaceutically active compounds in the environment has been recognized as one of the prevailing problems in ecological risk assessment and chemistry, although pharmaceutical analysis has addressed a very small percentage of compounds, and the analytical methods developed to determine them are very scarce [93].

Several methods have recently been developed for the analysis of quite a number of pharmaceutical residues in the environment; however, most of them applied to aqueous samples. In order to provide more information concerning occurrence, fate and effects of veterinary pharmaceuticals in the terrestrial environment, a number of theoretical models can identify where and when measurable concentrations will occur, but it is necessary to calibrate and to validate the models using real data [94].

In order to detect, identify and quantify pharmaceutical residues released into the environment and accumulated in river and marine sediments, and in agricultural soils amended with animal manure, analytes need to be isolated from the sample matrix and concentrated to some extent, because of the extremely low level of concentration at which they occur [89]. Because there is often strong interaction between the drug residues and soils or sediments, the compounds are difficult to extract. The isolation from environmental solid samples therefore encompasses optimization of the physical properties of the extracting solvents, especially temperature and pressure, in order to enhance their capacity to extract analytes from a variety of solid matrices by dropping the surface tension and increasing analyte solubility and diffusion. Methodologies based on MAE are presented in Table 5.

Published analytical methods for these compounds are typically specific to a simple contamination or pharmaceuticals class, although Rice and Mitra [83] developed an analytical method for the simultaneous detection and quantification of eight structurally diverse PPCPs (among them: a stimulant, a anti-histamine drug, and three anti-inflammatory-analgesics) in solid environmental matrices, i.e. soil and sediment. MAE was chosen for the separation of the target PPCPs from solid matrices, as it has extraction efficiency comparable to traditional Soxhlet methods, but requires less time and solvent volume. Using this MAE method, three pharmaceutical compounds were detected in natural sediment samples at nanogram per gram to microgram per gram concentrations. Cueva-Mestanza et al. [90] also developed a time and cost-effective method for the simultaneous determination of eight common pharmaceutical compounds including anti-inflammatory drugs (ketoprofen, naproxen, ibuprofen), lipid regulating agents (bezafibrate, clofibric acid), a β-blocker (propranolol), an antiepileptic (carbamazepine) and an analgesic (phenazone) in sediment samples. They explored a new possibility for the application of MAE using micellar media as extractants (MAME). This methodology uses a non-ionic surfactant (polyoxyethylene 10 lauryl ether, POLE) as extractant, and SPE to cleanup and to preconcentrate these eight pharmaceutical compounds in solid samples, following determination by LC using UV–DAD detection. Finally, the optimized method was successfully applied to the analysis of target compounds in sediment samples with different characteristics. The performance and application of this method to sediment samples is important due to the difficulty in extracting the pharmaceuticals from such complex matrices. In fact, there are very few publications that cover these types of matrices. The authors [95] applied the same methodology to the analysis of six pharmaceutical compounds in molluscs. Method validation was carried out using conventional Soxhlet extraction, and the method was successfully applied to determine the target pharmaceuticals in spiked samples of several kinds of molluscs with recovery rates of over 80%. Therefore,

Table 5
Pharmaceutical compounds.

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
CAF, DPH HCl, IBU, KET, NAP, among others	Soil and sediment (3 g)	1. Dried. 2. Homogenized.	800 W, dichloromethane: methanol (2:1)	1. Centrifugation (1000 rpm, 5 min). 2. Concentrated, fractionated. 3. Derivatization (pyridine:BSTFA, 2:1). 4. Silica micro-column cleanup, evaporation, reconstitution hexane.	GC–MS	25 but 1.57 DPH HCl			50–10,000 ng g^{-1} (d.w.)	[83]
KET, NAP, IBU, BEZ, CA, PRO, CAR, PHE	Sediment (2 g)	1. Dried.	Multivariate factorial design or central composite design: MAME, 8 mL water 2.75% POLE (5%, v/v), 500 W, 6 min	1. Filtration. 2. Addition of 14 mL pH 3.0 water. 3. SPE (OASIS HLB), washed with 2× 5 mL water, eluted with 2× 0.75 mL methanol.	HPLC–DAD	>70 (but 6 PHE)	<46 ng g^{-1} (but 167 ng g^{-1} BEZ)	<11	No real contaminated samples were evaluated.	[90]
CAR, CA, KET, NAP, BEZ, IBU	Mollusc (1 g)	1. Dried. 2. Homogenized.	MAME, 10 mL POLE 3%, 6 min, 500 W	1. Filtration (0.45 μm nylon membrane). 2. SPE (OASIS HLB), 5 mL of extract, addition of 14 mL of acidic water (pH = 3), rinsed with 2× 5 mL Milli-Q water, elution with 2× 0.75 mL methanol.	LC–DAD	>85	0.03 (NAP)–0.22 (CAR) μg g^{-1}	<12		[95]
FQs: NOR and CIP	Soil (0.2 g spiked soil) (0.1 g natural soil)	1. Dried under nitrogen. 2. Sieved (<1 mm).	Factorial design optimization: dynamic MAE, 120 W, 5 min, 1.2 mL min^{-1} (2.5 mL water, 3 cycles)	1. On-line derivatization.	Flow injection manifold, LC–FL	>95	0.15 μg g^{-1}	<7.29	3–9.8 μg g^{-1}	[96]
OXO and FLU	Soil and sediment (0.5 g)	1. Oven-dried (110 °C). 2. Sieved (<90 μm).	90 °C, 22 min, 10 mL of 1 M phosphoric acid buffer at pH 2, 10 mL dichloromethane	1. Centrifuged (4000 rpm, 5 min). 2. Rinsed with 2× 5 mL dichloromethane. 3. Addition of 2 mL of 1 M NaOH. 4. Centrifugation (10 min at 4000 rpm). 5. Addition of 1 mL 0.6 M oxalic acid and filtration (0.45 μm nylon membrane).	LC–FL	>82	1.3–2.4 μg kg^{-1}	3.8–4.1		[99]
6 SAs	Soil (1 g)	1. Sieved (<2 mm).	3 mL acetonitrile, 0.5 mL water, 15 min, 115 °C	1. Rinsed with 1 mL acetonitrile:water (1:1) and centrifuged. 2. Volume adjustment to 5 mL with aqueous formic buffer pH 3.4. 3. 0.7 mL were diluted to 10 mL with aqueous formic buffer pH 3.4 to reduce acetonitrile content to 5%. 4. SPE, elution with 1 mL of acetonitrile. 5. Derivatization.	LC–FL	>85 (but 60 for SCP)	1.0–6.0 ng g^{-1}	3–7	No real contaminated samples were evaluated.	[100]
SDZ and its two main metabolites	Soil (10 g)	1. Dried. 2. Homogenized. 3. Sieved.	150 °C, 15 min, acetonitrile:water (1:4, v/v)		HPLC–MS/MS Extracted radioactivity	66			4.46 μg g^{-1} (SDZ)	[101,104]

DIC, NAP, KET, IBU	River sediments (5 g)	1. Dried. 2. Crushed, and sieved.	40 mL, 1200 W, 170 °C, 40 min (heating ramp to 170 °C for 15 min)	1. Centrifuged (3500 rpm, 10 min). 2. Washed (3× 10 mL methanol). 3. Centrifuged. 4. Cleanup with SPE (StrataX reversed-phase tubes), eluted with 1.5 mL methanol. 5. Dried under nitrogen, reconstitution with 0.5 mL toluene. 6. Derivatization with addition of 50 μL of MSTFA.	GC–MS	>81%, but 46% DIC	0.03–0.08 μg g^{-1}	<11	0.06 μg g^{-1} (NAP), 0.32 μg g^{-1} (KET)	[106]
IBU, NAP, KET, DIC	Sludge (0.5 g)	1. Freeze-dried.	50 mL water, preheating 700 W (5 min) 60 °C, then 600 W (5 min up to 100 °C); extraction 700 W and 100 °C (30 min)	1. Addition of 0.5 g neutral alumina and 0.25 g aluminium sulphate, shake (10 min). 2. Centrifuged (10 min). 3. SPE (Oasis HLB). 4. Evaporation to dryness. 5. Derivatization (hexamethyldisilazane, trifluoroacetic acid and hydroxylamine-HCl in pyridine. 6. Dilution (hexamethyldisilazane).	GC–MS (SIS)	83–104	15–22 ng g^{-1} (LOQ)	<20	28 76 ng g^{-1} (mixed sludge) 23–138 ng g^{-1} (activated sludge)	[107]

BEZ: bezafibrate. BSTFA: bis(trimethylsilyl)trifluoroacetamide. CA: clofibric acid. CAF: caffeine. CAR: carbamazepine. CIP: ciprofloxacin. DAD: diode array detector. DPH HCl: diphenylhydramine hydrochloride. d.w.: dry weight. FL: fluorescence detector. FLU: flumequine. FQs: fluoroquinolones. IBU: ibuprofen. KET: ketoprofen. MAME: microwave-assisted extraction using micellar media as extractants. NAP: naproxen. NOR: norfloxacin. OXO: oxolinic acid. PHE: phenazone. POLE: polyoxyethylene 10 lauryl ether. PRO: propranolol. SPE: solid phase extraction. DIC: diclofenac. LOQ: limits of quantification. MSTFA, *N*-methyl-*N*-(trimethylsilyl)trifluoroacetamide. SAs: sulfonamides. SCP: sulfachloropiridazine. SDZ: sulfodiazine.

the developed MAME–SPE–HPLC method may be considered to be a valid alternative to other conventional extraction procedures for the study and control of the sea environment, allowing the determination of the degree of pollution in these organisms.

4.4.1. Antibiotics

Antibiotics are pharmaceuticals of particular environmental concern. Among them, quinolones have been used in human and veterinary medicine for over a decade; during this time, their entry into the environment has been continuous [93]. Quinolones belong to the family of gyrase inhibitors. They show striking potency against enteric Gram-negative bacilli, lesser activity against non-enteric Gram-negative bacilli and staphylococci, and generally marginal activity against streptococci and anaerobes. Fluoroquinolones (FQ) are probably among the most important class of synthetic antibiotics because of their broad activity spectrum and good oral absorption [96]. Ciprofloxacin is the most widely prescribed FQ in the world; the second is ofloxacin, followed by levofloxacin, lomefloxacin, norfloxacin, sparfloxacin, clinafloxacin, gatifloxacin, moxifloxacin sparfloxacin, and trovafloxacin. Norfloxacin is very common in Europe but is no longer used in the US. Data on outpatient quinolones used in Europe, collected from 25 countries, show that second-generation quinolones account for more than 50% of quinolone use (mainly ciprofloxacin) except for Croatia, where first-generation quinolones are most used (mainly norfloxacin). Use of second and/or third-generation FQs has increased at the expense of first-generation FQs. The new so-called respiratory quinolones (levofloxacin and moxifloxacin) account for more than 10% of FQs used [97]. The ubiquitous occurrence of FQs in the environment emphasizes that proper environmental risk assessment for these substances is essential. Unfortunately, most studies are restricted to the detection of FQs in aqueous matrices; their behaviour and effect in the environment are widely unknown. The sewage sludge and manure containing FQs are usually applied to agricultural field as fertilizers, so the non-metabolized drugs can accumulate in the soil and affect terrestrial organisms. The effect of such contamination on terrestrial biota has been investigated under laboratory conditions and on soils where different plant species were demonstrating that the drugs altered the normal post-germinative development of the plants and the growth of roots, hypocotyls and leaves. Moreover, FQs can pass into surface and ground water after rain, depending on their mobility in the soil system, and affect aquatic organisms. Among the possible effects, a drug-resistant bacterium is increasingly observed [98]. For this reason, it is necessary to monitor their presence in the environment.

Morales-Muñoz et al. [96] reported an extraction-monitoring approach for two FQs (namely, norfloxacin and ciprofloxacin) in soil samples. The use of a dynamic MAE system (using pure water as leaching agent) coupled with a flow injection manifold that acts as interface between the extractor and the detector provides a fully automated screening approach. The removal of the analytes by MAE allows the acceleration of the sample preparation step. Moreover, the dynamic extraction system facilitates coupling the extraction with the other steps of the analytical process. The analytes were monitored after derivatization based on the energy transfer from FQs to Tb^{3+} in the presence of tri-*n*-octylphosphine oxide in weakly acidic (pH 5.5) micellar solution of cetylpyridinium chloride. The mean recoveries from soil samples spiked with 5 and 0.5 μg g^{-1} of each analyte were 95.2 ± 4.16% and 98 ± 5.21%, respectively. The within-laboratory reproducibility and repeatability, expressed as RSD, were 7.29 and 5.80%, respectively. Prat et al. [99] developed a simple and effective method based on MAE and LC-fluorescence for trace determination of flumequine and oxolonic acid, two quinolone antibacterial agents which have been widely used as veterinary drugs in food producing animals, in sediments and soils samples. The extraction of the analytes consisted

of liquid–liquid partitioning between a homogenized sample in an aqueous buffer solution and a non-miscible organic solvent. MAE was investigated to improve the speed and efficiency of the extraction process. They concluded that, although MAE introduces some complexity into the procedure, the benefits, in terms of high recoveries (79–94%) and less dependence on the sample nature, make this technique the option of choice. Thus, MAE in combination with a simple cleanup based on LLE and final quantification by LC with fluorimetric detection enables determination of these target compounds in soil and sediment samples at relevant concentration levels for environmental analysis, up to the low microgram per kilogram range.

In European countries, sulfonamides (SAs) are one of the most widely administered groups of antibiotics in animal husbandry [100,101]. For instance, after fertilization of agricultural fields by application of manure, SA residues occur in soils in substantial amounts [91,102,103]. SAs then persist in the environment and due to their relatively high mobility they can enter groundwater and be transported in aquifers and surface waters. Papers devoted to the analysis of SAs in environmental solid samples, such as soils, sediments and sewage sludge are scarce. The most critical part of the analysis is the extraction of the analytes from the matrix. The ideal extraction method should be efficient and not dependent on the nature of the soil. Therefore, the validation of extraction methods should include assays with different soils, in order to ensure that they provide reliable results. Raich-Montiu et al. [100] developed a robust and efficient extraction method for trace determination of six SAs used as veterinary drugs in agricultural soils. MAE and ultrasound-assisted extraction were studied to improve the speed and efficiency of the extraction process. Experiments using MAE enabled extraction of SAs from soil samples with high absolute recovery rates (>85% with the exception of sulfachloropiridazine, with recovery rates about 60%) and little dependence of the nature of the soil sample. Förster et al. [101,104] developed an efficient and reliable extraction method for one of the most frequently used SAs, sulfadiazine (SDZ) (including its two main metabolites: *N*-acetyl-SDZ and 4-hydroxy-SDZ) from manure-amended soils. They concluded that extraction yields of individual compounds in MAE exceeded those for the best PLE method for SDZ (>50% increase) and were similar for *N*-acetyl-SDZ and 4-hydroxy-SDZ. Therefore MAE is a slightly superior extraction technique for aged SDZ residues in soils, as compared with PLE, and it offers more flexibility regarding the amount of sample to be extracted.

4.4.2. Anti-inflammatory drugs

Consumption of non-steroidal anti-inflammatory drugs (NSAIDs) is increasing and with it the danger of environmental pollution by pharmaceutical residues. Many publications on the effects of NSAIDs on living organisms show their toxicity to numerous animal species [105]. Four widespread NSAID representatives, diclofenac, naproxen, ketoprofen and ibuprofen were extracted from sediment samples using different extraction procedures: Soxhlet extraction, ultrasonic extraction, PLE, SFE and MAE [106]. The highest extraction efficiencies were obtained with PLE coupled with SFE. Nevertheless, MAE was chosen as the most effective extraction method because of the high extraction efficiencies (>80%, but 46% for diclofenac), low standard deviations (RSD < 11%), low solvent consumption and, lower extraction time per sample. While PLE–SFE used up to 80 mL of solvents and 50 mL of CO_2 per sample, MAE required 40 mL of solvents per sample. Extraction time for PLE–SFE was from 75 to 90 min per sample, whereas extraction time for MAE was 2 h for 16 samples, averaging about 8 min per sample.

Dobor et al. [107] presented a sample preparation procedure for determination of selected acidic pharmaceuticals (ibuprofen, naproxen, ketoprofen, and diclofenac) in sewage sludge based on MAE using water as extractant, and a new purification procedure applying a modified dispersive SPE followed by the conventional SPE technique. The determinations of drugs in the purified extracts were performed by GC–MS in selected ion storage mode (SIM) after derivatization by hexamethyldisilazane, trifluoroacetic acid and hydroxylamine-HCl in pyridine. The obtained recoveries were ranged from 80 to 105%. The developed sample preparation method was applied to real sewage sludge samples and the measured concentrations of acidic drugs were in the range of 10–150 ng g^{-1}.

4.5. Estrogens

Estrogens are a group of steroid hormones defined by their chemical structure and by their effect in the estrous cycle. They act as EDCs (i.e. substances that interfere with the endocrine system, as it was mentioned before) and disrupt the physiological functions of hormones [108]. Estrogens may originate from natural processes and industrial activities. Natural hormones such as 17β-estradiol and estrone are derived from excreta of humans and livestock, and 16α-hydroxyestrone from the hepatic metabolite of the natural estrone. Man-made substances include synthetically produced hormones, e.g. 17α-ethynylestradiol and industrial chemicals, e.g. BPA, 4-nonylphenol and 4-*tert*-octylphenol associated with plastics, household products and industrial processes. In recent years, there has been increasing attention toward the potential effects of EDCs in aquatic environments on human and wildlife endocrine systems, e.g. the feminization of male fish, abnormal reproductive processes and the development of testicular and prostate cancer even at the low concentrations down to 1 ng L^{-1} [67,109,110]. Numerous estrogenic compounds are excreted by human bodies and, as a consequence, they reach the aquatic environment daily via sewage systems. Domestic wastewaters are recognized as a main source of contamination for these new pollutants [108]. Hydrophobic organic pollutants in aquatic environments tend to deposit and accumulate on the solid phases such as sediments, although the magnitude of which is dependent on estrogen (they have moderate to high hydrophobicity) and sediment properties. From these sinks they have the potential to bioaccumulate in, and cause endocrine disruptions to, benthic invertebrates and enter the food chain. It is therefore essential that developed methods can simultaneously extract and accurately quantify large groups of these chemicals from complex environmental samples. Limited study is devoted to the analysis of estrogens from solid samples because of the complexity of sample processing and requirement of low LODs. Recently, different extraction and determination methods for estrogens in solid phases have been developed using conventional extraction systems coupled with chromatography detection techniques. Soxhlet extraction, sonication, and PLE are the most commonly used techniques in the extraction of organic pollutants from solid matrices. Little work has been completed on the MAE of estrogens from environmental particulate samples such as sediments. Those available up to now are presented in Table 6. Liu et al. [50] worked in the development of a reliable MAE technique for the simultaneous recovery of 17β-estradiol, estrone, 17α-ethynylestradiol, 16α-hydroxyestrone, among other compounds, from river sediment samples, followed by GC–MS analysis. The extraction efficiency by microwave-assisted system was similar for all the compounds compared with the results from ultrasonication extraction experiments. However, the advantages of MAE included low solvent consumption (25 mL) and short extraction time (15 min). The developed method was then applied to the extraction and analysis of EDCs from natural sediment samples, collected from rivers Ouse and Uck of UK, and the results revealed the presence of the target compounds in some river sediment samples in the low nanogram per gram range (2–12 ng g^{-1}). Hibberd et al. [51] developed a trace analytical method for the determi-

Table 6
Estrogens.

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
E1, E2, EE2, 16α-hydroxyestrone, among others	Sediment (5 g dry mass)	1. Addition of copper granules.	25 mL methanol, 110 °C, 15 min	1. Wash with 3× 15 mL of methanol and centrifugation (2500 rpm, 5 min). 2. Rotary evaporation to 1 mL. 3. Silica gel column cleanup, elution with 20 mL ethyl acetate:hexane (4:6). 4. Evaporation to 0.5 mL. 5. Derivatization with 50 μL pyridine and BSTFA (1% TMCS).	GC–MS	73.4–123	0.2–0.4 ng g^{-1}	<16.4	2–12 ng g^{-1}	[50]
E1, E2, 16α-hydroxyestrone, EE2, among others	Sediment (3 g)	1. Lyophilized. 2. Grounded and sieved (<500 μm).	25 mL methanol, 2 g copper granules, 110 °C, 15 min, 7 min ramp, at 200 psi	1. Rinsed with 3× 15 mL methanol. 2. Volume reduction to 1 mL. 3. Addition of 500 mL water. 4. SPE extraction, elution with 15 mL of ethyl acetate, solvent reduction to 0.5 mL. 5. Derivatization with 50 μL pyridine and BSTFA.	GC–MS/MS	86–102	0.05–0.14 ng g^{-1}	<10.9	<11.2 ng g^{-1}	[51]
E1, E2, DES, among others	Marine sediments (1 g)	1. Lyophilized. 2. Sieved through a 0.5-mm screen.	FMASE, 100 W, 5 cycles, 120 s, 35 mL dichloromethane	Dichloromethane extracts: 1. Evaporation to dryness. 2. Reconstitution with 200 μL of ethyl acetate. Water extracts: 1. LLE with hexane and 500 mg NaCl. 2. Evaporation to dryness. 3. Reconstitution with 200 μL of ethyl acetate.	GC–MS/MS	85–91	0.4–4.0 pg g^{-1}	<8	2.5 μg kg^{-1} (E1) 4 μg kg^{-1} (E2)	[52]
E2	Soil and sediment (3 g)	1. Dried. 2. Homogenized.	800 W, dichloromethane: methanol (2:1)	1. Centrifugation (1000 rpm, 5 min). 2. Concentrated, fractionated. 3. Derivatization (pyridine:BSTFA, 2:1). 4. Silica micro-column cleanup, evaporation, reconstitution hexane.	GC–MS	89.6			N.D.	[83]
E1, E2, E3, EE2, MeEE2, Pg, No, DN, E2G, E2S	Particulate phase of river water and STP effluent (15 and 150 mg)		FMASE, 30 W, 5 min, 10 mL of methanol:Milli-Q water (55:45, v/v)	1. Centrifugation (4500 rpm, 5 min). 2. Evaporation. 3. Purification with Oasis HLB and NH_2 cartridges and elution of steroid conjugates with 5 mL methanol:water (6:4, v/v) with 5×10^{-3} M of TEA; and 8 mL of methanol (free steroids). 4. Derivatization (30 μL of a mixture of MSTFA, mercaptoethanol, and NH_4I.	GC–MS	72–91	0.4–1.9 ng g^{-1}		N.D.	[111]
E1, α-estradiol, E2, E3, EE2, 17β-estradiol-17-acetate, among others	River sediment (1 g)	1. Grounded and sieved (1.0 mm). 2. Homogenized.	10 mL water:methanol (25:75, v/v), 100 °C, 10 min	1. Evaporation to dryness and reconstitution with 3 mL water:methanol. 2. SPE, OASIS WAX, elution with 6 mL water:THF (60:40) 5% NH_4OH. 3. Rotary evaporation and reconstitution with 100 μL water:acetonitrile (70:30). 4. Filtration through a 0.45-μm nylon membrane filter.	LC–MS/MS	82.7–107.3	0.14–0.98 ng g^{-1}	4.2–9.6	0.31–2.37 ng g^{-1}	[112]

Table 6 (*Continued*)

Analyte	Sample	Sample pre-treatment	MAE conditions	Extract treatment	Determination	Recovery %	LOD	RSD %	Concentration in real samples	Ref.
E1, E2, EE2	River sediment (1 g)	1. Addition of 1 mg of BHT.	5 mL methanol, 90 °C, 5 min	1. Centrifugation (1680 × *g*, 5 min), washed, evaporation, reconstituted 4.5 mL sodium acetate buffer and 0.5 mL methanol. SPE purification, elution 7 mL ethyl acetate, evaporated and reconstitution with 500 μL cyclohexane:ethyl acetate (9:1, v/v), silica gel cartridges	LC–TOF-MS, LC–MS/MS	82.1–97.8	200–500 pg g^{-1} (LC–TOF-MS); 15–40 pg g^{-1} (LC–MS/MS)	<20.4	0.34–3.30 ng g^{-1}	[113]
E1, E2, coprostanol, testosterone	Mussels (40 g)	1. Homogenized.	50% acetone in hexane, 80 °C, 20 min, 210 W	1. Acidification with 50 mL of concentrated hydrochloric acid. 2. Extracted with 3 × 20 mL dichloromethane. 3. The organic layer was evaporated to dryness by rotary evaporation. 4. Derivatization with 5 mg of K_2CO_3, 50 μL PFB-Br and 50 μL of 5% 18-crown-6 in acetone. 5. Silica gel column, elution with 30 mL of 50% acetone in hexane, evaporation to dryness and addition of 100 μL of 1% acetone in isooctane.	GC–MS	21–48	3 ng g^{-1}	<16	Coprostanol: 32 μg g^{-1}	[114]

BSTFA: bis(trimethylsilyl)trifluoroacetamide; DES: diethylstilbestrol; DN: d-norgestrel; E1: estrone; E2: 17β-estradiol; E2G: 17β-estradiol-17-glucuronide; E2S: 17β-estradiol-3-sulfate; E3: estriol; EE2: 17α-Ethynylestradiol; FMASE: focused microwave-assisted Soxhlet extraction; LLE: liquid–liquid extraction; MeEE2: mestranol; MSTFA: 2,2,2-trifluoro-N-methyl-N-trimethylsilyl-acetamide; N.D.: not detected; No: norethindrone; Pg: progesterone; SPE: solid phase extraction; STP: sewage treatment plant; TEA: triethylamine; TMCS: trimethylchlorosilane; BHT: butylated hydroxytoluene; PFB-Br: pentafluorobenzyl bromide; THF: tetrahydrofuran; TOF: time-of-flight.

nation of seven potent EDCs in water and sediments, based on SPE and MAE followed by GC–MS/MS. The method was optimized and provided increased selectivity and sensitivity with lower LODs than earlier methods based on GC–MS. Improved cleanup procedure removed matrix interferences and increased recovery in sediment samples. Finally, the method was successfully used to determine the concentrations of the target EDCs in water and sediment samples finding levels up to 11.2 ng g^{-1}. Morales-Muñoz et al. [52] studied the application of FMASE to the determination of compounds with different polarities (among them estrone, 17β-estradiol, and diethylstilbestrol) in marine sediments. Quantitative recoveries at real environmental concentrations (low nanogram per gram) were obtained for these three compounds using both the proposed method and conventional Soxhlet. Soxhlet extraction using water as extractant for 12 h was less efficient than the proposed FMASE method with water (50 min). The extraction efficiency using dichloromethane was similar for both FMASE and Soxhlet although the difference in time extraction should be considered (25 min vs 12 h). In the work of Rice and Mitra [83], the presence of 17β-estradiol in soils and sediments was also investigated. With the application of GC–MS/MS as the determination technique, they reached LOD in the low picogram per gram levels. Labadie et al. [111] analyzed 10 steroidal hormones in river water, effluent water, and particulate phase. The glass-fiber filters (pore size 0.7 μm) used for filtration of 3 L samples (equivalent to 15 mg and 150 mg of particulate phase of river water and effluent, respectively) were directly extracted by MAE with 10 mL of methanol/Milli-Q water (55:45, v/v). The extracts were then centrifuged at 4500 rpm for 5 min. Recoveries of all analytes were above 70% (72–91%) and the LODs were in the range 0.4–1.9 ng g^{-1}. Matějíček et al. [112] evaluated a quick and sensitive HPLC–MS/MS method using MAE followed by a cleanup step through SPE on the ion-exchange sorbent Oasis WAX, for the simultaneous separation and quantification of estrogens (α-estradiol, β-estradiol, estriol, estrone and ethynylestradiol) and estrogen conjugates (E1, E2, E3-sulfates; E1, E2-glucuronides and E2-acetate) in samples of river sediments. Comparing Soxhlet extraction with MAE, the last has been found to be more suitable for the simultaneous extraction of both, free and conjugated estrogens, from the sediment samples. The reasons are the higher MAE recovery (1 g of sediment spiked with 20 ng of each analyte; 82.7–107.3 and 74.5–82.4% for MAE and Soxhlet extraction, respectively), better MAE RSD values (4.2–9.6 and 6.5–13.7% for MAE and Soxhlet, respectively), and shorter extraction times (10 and 70 min for MAE and Soxhlet, respectively). Repeatabilities of the MAE on day-to-day and 5-day bases were 6.4–12.1 and 7.2–12.9%, respectively. Labadie and Hill [113] developed a simple and reliable method for the determination of estrone, 17β-estradiol and the synthetic estrogen 17α-ethynylestradiol in surface sediment samples at sub-nanogram per gram level using LC–MS techniques. The developed method is based on MAE, SPE and LC–MS with an electrospray (ESI) interface. One of the objectives of this work was to compare the suitability and the performances of LC–TOF-MS and LC–MS/MS for the determination of estrogens in river sediment. LC–MS/MS was approximately 13 times more sensitive than LC–TOF-MS. Method detection limits achieved by LC–MS/MS ranged from 15 to 40 pg g^{-1}. The occurrence of estrogens in sediments collected at selected locations in the River Ouse (Sussex, UK) catchment was investigated by the application of the previously described LC–MS/MS method. Results showed the presence of the target analytes in the low nanogram per gram range (0.34–3.30 ng g^{-1}).

A method for the determination of coprostanol and steroids including estradiol-17β, estrone and testosterone, in surface water, effluent water, and mussels, was developed by Cathum and Sabik [114]. The method is based on the derivatization of steroids containing hydroxyl groups with pentafluorobenzyl bromide, followed

by GC–MS determination. Estradiol-17β and estrone were successfully derivatized by this method, whereas coprostanol (a sterol compound) and testosterone showed no spectra of the derivatized form, and were therefore determined as free compounds. Mussels were extracted using a microwave extraction system. The method detection limits of estradiol-17β, estrone, testosterone and coprostanol were 3 ng g^{-1} for mussel. Recoveries in spiked mussel for the same chemicals ranged from 21 to 48%. Using this method, only coprostanol was found in effluent and mussel samples at concentrations of 14,667 ng L^{-1} and 32,252 ng g^{-1}, respectively.

The application of MAE for the template extraction when molecular imprinted polymers are used in the extraction of β-estradiol from water was developed by Bravo et al. [115]. Molecular imprinting has become a promising technique that provides polymers with specific recognition properties. The process involves the formation of a molecular complex between functional monomers and a molecule that acts as a template (imprinting molecule) in the presence of an appropriate solvent, followed by polymerization in the presence of a crosslinker. Removal of the template from the polymer leaves specific sites complementary in shape and functionality to the molecule that was imprinted. These sites provide the capacity for specific rebinding with the template. A critical step in the molecular imprinting technique is the extraction of the template from the imprinted polymer. It is known that a small portion of the template remains un-extracted even after extensive washing, and this can cause problems since it might bleed from the polymer during the elution step. Therefore, methods that can reduce this bleeding to acceptable levels are being sought. Usually, the extraction of the template from the molecular imprinted polymer is undertaken by washing several times with a solvent (incubated) or by Soxhlet extraction until the analyte is undetectable in the washing solution. Despite its good results, the Soxhlet extraction method has the drawback that up to 24 h are necessary for the complete removal of the imprinted molecule. In that work, the template underwent MAE with the aim of reducing this time and increasing extraction efficiency. Finally they concluded that MAE is effective for achieving efficient extraction of the template and should be used as a routine post-treatment step with imprinted polymers.

5. Conclusions

The MAE technique has been successfully applied to the extraction of the most of the families of emerging pollutants (covering different groups of compounds with very different physicochemical properties), from a wide range of environmental and biota samples. The obtained extracts can be analyzed, mainly, by GC or LC coupled to different detectors, obtaining LODs in the low nanogram per gram level in the most of the cases. MAE is rapid and provides good extraction efficiencies comparable to those obtained with classical techniques (Soxhlet, LLE) and other more recent ones such as SFE or PLE, with acceptable reproducibilities. Among MAE advantages, the great reduction in the extraction time and solvent consumption, as well as the opportunity to perform multiple extractions, increasing the sample throughput, must be emphasized. Optimization of MAE conditions is rather easy owing to the low number of influential parameters (i.e. matrix moisture, nature of the solvent, time, power, and temperature in closed vessels), as compared to other extraction techniques such as SFE. The reasonable cost of the equipment should be also taken into account. Overall, MAE appears to be a good alternative extraction method for the determination of organics in environmental samples because it is rapid, effective, allows simultaneous extractions and is environmentally friendly. It can be used as a rapid screening tool, and also to obtain detailed information on the sources, behaviour and fate of emerging pollutants in environmental matrices.

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