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Review

Application of accelerated solvent extraction in the analysis of organic contaminants, bioactive and nutritional compounds in food and feed

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ABSTRACT

Accelerated solvent extraction (ASE) has become a popular green extraction technology for different classes of organic contaminants present in numerous kinds of food and feed for food safety. The parameters affecting ASE efficiency and application advancement of ASE in the analysis of organic contaminants, natural toxins compounds as well as bioactive and nutritional compounds in animal origin food, plant origin food and animal feed are reviewed in detail. ASE is a fully automated and reliable extraction technique with many advantages over traditional extraction techniques, so it could be especially useful for routine analyses of pollutants in food and feed.

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1. Introduction

Recent years, food safety has become an issue of high priority to many governments. Consumers also have well developed concerns about food safety and an interest in organic products. Therefore, in the field of food safety, scientists and regulatory agencies need to identify any potential risks to consumers related to the consumption of food. The analysis of chemical contaminants in food has grown considerably in recent years. These chemical contaminants can be broadly classified into 4 main categories: veterinary drugs, pesticides, persistent environmental chemicals and naturally occurring toxicants [1]. The World Health Organization (WHO) and other international organisms have pointed out the risks associated to the overuse or misuse of antibacterial treatments, both in human medicine and veterinary practices [2]. The determination of trace residues and contaminants in food has been of growing concern over the past few years.

The complex food matrices and the different physicochemical characteristics of the antibacterial families make difficult the development of analytical methods appropriate for a great variety of antibacterial/food commodity combinations. Therefore, sample preparation is one of the key issues in food analysis, because it can be a source of inaccuracy, as well as a limitation for the development of high-throughput methods [3]. Therefore, for the multi-class determination, generic sample preparation procedures are necessary to simultaneously extract a broad range of antibacterial and banned chemicals from different food matrices, down to their maximum residue limit (MRL) or minimum required performance level (MRPL). Otherwise, quantification is sometimes a very difficult issue because of matrix interferences. Difficulty in determination using liquid chromatography–tandem mass spectrometry (LC–MS/MS) systems could result from co-eluting compounds or matrix effects [4–8]. These unwelcome effects can severely affect method's accuracy and precision.

Recently, LeDoux [9] has reviewed the analytical methods applied to the determination of pesticide residues in foods of animal origin. During recent years, modern extraction and clean up techniques for sample preparation were developed [10–12]. These techniques meet the need of multi-residue determination for singe class or several classes of substances in samples of different origin, often present at trace levels. Recent developments and applications of microwave-assisted extraction (MAE) [13] and supercritical-fluid extraction (SFE) [14] have been reviewed. Accelerated solvent extraction (ASE) has received different names, such as pressurized liquid extraction (PLE), pressurized solvent extraction (PSE), high-pressure solvent extraction (HPSE), pressurized hot solvent extraction (PHSE), high-pressure, high temperature solvent extraction (HPHTSE), pressurized hot water extraction (PHWE) and subcritical solvent extraction (SSE). ASE is a new technique for sample preparation [15]. Giergielewicz-Mozajska et al. evaluated the performance of ASE in the analysis of environmental solid samples [16]. Application of superheated water extractions in soils and environmental solids was reviewed in 2002 by Smith [17]. Teo et al. [18] reviewed in 2010 the application of PHWE in and contaminants in environmental samples including soil and sediments, as well as organic contaminants in plant and food. Nieto et al. [19] reviewed the application of PLE in extraction of pharmaceuticals and personal-care products from sewage sludge. PLE in the analysis of food and biological samples was reviewed in 2005 by Carabias-Martínez [20]. ASE is a solid–liquid extraction process performed at high temperatures (50–200 °C) and high pressures (10–15 MPa), its main advantages over traditional extraction methods being dramatic decreases in the amount of solvent used and the extraction time. Nowadays, ASE is considered as an attractive and alternative technique for extracting organic compounds from solid

environmental, biological matrices and food applications. ASE combined the benefits of high-throughput, automation and low solvent consumption. It is becoming increasingly to be an important sample preparation technique in food analysis, although expensive lab-equipment is required.

In this review, the main parameters affecting ASE efficiency, namely the temperature, pressure, solvent, matrix composition, operation mode in terms of extraction time/flow rate and modifiers/additives are covered. The current review will focalize on the application progress of ASE in analysis of contaminants in animal origin foods, plant origin foods and feedstuffs for food safety analysis. It is noted that there is a steady growing trend to use ASE to extract contaminations, bioactive and nutritional compounds from food and feed materials.

2. Parameters affecting ASE efficiency

The principle of ASE has been reviewed in comprehensive studies [15–20]. Briefly, the efficiency of the extraction depends on the nature of the sample matrix, the analyte to be extracted and the location of the analyte within the matrix.

The desorption of analytes from solid samples can be achieved via three steps during the extraction, that is firstly desorption from a solid particle, then diffusion through the solvent located inside a particle pore, finally and transfer to the bulk of the flowing fluid [21]. Each step depends on many factors, which can be varied by temperature and pressure modification. An ideal extraction method should be rapid and simple, yield a quantitative recovery of target analytes without loss or degradation, offer fully automated extractions and generate little laboratory waste.

2.1. Effect of temperature

High temperature is one of the most important parameter for ASE. The use of high temperatures during the extraction process affects the properties of a solvent. It increases diffusion rates and the capacity to solubilize analytes. Interactions between analytes and matrix components are weakened, and there is a decrease in viscosity and surface tension. With the use of high pressure in the extraction process, the solvent is kept in a liquid state when temperatures at or above the boiling point are being used. It also improves the extraction efficiency by forcing the solvent into areas that would not normally be contacted using atmospheric conditions [15]. High temperatures will increase solubility and mass transfer, but selectivity also decreases. In addition, high temperatures might affect thermo-labile compounds that are subject to disintegration and hydrolytic degradation [22].

A temperature of 40 °C was chosen for ASE of ochratoxin A (OTA) from rice with recoveries of 90%, but increased above 40 °C; the extraction efficiency decreased because matrix components are co-extracted [23]. Golet et al. [24] studied the effect of temperature on the extraction efficiency of two fluoroquinolones by varying the temperature in the range 50–150 °C with increments of 25 °C. The extraction efficiency increased in the range 50–100 °C; however, in the range 100–150 °C, the extraction efficiency remained constant. Tetracyclines (TCs) in muscle and liver samples were extracted at various temperatures (40–80 °C), with the recovery ranged from 69% to 94%. Extraction efficiency showed an optimum at 60 °C. Above it, recoveries decreased, probably due to decompositions of the TCs or increased formation of 4-epimers. Another problem is that in high temperature, the extract was not clear which may be due to the matrix dispersion of the tissues. Recoveries were also low at below 50 °C, most like due to the inefficient desorption and dissolution of the TCs [25].

2.2. Effect of pressure

In ASE, pressure is another important parameter which may influence compound recovery. The main reason why high pressure is used during the extraction process is to keep the solvent in a liquid state at elevated temperatures far above the boiling point. High pressures improve the extraction efficiency also by "pushing" the solvent into pores and in this way making the analytes available. Nevertheless, no relationship between pressure and recovery was observed either during the extraction of polycyclic aromatic hydrocarbons from food.

The effect of pressure (1000–2000 psi) on the extraction efficiency of wheat samples spiked with zearalenone (ZON) and α-zearalenol (α-ZOL) was evaluated using a static time of 5 min and a methanol/acetonitrile mixture (50:50, v/v) and a temperature of 70 °C. The obtained recoveries for both species were always higher than 86% for ZON and 91% for α-ZOL, and there were no significant differences for the values obtained at 1000, 1500 or 2000 psi. However, an increase of the applied pressure to 2000 psi resulted in darker extracts, with broad peaks at the beginning of the chromatogram due to the co-extraction of other matrix components [26]. This is considerably higher than the minimum pressure to keep the solvent liquid. With increased density, the solvating power of the extraction solvent is increased. But at higher densities, the diffusion coefficients decreased, which could lead to low recoveries due to the kinetics of the extraction process [27]. For the extraction of organotin compounds from biological samples, higher extraction pressure and temperature resulted in extracts loaded with compounds of high molecular mass (lipids, proteins) that interfere with subsequent analysis steps. On the other hand, operation at low pressure, close to 500 psi, the lowest possible with the ASE 200 extractor, becomes unstable (overfilled collection vials), because of difficulties in maintaining the set pressure [28].

2.3. Effect of type and composition of solvents

In general, physicochemical properties such as boiling point, polarity, specific density (influences a penetration into the sample matrix) as well toxicity (makes a workplace hazard) should be considered when choosing extraction solvent. The selection of a suitable extraction solvent is the first challenge in ASE method development. ASE can be performed with a wide range of solvents except for strong bases and acids as well as those with an autoignition temperature of 40–200 °C (e.g., carbon disulfide, diethyl ether, and 1,4-dioxane). Several solvents such as methanol, water, toluene, dichloromethane, ethyl acetate and acetonitrile have been used to ASE for the preparation of food and feed samples. PHWE is a feasible green solvent extraction method. Various reports have shown that at certain temperature and applied pressure, the polarity of water can be varied close to those of alcohols. Thus, it can dissolve a wide range of medium and low polarity analytes. Hence, PHWE has steadily become an efficient and low cost method of extraction for less-polar organic components from food and feed samples.

Water is a good solvent to extract oxytetracycline (OTC), tetracycline (TC), chlortetracycline (CTC), minocycline (MINO), methacycline (MTC), demeclocycline (DEMC) and doxycycline (DOX), and the results for muscle sample were good, however, for analysis of liver, there were strong interferences with TC and OTC, probably due to impurities extracted by water from these samples. The water/acetonitrile solution mixture is not suitable for CTC, MINO and DEMC because of variable recoveries from liver samples, further more, there was an obvious interference with OTC in the chromatogram. When trichloracetic acid (TAC) solution (pH 4.0) mixed with acetonitrile in the rate of 1:2 (v/v) the interference was eliminated and the recoveries were stable [25]. Methanol is still the

solvent with the best recovery values. The use of methanol can be pointed out as a general advantage for extracting because in this way the use of halogenated solvents is avoided.

The polarity of the extraction solvent should closely match that of the target compounds, but, in some cases, solvent mixtures of polar and non-polar solvents give higher recoveries. Solvent mixtures with different methanol content were tested to obtain maximum recovery of the analytes. Since 2, 4-dimethylaniline (2, 4-DMA) is much more polar than amitraz, more n-hexane in the extraction solvent will result in a very satisfactory recovery for amitraz but not for 2, 4-DMA and vice versa when more methanol is used. The results obtained via the experiment with the ratio of n-hexane and methanol continuously varied from 5% n-hexane and 95% methanol to 20% n-hexane and 80% methanol at 5% steps showed that the best extraction for both amitraz and 2, 4-dimethylaniline (2, 4-DMA) was obtained when n-hexane/methanol is at a ratio of 1:9 (v/v) [27]. The four extracting systems {McIlvaine buffer (pH 3)/acetonitrile, ammonium acetate buffer (pH 4.5)/acetonitrile, 2% trichloroacetic acid/acetonitrile, 6% perchloric acid/acetonitrile} were compared for the extraction of malachite green (MG), lipophilic leucomalachite green (LMG), gentian violet (GV), and leucogentian violet (LGV) under the same ASE conditions. It was found that the system of 2.5 mL McIlvaine buffer (pH 3)/10 mL acetonitrile obtained the best result [29].

2.4. Effect of modifiers and additives

The addition of some organic, inorganic modifiers and additives may enhance the solubility of analytes in solvent and increase the interactions of target analytes with solvent. They can also alter the physicochemical properties of solvent at elevated temperature. In some cases, solvent modifiers, such as a surfactant, it has been used to extract phthalates from fish tissues [30]. The addition of 0.03% (w/v) complexing agent (tropolone) considerably improved the recovery of monobutyltintrichloride (MBT) by increased by 60% compared with use of solvent containing 90% (v/v) methanol without tropolone [28]. MBT complexation with tropolone produces molecules which are less polar and less soluble in the medium-polarity solvent, and thus extraction efficiency drops. On the other hand, shielding of the original analyte molecules hampers their interactions with the protein matrix, increasing extraction efficiency.

2.5. Effect of matrix composition

The effect of sample matrix depends on sample composition. Food samples can differ significantly in their physical–chemical properties, type of compounds present, or granulation (particle diameter). These parameters affect the sorption and retention of analytes. The complexity of analytical procedure increases with the number of organic compounds present in the sample. Under same ASE conditions, same analyte in different matrices has different extraction efficiency, for instance, recoveries of polychlorinated biphenyls (PCBs) were 110% for vegetable feedstuff, 89% for poultry feed, 81% for mackerel oil and 77% for pork fat [31]. In order to solubilize the analytes during the extraction, proper conditions should be used to overcome the interactions between the organic fraction and analytes. This often results in some components of the matrix being co-extracted with the analytes. These co-extracted substances should be removed usually before the final analysis.

2.6. Effect of extraction mode

The extraction process can be conducted in a static or dynamic mode. In the static extraction mode, the critical factors are the temperature and time of the extraction. The efficiency of the extraction depends on the solubility of the analyte in the static process. The static process begins with heating the cell with the sample to an appropriate temperature during the equilibration time, which lasts approximately 5 min, and is followed by a so-called static extraction process. During this process, the analytes are isolated from the sample under stable static conditions. The static process can be repeated several times if low recoveries are obtained in a single stage. The dynamic variation of ASE extraction improves mass transfer, but this type of extraction is rarely used, mainly because of higher solvent consumption compared with the static process [16]. The two modes have been used for the extraction of 12 sulfonamides (SAs) with water using dynamic mode at 1 mL/min, or using 8 min static time and one static cycle at 160 °C under 1500 psi pressure [32,33].

In the static extraction mode, the lengthy exposure to solvents allows the matrix to swell and improves the penetration of the solvent into the sample interstices and the contact of the solvent with the analytes. Four consecutive extractions of amitraz and its metabolite from the same food animal tissue sample were made to optimize the number of cycles [27]. Significant amounts of the analytes were found in the second extract but the recoveries for both compounds were considered negligible in the fourth cycle. To save solvent and time, three extraction cycles were used, allowing fresh solvent to be introduced.

In the static extraction mode, its extraction efficiency strongly depends on the partition-equilibrium constant and solubility of compounds at elevated temperatures. Thus, highly concentrated samples or low solubility analytes may lead to incomplete extraction due to limited volume of solvent used.

A combination of static–dynamic modes of PHWE was described [34]. The oven was brought up to the temperature of 75 °C as quick as possible. The inlet valve was closed for 20 min (static extraction time) and then, both the inlet and outlet valves were opened; meanwhile fresh water was pumped through the extraction chamber at 0.5 mL/min for 30 min (dynamic extraction time). The static–dynamic modes have been used for the extraction of N-methylcarbamates from different fruits and vegetables.

2.7. Effect of other parameters

Before the extraction, the pretreated samples usually are ought to be mixed with some inert material in order to avoid the aggregation of sample particles that might alter extraction efficiency. ASE often requires dispersion of the sample with an inert material, such as EDTA-washed sand [25], basic alumina [29], sodium sulfate [31], and quartz sand [32] as well as diatomaceous earth [33].

At the end of the extraction the sample is usually rinsed with portions of fresh solvent. Then the entire system is purged with nitrogen. The two steps aim at the removal of all of the sample residues from the ASE system in order to improve the analyte recovery and to prepare the system for the next extraction process.

There are three parameters (i.e., preheating time, flush volume and purge time) that do not significantly affect the recoveries of the target analytes and these are fixed in accordance with the literature to ensure good extraction efficiencies. Preheating time is the time when the cell is kept in the oven at the selected temperature before the solvent is added, 5 min usually being enough to ensure the cell is at the fixed temperature. Flush volume is the percentage of fresh volume introduced into the cell after the static time to drag the analytes toward the collection vial. This volume ensures that all analytes are eluted and is closely related to the final volume. Different flush volumes have been used to extract analytes; in general, a flush volume of only 60% was enough to push the analytes extracted out of the cell.

3. Application of ASE in analysis of animal origin food

3.1. General

Pre-treatment of the sample is needed to assure good contact between the solvent and the matrix in the extraction process.

Prior to loading in the extraction cell, the sample is often pretreated in some way, involving sieving or grinding, because the diffusion of analytes from the sample to the solvent extract can be increased considerably by decreasing particle size. Drying the sample (except for volatile compounds) by vacuum ovens, freeze-drying or lyophilization is also important, especially, when non-polar solvents are to be used in extraction, since any moisture in it may diminish extraction efficiency. Drying agents such as sodium sulfate, diatomaceous earth or cellulose have frequently been employed for this purpose. The extraction of wet samples using water as the extraction solvent is very useful because, in some cases, it permits the elimination of this drying step, thereby minimizing sample pre-treatment.

The use of more polar solvents (acetonitrile, methanol, ethyl acetate, etc.) or solvent mixtures (n-hexane-acetone, n-hexane–acetonitrile, etc.) can assist the extraction of wet samples, making this drying step less crucial. Despite good selection of the drying agent, some water may sometimes be co-extracted, thus interfering in later steps (clean-up, extract concentration, or direct analysis).

After ASE procedure, in the some case, clean up to the extract is required. Solid-phase extraction (SPE), solid-phase micro extraction (SPME), gel permeation chromatography (GPC), matrix solid-phase dispersion (MSPD) and liquid–liquid extraction (LLE) have been used for the clean up prior to analysis.

The final separation and determination were achieved by using a series of analytical methods: gas chromatography (GC) with flame-photometric detection (FPD) or flame-ionization detector (FID), capillary gas chromatography (CGC), high-performance liquid chromatography (HPLC) with diode-array detection (DAD), fluorescence detection (FLD) or ion-trap detection (ITD), hydrophilic interaction chromatography (HILIC), high-speed counter-current chromatography (HSCCC), capillary electrophoresis (CE), mass spectrometry (MS), atomic fluorescence spectrometry (AFS) and GC/CGC/LC/EC–MS as well as GC/LC–MS/MS. The conditions of ASE and final analytical methods for the determination of veterinary drugs, pesticides, other organic pollutants, bioactive and nutritional compounds in animal origin foods are summarized in Table 1. Analytical strategy for multi-residue analysis is summarized in Fig. 1.

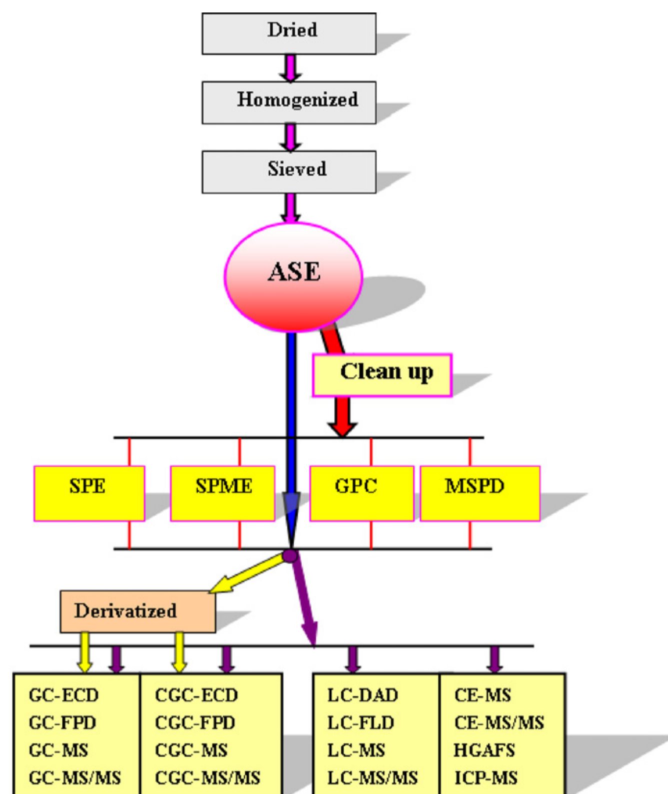

Fig. 1. Analytical strategy for multi-residue analysis of organic contaminations, bioactive and nutritional compounds in food and feed samples.

3.2. Veterinary drugs

3.2.1. Typical multi-residue analysis

One representative example is the application of ASE to multi-class residue extraction. Carretero et al. [35] developed an ASE–LC–MS/MS method for determining trace levels of 31 antimicrobials, including β-lactams, lincosamides, macrolides, quinolones, sulfonamides, tetracyclines, nitroimidazoles and trimethoprim. The extraction method required pre-homogenization of the meat with EDTA-washed sand and subsequent one-static-cycle extraction for 10 min with 40 mL of water at 1500 psi and 70 °C. The method was validated according to the European Union requirements (2002/657/EC). The method validation in meat, according to the Commission Decision No. 2002/657/CE, showed that it is simple, rapid, rugged, sensitive and specific. Additionally, limit of detection (LOD) and limit of quantification (LOQ) pointed out that residue concentration 100 times lower than the MRLs can be determined.

3.2.2. Sulfonamides

Sulfonamides (SAs) comprise a large number of synthetic bacteriostatic compounds. Analysis of SA residues in foodstuffs is of particular concern because of the potential carcinogenic character. To ensure the safety of food for consumers, regulation 281/96 of the EU Commission has laid down MRLs of 100 ppb of SAs as a total in cattle tissues. The U.S. Food and Drug Administration (FDA) has set safety levels of 100 ppb for individual SAs in bovine tissues and 100 ppb of sulfadimethoxine and zero tolerance level of sulfamerazine in fish [36].

Since SAs are polar and medium-polar compounds, with higher solubility in water, so water can be used commonly as solvent of ASE for extraction of SAs. A simple and rapid method able to determine residues of 12 SAs antibacterials including sulfadiazine, sulfathiazole, sulfapyridine, sulfamerazine, sulfameter, sulfamethizole, sulfamethazine, sulfamethoxypyridazin, sulfachloropyridazine, sulfamethoxazole, sulfamonomethoxine, sulfadimethoxine and sulfaquinoxaline in cattle and trout muscle tissues is presented with LOQ of 6.15 ppb for SAs in bovine muscle tissue and 3.13 ppb in trout fillet [32]. This method is based on MSPD technique with hot water as extractant followed by LC–MS. Afterward, following this ASE method and using clean up on Oasis HLB cartridge, a CE–MS/MS method was proposed and validated for the identification and simultaneous quantification of 12 SAs in pork meat [33]. Gentili et al. [37] have described a new LC–MS/MS method for the rapid extraction and unequivocal confirmation of 13 SAs in raw meat and infant foods. This study has taken matrix-induced suppression of ionization into account, by comparing standard and matrix-matched calibration curves. Four of the 13 monitored SAs have been detected in some baby foods and raw meat samples, using the described methodology. This work shows that the environmentally friendly and inexpensive water, besides being an effective extractant for polar and medium-polar contaminants in biological matrixes, produces sufficiently clean extracts requiring

Table 1
Application of ASE in analysis of animal origin food.

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
7 tetracyclines	Muscle and liver	Trichloracetic acid/ACN (1:2, v/v)	60/65 bar	Static time 4 min Static cycles 2		HPLC–UV	75.0–104.9%; LOQ < 15 μg/kg	[25]
12 sulfonamides	Cattle and fish muscle tissues	Water	80/–	Dynamic, at 1 mL/min for 5 min.		LC–MS	LOQ 3–14 ppb	[32]
12 sulfonamides	Pork meat	Water	160/1500 psi	Static time 8 min Static cycles 1	SPE	CE–MS/MS	76–98%; LOQ 46.5 μg/kg	[33]
31 antimicrobials	Meat	MeOH/water (25:75, v/v)	70/1500 psi	Static time 10 min Static cycles 1		LC–MS/MS	75–99%; LOQ 10–50 μg/kg	[35]
13 sulfonamides	Raw meat and infant foods	Water	160/100 atm	Static time 5 min Static cycles 1		LC–MS/MS	70–101%; LOD below 2.6 ppb	[37]
5 sulfonamides	Beef	ACN	120/10 MPa.	Static time 10 min Static cycles 1		HPLC–UV	89.0–107.8%; LOD 0.011 mg/kg	[38]
Fluoroquenolones	Eggs	Phosphate buffer 50 mM pH 3.0/ACN (50:50, v/v)	70/1500 psi	Static time 5 min Static cycles 3		LC–FLD	67–90%	[39]
Antibiotic (avoparcin)	Kidney	Water/30% ethanol (v/v)	75/50 atm	Static time 5 min Static cycles 3	SPE	HILIC–UV	108%	[40]
Aminoglycoside antibiotics	Bovine milk	Water	70/–	Dynamic mode at 1 mL/min for 4 min		LC–MS/MS	70–92%; LOQ 2–13 ng/mL	[41]
Dexamethasone and its b-epimer betamethasone	Bovine liver	n-Hexane/ethyl acetate (1:1, v/v)	50/10 MPa	Static time 5 min Static cycles 1		LC–MS/MS	74.4–77.4%; LOQ 1.0 mg/kg	[42]
8 glucocorticoids	Muscle of swine, cattle, and sheep	n-Hexane/ethyl acetate (50:50, v/v)	50/1500 psi	Static time 5 min Static cycles 2		LC–MS/MS	70.1–103; LOD 0.5–2 μg/kg	[43]
Anabolic steroids	Kidney fat	ACN	50/1500 psi	Static time 5 min Static cycles 1	SPE	LC–MS/MS	17–58%; CCα < 2 ng/g, CCβ 0.3–0.9 ng/g.	[44]
Macrolides	Meat, fish muscle	MeOH	80/1500 psi	Static time 15 min Static cycles 2		LC–MS/MS	77–90%;	[45]
11 benzimidazoles and 10 metabolites	Muscles and livers	ACN/n-hexane	60/1500 psi	Static time 5 min Static cycles 1		LC–MS/MS	70.1–92.7%; LOQ 0.02–0.5 μg/kg	[46]
Barbital, amobarbital and phenobarbital	Pork	Acetrinile	100/10.3 MPa	Static time 5 min Static cycles 2	SPE	GC–MS	84.0–103%; LOQ 1 μg/kg	[47]
Heterocyclic amines	Cooked beef	Dichloromethane/acetone (50/50, v/v)	80/1500 psi	Static time 10 min Static cycles 3		LC–MS/MS	45–79%; LOD 0.02–1 ng/g	[48]
Malachite green, gentian violet and their leuco-metabolites	Shrimp and salmon	McIlvaine buffer (pH 3)/ACN/n-hexane (2/10/2, v/v)	60/1500 psi	Static time 5 min Static cycles 1	SPE	LC–MS/MS	82.1–102.9%; CCα 0.005–0.012 mg/kg, CCβ 0.08–0.13 mg/kg	[29]
109 pesticides (including isomers	Pork, beef, chicken, fish	ACN	80/1500 psi	Static time 5 min Static cycle 2	GPC	GC–MS	62.6–107.8%; LOD 0.3 g/kg	[49]
Polychlorinated biphenyls, organochlorine pesticides	Fish tissue	n-Hexane/dichloromethane (1:1, v/v)	60–90/10 MPa	Static time 5 min Static cycles 3	GPC	HRGC–ECD		[50]
Lipids and extractable organochlorine (EOCl)	Fish	n-Hexane/acetone (3:1, v/v)	55 and 100/1500 psi	Static time 5 min Static cycles 2	Wash with water (pH 3)	NAA	99% for EOCl	[51]
59 organohalogen compounds	Swine liver, heart, kidney, and cattle adipose tissues	Dichloromethane/acetone (1:1, v/v)	100/1500 psi	Static cycles 2	GPC	GC–MS	40.9–111% for adipose, 43.7–110% for heart, 37.6–90.0% for kidney; 24.3–106% for liver	[52]
Organochlorine pesticides, polychlorinated biphenyls, polychlorinated naphthalenes	Harbor seal (*Phoca vitulina*) tissue	n-Hexane/methylene chloride (1:1, v/v)	100/20mPa	Static cycles 3	Activated carbon/silica gel column	GC–MS	45–86%; LOQ 0.7–1.9 pg/g	[53]

Table 1 (*Continued*)

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
22 organochlorine pesticides, 23 organophosphorus pesticides	Chicken meat	Ethyl acetate	120/1800 psi	Static time 5 min Static cycles 2	GPC	GC–MS/MS	62–93%; LOQ 0.19–7.1 ng/g	[55]
50 pyrethroid electronegative pesticides	Pork, beef, chicken, fish	ACN	80/13.8 MPa	5 min (2)	GPC	GC–GC–μ-ECD	63.8 ± 2.4–103.5 ± 9.2%; LOD: 0.04–2.6 g/kg	[56]
12 carbamates	Animal origin foods	ACN	80/2000 psi	5 min (2)	GPC	GC–GC–FLD	62.1/8.8–104%; LOD: 0.24–1.02 μg/kg	[58]
Carbamates	Bovine milk	Water	90/–	Dynamic mode at 1 mL/min		LC–MS	76–104%; LOQ 3–8 ppb	[59]
Atrazine	Beef kidneys	Water/30% ethanol	100/50 atm	Static time 10 min Static cycles 3	MSPD	GC–MS	104–111%; LOD 20 ng/g	[60]
Amitraz and its metabolite	Food animal tissues	n-Hexane/MeOH (1:9, v/v)	60/120 bar	Static time 2 min Static cycles 3	SPE	GC–ECD GC–MS	72.4–101.3% for GC–ECD, 77.4–107.1% for GC–MS; LOQ: 10 μg/kg for GC–ECD, 5 μg/kg for GC–MS	[27]
4,4′-DDE, 4,4′-DDD,; 4,4′-DDT, chlorpyrifos and malathion	Baby food and adult-diet samples	ACN	80/2000 psi	Static time 5 min Static cycles 3	SPE	GC/MS	LOQ 0.3 ppb	[61]
7 neonicotinoid insecticide	Bovine muscle and liver	Water	80/10 MPa	Static time 5 min Static cycles 2	SPE	LC–ESI-MS/MS	83.2–101.9%; LOQ 2.5–5.0 μg/kg	[62]
Lettuce, avocado, lemon	Benzoylurea insecticides	Ethyl acetate	80/1500 psi	Static time 5 min Static cycles 2		LC–MS/MS	58–97%; LOQ 0.002–0.01 mg/kg	[63]
Polychlorinated biphenyls, polycyclic aromatic hydrocarbons	Mussel and fish	DCM	100/13.8 Mpa	Static time 5 min Static cycles 1	GPC	GC–MS		[64]
9 polychlorinated biphenyls	Fish tissue	DCM	125/–	Static time 3 min		GC–ECD		[65]
Polychlorinated biphenyls, lipids	Fish tissue	n-Hexane	125/1500 psi	Static time 5 min Static cycles 2		GC–ECD		[66]
14 polychlorinated biphenyls, 9 dioxins	Fish tissue	n-Hexane/2-propanol (3:2)	100/1000 psi	Static time 5 min Static cycles 1		GC–ECD		[67]
7 polychlorinated biphenyls,	Fish meal and feed samples	n-Heptane	100/–	Static time 5 min Static cycles 2		GC–MS	89–103%	[68]
7 polychlorinated biphenyls	Milk powder (CRM), cod-liver oil (CRM)	n-Hexane	100/10.34 MPa	Static time 5 min Static cycles 2		GC–MS	70 and 72%	[69]
Polychlorinated dibenzo-*p*-dioxins, polychlorinated biphenyls	High-fat-content samples	n-Hexane	/1500 psi	Static time 5 min Static cycles 2	GPC	GC–HRMS	44–132%	[70]
Five types of fat retainers	Fat-containing samples	n-Hexane	100/1500 psi	Static time 5 min Static cycles 2		GC–MS	96–133%; LOQ 1 ng/g	[71]
Polychlorinated biphenyls	Eggs and mussels (CRM)	DCM/pentane (15:85, v/v)	40/2000 psi	Static time 10 min Static cycles 2		GC–ECD GC–MS/MS	90–106%; LOD 0.001–0.004 for GC–ECD and 0.002–0.07 ng/g for GC–MS–MS	[72]
Polychlorinated biphenyls	Fish meal and animal feed	n-Heptane	100/–	Static time 5 min Static cycles 2		GC–ECD	90–93%	[31]
Polychlorinated biphenyls, polychlorinated dibenzo-*p*-dioxins	Meat and fish	DMSO/ACN (1:9, v/v)	180/2000 psi	Static time 15 min Static cycles 1	Silica gel-activated carbon column	HRGC/HRMS	>60%; LOD 0.058–5.7 pg/100 mL	[73]

Table 1 (*Continued*)

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
Polychlorinated biphenyls, DDT, toxaphene, chlordane, hexachlorobenzene, hexachlorocyclohexanes, and dieldrin	Fish tissue	Ethyl acetate/n-hexane (1:1, v/v)	125/10 MPa	Static time 10 min Static cycles 2	GPC SPE	GC–ECD	>70%; LOD 0.2 μg/kg	[74]
22 polychlorinated biphenyls	Foodstuffs	n-Hexane	40/12 MPa	Static time 5, 7 or 10 min Static cycles 2		GC–ECD	83–133%; LOD < 0.2 ng/g	[75]
Polybrominated diphenyl ethers	Fish	n-Hexane/dichloromethane 90:10 (v/v)	100/–	Static time 5 min Static cycles 3		GC–MS/MS	83–108%; LOQ 34–68 pg/g	[77]
Polychlorinated biphenyls, polybrominated diphenyl ethers	Fish sample and soil	n-Hexane/acetone (1:1, v/v)	150/1500 psi	Static time 8 min Static cycles 3	GPC	GC–MS	77–118%; LOD: < 1.52 pg/g for PCBs, 24.8 pg/g for PBDEs	[78]
Polybrominated biphenyls	Fish samples	n-Hexane	100/–	Static time 5 min Static cycles 3	Silica gel	GC–MS/MS	>91%; LOD 0.03–0.16 ng/g	[79]
Nonylphenol and its ethoxylates	Fish tissue	DCM	/6.9 MPa	Static time 10 min Static cycles 3	SPE	HPLC–FLD	74–125%; LOQ 34–171 ng/g	[80]
Alkylphenols and alkylphenols ethoxylates	Egg and fish tissue	ACN (egg sample) DCM	Ambg/1000 psi	Static time 10 min Static cycles 3	SPE	LC–MS/MS; LC–FLD	96%; LOQ 4–12 ng/g in eggs, 6–22 ng/g in fish	[81]
4-t-Octylphenol, 4-nonylphenols, and bisphenol A	Fish liver	Acetone/n-hexane (1:1, v/v)	100/1500 psi	Static time 5 min	Florisil column	LC–ESI-MS	>98%; LOD 5–20 ng/g	[82]
Nonylphenol, octylphenol, bisphenol A	Pork, fish, rabbit, duck meat and chicken	MeOH–water (90:10, v/v)	125/800 psi	Static time 3 min Static cycles 4		LC–MS/MS	91.5–101.3%; LOQ 0.20–100 μg/kg	[83]
Bisphenol A, octylphenol, and nonylphenol	Powdered milk infant formulas	Ethyl acetate	70/1500 psi	Static time 10 min Static cycles 1		LC–MS/MS	84–101%; LOQ 0.016–0.010 mg/kg	[84]
Polycyclic aromatic hydrocarbons	Smoked meats	n-Hexane	100/1500 psi	Static time 5 min Static cycles 2	Florisil column	GC–MS	54–102%	[85]
Polycyclic aromatic hydrocarbons	Smoked meats	n-Hexane	100/100 bar	Static time 10 min Static cycles 2	GPC	GC–MS	91–97%	[86]
Polycyclic aromatic hydrocarbons and their derivatives	Fish tissue	n-Hexane/acetone (1:1, v/v)	100/10 MPa	Static time 5 min Static cycles 1	GPC	HPLC–FLD	LOQ 0.3 μg/kg	[87]
Polycyclic aromatic hydrocarbons	Trout and sardine	Water + SDS	200/–	Static time 15 min Static cycles 4	SPE	HPLC–FLD	98.3–102.1%; LOD 0.022 μg/mL	[30]
Polycyclic aromatic hydrocarbons	Smoked food	90%methylene chloride and 10% ACN	100/1500 psi	Static time 5 min Static cycles 2	Florisil column	GC–MS	LOD 0.002–0.1 μg/mL	[88]
Polycyclic aromatic hydrocarbons	Smoked meat products and liquid smokes	n-Hexane	100/100 bar	Static time 10 min Static cycles 2	GPC	GC–MS	75–110%	[89]
Polycyclic aromatic hydrocarbons	Mussel tissue	Dichloromethane/acetone (1:1, v/v)	125/1500 psi	Static time 5 min Static cycles 1	GPC	LC–FLD LC–MS	70–110%; LOQ 0.1–0.25 mg/kg	[90]
Organometallic species of As, Sn and Hg	Sediments and an oyster tissue	50% acetic acid in MeOH	100/1500 psi	Static time 3 min Static cycles 5		GC–ICP-MS LC–ICP-MS	80% (dimethylarsinic acid, DMA)–99%for arsenobetaine (AsB). Dibutyltin (DBT), tributyltin (TBT)	[91]
Butyl- and phenyltin compounds	Harbor porpoise (*Phocoena phocoena*) liver	MeOH/water (9:1, v/v)	125/800 psi	Static time 3 min	Derivatization with $NaBEt_4$	GC–FPD	LOD 6–10 ng(Sn)/g and 7–17 ng(Sn)/g for butyl- and phenyltin, respectively	[28]

Table 1 (*Continued*)

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
Musk compounds	Freshwater fish	Ethyi acetate/n-hexane (I:5, v/v)	80/10.104 kPa	Static time 5 min Static cycles 2		GC–MS	75–93%; LOD 0.5–2.0 ng/g	[92]
Pacific ciguatoxin-1	Fish flesh	MeOH	75/1500 psi	Static time 5 min Static cycles 2	SPE	LC–MS/MS	49–85; LOQ 0.01 μg/kg	[93]
2-Alkylcyclobutanones, 2-docecylcyclobutanone, 2-tetradecylcyclobutanone	Fat-containing foodstuffs irradiated with γ-rays	Ethyl acetate	100/1500 psi	Static time 5 min Static cycles 2	silica gel mini column.	GC–MS	70–105%; LOD 1–3 ng/g	[94]
Isopropylthioxanthone	Milk, yoghurt and fat	Cyclohexane/ethyl acetate (1:1, v/v)	100/14 MPa	Static time 5 min Static cycles 2		HPTLC–FLD	For 100%, LOD 0.13 μg/kg; for 6–70%, LOD 0.2–2.5 μg/kg	[95]
Total fat	Powdered infant formula	n-Hexane/acetone (4:1, v/v)	125/–	Static time 3 min Static cycles 5		Gravimetry GC–FID		[96]
Total fat	Meat	Petroleum ether or n-hexane	125/–	Static time 2 min Static cycles 2/1		Gravimetry		[97]
Total fat	Dried milk products	Hexane/DCM/MeOH	80/–	Static time 1 min Static cycles 3		Gravimetry, GC HPLC–FLD		[98]
Total fat	Dairy products	n-Hexane/isopropanol petroleum ether/acetone	100–120/	Static time 3 or 2 min Static cycles 1		Gravimetry		[99]
Total fat	Dairy products	n-Hexane, DCM, MeOH, petroleum ether, acetone	80–120/–	8–10 min		Gravimetry		[10]
Unbound fat	Snack foods and dog biscuits	Petroleum ether, n-hexane, chloroform	125/–	Static time 5–25 min Static cycles 1–3		Gravimetry		[101]
Total lipids	Poultry meat	Chloroform/MeOH (2:1, v/v)	120/20 MPa	Static time 10 min Static cycles 2	LLE	TLC; CGC	97.8%	[103]
Total lipids	Fish tissue	60% chloroform/40% MeOH; 60% n-hexane/40% isopropanol; 100% methylene chloride	100/13.8 MPa	Static time 5 min Static cycles 2		GC–FID	80–120%	[104]
Total fatty acids	Cereal lipids and animal	Chloroform/MeOH Isopropanol/n-hexane	120/–	Static time 5 min Static cycles 2		GC		[105]
Oxysterol	Egg-containing food	n-Hexane/isopropanol (3:2, v/v)	60/15 Mpa	Static time 10 min Static cycles 2		GC–FID		[106]

Note: ACN – acetonitrile, DCM – dichloromethane, DMSO – dimethyl sulfoxide, MeOH – methanol, SPE – solid-phase extraction, GPC – gel permeation chromatography, LLE – liquid–liquid extraction, LOD – limit of detection, LOQ – limit of quantification, CCα – detection capability, and CCβ – decision limit.

little or no manipulation before final analysis by LC–MS. These methods can be used in the food quality and safety control areas.

3.2.3. Antibiotics

Tetracyclines (TCs) antibiotics were widely used in animal husbandry. Due to the widespread misuse, antibiotic residues in products of animal origin have been a growing concern to consumers. The residues of these molecules can be directly toxic and cause allergic reactions in some hypersensitive individuals. A simple and especially rapid method using ASE and HPLC was developed for the quantitative determination of representative members of TCs antibiotic class in muscle and liver of porcine, chicken and bovine [25]. The method could be useful to determine TCs residues in contaminated animal muscle and liver.

ASE has been applied for extraction of quinolones (QNs) from meat and eggs [35,39]. Whole eggs were firstly homogenized and then, aliquots were mixed with a dispersing agent (diatomaceous earth) before extraction. The obtained extracts did not require further clean up. The ASE–LC–FLD method has been successfully applied to the determination of enrofloxacin and its metabolite ciprofloxacin in incurred eggs from enrofloxacin-treated hens, showing that the method could be useful for screening contamination or illegal use of QNs in laying hens [39].

A new approach is presented for the determination of avoparcin in tissue [40]. The samples were extracted by ASE at 75 °C and 50 atm. In situ sample clean up was achieved by using MSPD. The aqueous extracts were concentrated by SPE on the HILIC material polyhydroxyethyl aspartamide. Five-millimeter HILIC column with UV detection was used for the separation of avoparcin. The retention time was less than 15 min with 47% aqueous component in acetonitrile and 15 mM TEAP as eluent. The average recovery of avoparcin from kidney samples was 108%.

A procedure for determining nine widely used aminoglycoside antibiotics in bovine whole milk is presented [41]. It is based on MSPD with heated water as extractant followed by LC–MS/MS using an electrospray ion source. MS data acquisition was performed in the MRM mode. Analyte recoveries ranged from 70% to 92%. The LOQs were between 2 ng/mL (apramycin) and 13 ng/mL (streptomycin). They are well below the tolerance levels set by both the European Union and the U.S. Food and Drug Administration.

Corticosteroid drugs are widely used to combat inflammatory diseases in food-producing animals. An ASE-SRM-LC–MS/MS method for the rapid extraction and unequivocal confirmation of two highly potent fluorinated synthetic corticosteroids, dexamethasone and its b-epimer betamethasone, in bovine liver was developed [42]. The proposed approach seems particularly useful for routine control of the illegal use of corticosteroids in food-producing animals. A multi-residues method using ASE and LC–ESI-MS/MS in negative mode with SRM mode has been developed for determination of eight glucocorticoids in muscle of swine, cattle, and sheep [43].

Synthetic gestagens have anabolic side effects and they are able to stimulate other anabolic steroids. To control the illegal use of gestagens in animals sensitive analytical methods are necessary. Some papers describe an analysis for one or more gestagens in kidney fat. A screening method has been developed for the determination of various anabolic steroids in kidney fat [44]. Fat samples are extracted and steroids are trapped "on-line" during ASE, followed by cleanup with C18 SPE. Compounds were finally analyzed by LC–MS. The method was validated using blank kidney fat and fat samples fortified at 2 ng/g. Accuracies are adequate when using isotopically labeled internal standards and the acquired validation data are satisfactory for a qualitative screening method. ASE has also been applied to the extraction of macrolides (MCs) from meat and fish samples before LC–MS/MS determination [45]. No interferences were found at the retention times of the MCs, which allows direct injection of the extracts without the need of further clean-up. But, relatively low recoveries were obtained for some of the analyzed compounds, e.g., erythromycin A (ERY A) with only 58% recoveries at the MRL level.

3.2.4. Benzimidazoles and barbiturate compounds

Benzimidazoles (BZDs) are anthelmintic agents widely used for the treatment of parasitic infections in food-producing animals. For the food safety risks, the use of BZDs in food-producing animals is controlled in China and the European Union. China and the European Union have recommended the MRL for BZDs ranged from 50 to 400 μg/kg and 60 to 5000 μg/kg, depending on the compound and matrix. Consequently, there is an urgent need to develop comprehensive control measures to monitor residues of BZDs in animal products.

A confirmatory and quantitative method of LC–MS/MS combined with an ASE using acetonitrile/n-hexane as the extraction solvent was developed for the determination of 11 benzimidazole and 10 metabolites of albendazole, fenbendazole and mebendazole in the muscles and livers of swine, cattle, sheep and chicken [46]. HPLC analysis was performed on a C18 column with gradient elution using acetonitrile and 5 mmol/L formic ammonium as mobile phase. The analytes were detected in the positive ion MRM mode by the LC–ESI-MS/MS analysis. The between-day relative standard deviations were no more than 10%. The method is simple, fast, robust and suitable for identification and quantification of BZDs residues in animal products.

Sedative barbiturate compounds were distributed into all tissue and organs in vivo. It is necessary to monitor their residues to protect the consumer's health. A GC–MS method combined with ASE, SPE and derivatization was developed for the determination of barbital, amobarbital and phenobarbital residues in pork [47]. The developed method provided an unequivocal identification and accurate quantification of three barbiturates.

3.2.5. Heterocyclic amines and malachite green

In recent years, many studies have focused on the role of certain heterocyclic amines (HAs) as mutagenic/carcinogenic compounds found in protein rich foods, such as meat and fish. HAs in meat extract samples were analyzed using an ASE and LC–MS/MS [48]. The run-to-run and day-to-day precisions with RSD lower than 13% achieved at both low (0.20 μg/g) and medium (1.0 μg/g) concentrations. This method reduces sample manipulation and total extraction time by nearly four-fold compared to conventional SPE. The optimized method was validated using laboratory reference material based on a meat extract, and was successfully applied to HAs analysis in several cooked beef samples.

As we all know, malachite green (MG) is a triphenylmethane dye and readily absorbed by fish and metabolically reduced to the lipophilic leucomalachite green (LMG). MG and LMG have potential health and environmental hazards. Numerous analytical methods have been published. Recently ASE has been used for the extraction of malachite green and gentian violet as well as their leuco-metabolites in shrimp and salmon before auto solid-phase clean-up and LC–MS/MS detection [28]. The limits of quantification were lower than the MRPL of EU, China, etc. The method was a reliable tool and could be applied to the testing of MG and GV, or LMG and LGV in aquatic products for surveillance programs.

3.3. Pesticides

3.3.1. Typical multi-residue analysis

In the reported studies from the literatures consulted for this review, products of animal origin were mostly analyzed for five main groups of pesticides, namely organochlorine pesticides (OCPs), organophosphorus pesticides (OPPs), carbamates,

pyrethroids, and triazines. Determination of pesticides in food is often complicated by the presence of fats and requires multiple clean up steps before analysis. Cost-effective methods are needed for analyzing the large number of samples generated in large-scale exposure studies.

Recently, a new analytical method was developed to simultaneously determine residues of 109 pesticides (including isomers) in the foods of animal origin [49]. Acetonitrile was selected for ASE for effectively extracting the pesticides from the fatty samples. The clean up was performed with an automated GPC clean up system. The prepared samples were analyzed with GC–MS in the SIM mode using one target and two qualitative ions for each analyte. The average recoveries of most pesticides were from 62.6% to 107.8% with RSD of 620.5% ($n = 6$).

3.3.2. *Organochlorine pesticides*

Organochlorine pesticides (OCPs) are persistent organic pollutants. As it is known, an important consideration when developing an extraction method for pesticide multi-residue analysis is the need to cover a wide range of different compounds with different properties in a single procedure.

ASE was used to extract OCPs and other related compounds in fish muscle tissue containing 3.2% (w/w) lipids with n-hexane-dichloromethane (1:1, v/v) or n-hexane-acetone (4:1) [50]. Crude extracts were purified by GPC employing Bio-Beads S-X3. Identification and quantification of target indicator OCPs were performed by high resolution-GC with two parallel ECDs. Zhuang et al. [51] evaluated comparatively ASE and polytron extraction for quantification of lipids and extractable organochlorine (EOCl) in fish. Both extractions can be used for determination of fish EOCl. A suitable extraction protocol for ASE is consecutive extractions of ground, freeze-dried filets with n-hexane–acetone at 55 and 100 °C. The lipid content given by polytron is higher than that by ASE. Differences in EOCl measurement between the two extraction methods depend on the source of fish or the chemical composition of fish EOCl. An analytical method has been developed for the quantification of 59 different persistent organohalogen compounds in biological organ tissues [52]. The optimum extraction and clean up procedures were examined using ASE, automated GPC on Biobeads S-X3 and automated SPE on silica-gel. Wang et al. [53] developed a GC–IT–MS method for the determination of OCPs and other organochlorine pollutants in harbor seal tissues. Tissue samples were homogenized, lyophilized and then extracted with n-hexane–methylene chloride (1:1, v/v). After lipid removal using a 40% H_2SO_4-modified silica gel column, OCPs were collected in one fraction. This method can effectively eliminate matrix interferences, and has high selectivity and sensitivity, and can be used to analyze OCPs and other organochlorine pollutants in harbor seal blubber, liver and kidney samples. The use of certified reference material, CRM 7404-a, as an useful tool had validated the reliability of ASE–GC–HRMS methods and quality assurance/quality control of analyses of OCPs and polychlorinated biphenyls (PCBs) in fish or similar sample matrices [54].

3.3.3. *Organophosphorus pesticides*

Organophosphorus pesticides (OPPs) are persistent organic pollutants. A rapid analytical method for 45 pesticides in three different types of meat matrix was developed [55]. The residues of OPPs and OCPs pesticides in meat samples were extracted using ASE with ethyl acetate, then clean up by GPC with Envirogel column and n-hexane-ethyl acetate (1:1, v/v) before final determination by GC–triple-quadrupole analyzer–MS detection system. Recoveries and precision values were 70.0–90.0% and 15%, respectively. The proposed analytical methodology was applied to the analysis of the pesticides in chicken, pork samples, and lamb samples.

3.3.4. *Pyrethroid pesticides*

A rapid method was developed to determine the multi-residues of 50 electronegative pesticides in the animal origin foods by capillary gas chromatography with μ-ECD. The electronegative pesticides in the animal origin samples could be extracted with acetonitrile by ASE and cleaned up by auto GPC and primary secondary amine PSA packing material. The LODs and the recoveries for the 50 electronegative pesticides were both satisfied with the requirement of pesticide residue analysis [56].

3.3.5. *Carbamate pesticides*

The use of carbamates for pest control has increased progressively in recent years. Owing to their broad spectrum of biological activity, carbamates can be used as insecticides, miticides, fungicides, nematocides, and molluscicides. Carbamate residues are of concern for food control because some of them have high acute toxicity. Some are suspected carcinogens and mutagens [57].

Carbamate pesticides in animal derived foods were determined with ASE–GPC and HPLC post column derivatization [58]. A simple, specific and rapid procedure for determining six largely used carbamate insecticides in bovine whole milk was presented [59]. This method is based on MSPD technique with heated water as extractant followed by LC–MS equipped with a single quadrupole and an electrospray ion source. This work has again shown that the environmentally friendly and inexpensive water, besides to be an effective extractant for polar and medium-polar contaminants in biological matrices, produces sufficiently clean extracts requiring little manipulation before final analysis by LC–MS.

3.3.6. *Amitraz pesticides*

Amitraz is a member of formamidine pesticide family. Increased concerns in recent years on possible health risk due to amitraz residues have greatly influenced our thinking and impelled us to set up monitoring programs to determine amitraz at low levels. Curren et al. [60] developed a novel extraction method that utilizes ethanol-modified subcritical water in combination with SPME for the removal of atrazine from beef kidney. A new method has been developed for the determination and confirmation of amitraz and its main metabolite, 2, 4-DMA, in food animal tissues by GC–ECD and GC–MS using ASE [27]. The use of GC–ECD combined with GC–MS is recommended for the analysis of large numbers of tissue samples requiring method ruggedness. The rapid and reliable method can be used for characterization and quantification of amitraz and its main metabolite residue, 2, 4-dimethylaniline, in liver and kidney samples of swine, sheep and cattle.

Chuang et al. [61] examined two extraction methods, supercritical fluid extraction (SFE) and ASE, coupled with various clean up techniques for the analysis of pesticides (4,4′-DDE; 4,4′-DDD; 4,4′-DDT; chlorpyrifos and malathion) in baby foods and adult-diet samples. The SFE-GC–MS method did not provide quantitative recoveries (<50%) of the pesticides spiked into fatty baby foods. ASE with CAN at 80 °C under 2000 psi and clean up with an ENVI-Carb SPE were used to determine target pesticides by ASE–ELISA and by ASE–GC/MS. Concentrations of these compounds ranged from <0.3 to 110 ppb.

3.3.7. *Neonicotinoid pesticides*

A rapid, sensitive, and environmental-friendly method has been developed for the simultaneous determination of seven neonicotinoid insecticides residues in bovine muscle and liver [62]. The sample preparation procedure was based on a high automated ASE combined with SPE cleanup. The target compounds were identified and quantitatively determined by LC–ESI-MS/MS operated in MRM mode. This validated method was successively applied to the determination of neonicotinoid insecticides in real samples from markets.

3.3.8. Benzoylureas pesticides

Benzoylureas (BUs) constitute an important group of pesticides with herbicide, insecticide, or acaricide activity that act as insect growth regulators. A method based on ASE and LC–MS/MS has been developed for determining nine BUs in fruit, vegetable, cereals, and animal products [63]. Samples (5 g) were homogenized with diatomaceous earth and extracted in a 22 mL cell with 22 mL of ethyl acetate at 80 °C and 1500 psi. After solvent concentration and exchange to methanol, BUs were analyzed by LC–MS/MS. LOQs (0.002–0.01 mg/kg) are equal or lower than MRLs established by the Codex Alimentarius. The use of LC–MS/MS attains the determination of BUs without further clean up, avoiding the presence of interferences during the quantification step.

3.4. Other organic contaminations

3.4.1. Organochlorines

Polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), polychlorinated naphthalenes (PCNs), and polychlorinated dibenzo-*p*-dioxins (PCDDs) are persistent organic pollutants. Determination of PCBs in fatty matrixes is important, however, the extraction of trace compounds in the presence of extractable major sample components such as lipids offers special problems. In gas chromatography, large amounts of injected fat may cause problems in the injector and at the top of the column. When using mass spectrometry detection, the ion source might become contaminated, causing impaired analytical performance. Extraction procedures often rely on Soxhlet extraction, in which the extracts contain large amounts of lipids that need to be removed. ASE is a relatively new technique applicable for the extraction of persistent organic pollutants from various matrices.

ASE, for the extraction of selected PCB from the reference materials, was evaluated in 1997 by Schantz et al. [64]. In 1998–2004, ASE has been used for the extraction of PCBs from different animal foods, such as fish tissue [31,65–68], cod-liver oil and milk powder [69], fat-content samples [70,71], eggs and mussels [72], and meat and fish [73] as well as cod liver and fish fillets [74]. Ramos et al. [75] have proposed the feasibility of ASE with in-cell purification and subsequent GC–micro-ECD detection for the determination of prioritary and toxic PCBs in a variety of foodstuffs.

3.4.2. Polybrominates

Polybrominated diphenyl ethers (PBDEs) are a class of chemicals extensively used as flame retardant additives in a wide variety of commercial and industrial products. They are released into the environment. Since an important human exposure route of PBDEs is through the diet, recent studies on PBDE levels in food have demonstrated that fish consumption significantly contributed to the total human exposure. Due to these findings, efforts have been undertaken to develop reliable methods to analyze these compounds in biota samples. PBDEs are currently analyzed using similar methods to those applied for polychlorinated biphenyls (PCBs) and other persistent organic pollutants [76]. A fast and simple method for the analysis of PBDEs in fish samples was developed using a one-step extraction and clean up by means of ASE combined with GC–IT–MS/MS [77]. The method was validated using the standard reference material SRM-1945 (whale blubber) and was then applied to the analysis of PBDEs in fish samples. For both PBDEs and PCBs, ASE and MAE were in general capable of producing comparable extraction results as the classical solvent extraction, and even higher extraction recoveries were obtained for some PCB congeners with large octanol–water partitioning coefficients (Kow) [78]. This relatively uniform extraction results from ASE and MAE indicated that elevated temperature and pressure are favorable to the efficient extraction of PCBs from the solid matrices. For PBDEs, difference between the results from MAE and ASE (or SOE) suggests that the MAE extraction condition needs to be carefully optimized according to the characteristics of the matrix and analyte to avoid degradation of higher brominated BDE congeners and improve the extraction yields. Recently, Malavia et al. [79] have described a fast and simple ASE method combined with GC–IT–MS–MS for the determination of polybrominated biphenyls (PBBs) in fish samples. The method is based on a simultaneous extraction/clean up step to reduce analysis time and solvent consumption. For the whole method, limits of detection ranging from 0.03 to 0.16 ng/g wet weight and good precision (RSD < 16%) were obtained.

3.4.3. Alkylphenols and bisphenol A

The ubiquity of alkylphenols and bisphenol A (BPA) in the environment is a worldwide scientific and public concern due to the persistence, toxicity and endocrine disrupting properties of these compounds. A simple automated extraction method for the determination of alkylphenolic compounds in fish tissue was reported [80]. Pressurized fluid extraction is used to extract ground fish tissue, and the resulting extract was purified on aminopropyl silica (APS) extraction cartridges. With no further sample preparation, nonylphenol (NP) and its ethoxylates, up to nonylphenol pentaethoxylate, were quantitated using HPLC–FLD. Analysis of extracts from fish liver containing alkylphenol contaminants can be hindered by the presence of co-extracted fats and proteins that interfere with chromatographic analysis. A quantitative method for the simultaneous determination of octylphenol, nonylphenol and the corresponding ethoxylates (1–5) in egg and fish tissue was presented based on ASE followed by SPE cleanup, using octadecylsilica or aminopropyl cartridges [81]. Tavazzi et al. [82] described a procedure for the analysis of octylphenol, nonylphenol, and bisphenol A in fish liver. This procedure combines simple and automated ASE with Florisil clean up to obtain clean and analyzable biological extracts for subsequent LC–MS determination of alkylphenols and bisphenol A. Interferences from lipids and proteins were avoided, enabling quantification of alkylphenol compounds at ppb levels in liver samples. The method can be satisfactorily applied to screening analysis of octyl- and nonylphenol, and bisphenol A in biological samples such as fish liver. A new method based on ASE with a subsequent cleanup step using amino-propyl SPE cartridges and LC–ESI-MS/MS was reported for the simultaneous determination of nonylphenol (NP), octyl phenol (OP) and bisphenol A (BPA) in different meats [83]. This method was applied to investigate the exposure levels of alkylphenols and bisphenol A in different kinds of meat available from Beijing markets. Investigation of the levels in commercial samples indicated that NP was ubiquitous in different types of meat at levels ranging from 0.49 to 55.98 μg/kg. Higher concentrations of NP and BPA were found in aquicolous animals. The maximum intakes of NP and BPA were estimated to be 11.2 and 1.4 μg/person/day, or 0.19 and 0.02 μg/kg bw. BPA, OP and NP have estrogen-like effects and chronic toxicity causing, at low doses, a variety of adverse effects. Ferrer et al. [84] developed an analytical method using ASE and LC–MS/MS for the simultaneous determination of BPA, OP and NP in powdered infant formulas and powdered skimmed milk. The positive samples were found; therefore, the content of these compounds must be monitored to meet consumer food safety concern.

3.4.4. Polycyclic aromatic hydrocarbons

Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous carcinogenic contaminants. The Scientific Committee on Food (SCF) has assessed the health risks to consumers associated with exposure to PAHs in foodstuffs (Report SCF/CS/CNTM/PAH/29 Final (4 December 2002). ASE has been used for the extraction of PAHs in trout and sardine [30], smoked food samples [85,86], and fish tissue [75,87].

Samples fortified with 16 PAHs were extracted by ASE, and the extracts were treated with sulfuric acid and Florisil, followed by GC–MS analysis [88]. Up to 12 PAHs were found to be present at concentrations ranging from 3 to 52 ng/g wet sample. Three PAHs were detected in a commercial smoked salmon sample. With smoked sausage and smoked pork tasso samples, the number of PAHs detected varied from 6 for one tasso sample to 12 for another. PAH concentration levels ranged from 3 to 52 ng/g wet sample. A GC–MS method for the determination of ten PAHs with four to six condensed aromatic carbon rings (including six PAHs) in smoked meat products and liquid smokes has been developed [89]. The method implies ASE and GPC for efficient lipid removal without saponification and ^{13}C-labeled PAH for quantification. The analysis of a standard reference material of the National Institute of Standards and Technology (mussel tissue, SRM 2977) resulted in a good accordance between measured and certified PAH concentrations. The determination of PAH contents in 26 samples of smoked meat products and liquid smokes further confirmed the analytical power of the new method and gave a first insight into the specific PAH patterns. Yusa et al. [90] reviewed briefly the analytical procedures used for PAHs determination in fish and shellfish. ASE–GPC–HPLC method has been evaluated as a fast alternative to methanolic saponification for the extraction of 12 PAHs from mussel tissue. The ASE method was validated using the standard reference material SRM 2977, a freeze-dried mussel tissue with naturally present organic contaminants.

3.4.5. Organometallic species

Wahlen and Catterick [91] described the development of ASE methodology that is capable of simultaneously extracting organometallic species of As, Sn and Hg in a semi-automated manner. The developed ASE method provides a significant improvement over many currently available routine monitoring methods for trace element speciation due to the fact that it is capable of extracting several species of toxicological interest simultaneously and quantitatively. Organotin compounds are widely used in agriculture and industry as fungicides, bactericides, and insecticides. To evaluate the fate of organotin compounds in the environment and the effectiveness of legal provisions controlling their use, many analytical methods have been developed. Wasik and Ciesielski [28] developed a method for species-selective analysis of organotin compounds in solid and biological samples. The procedure is based on ASE of analytes and includes extraction of the tin species with a methanol–water (90% methanol) solution of acetic acid–sodium acetate containing tropolone (0.03%, w/v), their ethylation with sodium tetraethylborate ($NaBEt_4$), and separation and detection by GC–FPD. The analytical procedure was validated by analysis of NIES No. 11 (fish tissue) certified reference material.

3.5. Bioactive and nutritional compounds

Draisci et al. [92] developed an ASE–GC–MS method for the determination of Musk compounds in freshwater fish samples. Wu et al. [93] described a sensitive and rapid extraction method using ASE combined with HPLC–MS/MS for the detection and quantification of pacific ciguatoxin-1 in fish flesh. ASE with ethyl acetate and clean up on silica gel mini column were used to determine 2-docecylcyclobutanone in γ-ray irradiated fat-containing foodstuffs by GC–MS [94]. Morlock and Schwack [95] have developed two new high performance thin layer chromatographic (HPTLC) methods for quantification of isopropyl-9H-thioxanthen-9-one (ITX) in milk, yoghurt and fat samples using ASE with a mixture of cyclohexane and ethyl acetate. Extraction of ITX from milk and yoghurt was performed by ASE with a mixture of cyclon-hexane and ethyl acetate.

The determination of fat in certain food products is difficult due to the binding of the fat by the matrix. Thus, traditional methods used to extract fat include a pretreatment step, generally with ammonium hydroxide, to denature or destroy the matrix structure. ASE has probed to be a good alternative to replace other extraction methods. Many ASE procedures have described for extraction of total fat from powdered infant formula [96], meat [97], dried milk products [98], and dairy products [99,100], as well as unbound fat from snack foods and dog biscuits [101].

Dietary fats are the most targeted nutrients related to chronic diseases. Among the different fats, some fatty acids can be used as functional ingredients. Ruiz-Rodriguez et al. [102] reviewed recent developments in FAs analysis. It is difficult to pursue direct ASE with acid- or base-hydrolyzed samples due to the corrosive nature of the reagents and material limitations. An ASE procedure was used for the quantitative determination of the fat content in homogenized poultry meat samples [103]. The recovery of total lipids obtained by ASE extraction was compared to those obtained by conventional methods, such as the Folch method and acid hydrolysis, followed by Soxhlet extraction. The compositions of the extracts from each method were determined by TLC analysis and the fatty acid composition of the extracts was analyzed by a CGC. Dodds et al. [104] described the adaptation of ASE for extracting total lipids from 100 mg of fish tissue. Their test demonstrates that micro scale ASE represents an effective and efficient alternative to traditional lipid extraction techniques based on quantity and composition of extracted lipid, surrogate recovery, and precision. Schäfer [105] has developed an ASE method for the quantitative determination of total lipids and fatty acid composition in plant and animal tissues. ASE and modified Folch procedure were compared in their ability to extract lipids from cereal, egg yolk and chicken breast muscle samples. Fatty contents and compositions of extracted lipids were determined by GC. Results indicate that ASE is a promising lipid-extraction system for the entire range of plant and animal tissues. The effectivity and reliability of GC–FID and LC/MS combined ASE for the determination of fatty acids have been approved using SRM 3250 Serenoa repens fruit and SRM 3251 Serenoa repens extract [107].

4. Application of ASE in analysis of plant origin food

The conditions of ASE and final analytical methods for the determination of pesticides, herbicides, other organic contaminations, natural toxins, bioactive and nutritional compounds as well as other organic contaminations in plant origin foods are summarized in Table 2.

4.1. Pesticides

4.1.1. Typical multi-residue analysis

The intensive development of agriculture means that more and more toxic organic and inorganic compounds are entering the environment. Because of their widespread use, stability, selective toxicity and bioaccumulation, pesticides are among the most toxic substances contaminating the environment. They are particularly dangerous in fruit and vegetables, by which people are exposed to them. It is therefore crucial to monitor pesticide residues in fruit and vegetables using all available analytical methods [108].

Of multi-residue methods for the determination of pesticides, three typical high-throughput and multi-class residue methods have been reported. An analytical procedure using ASE and CGC with ECD and FPD was developed to simultaneously determine residues of 28 compounds selected from eight pesticide classes in fruits and vegetables [109]. 24 of the 28 pesticides gave recoveries of more than 70% with a coefficient of variation less than

Table 2
Application of ASE in analysis of plant origin food.

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
28 pesticides (8 classes)	Fruit, vegetables	Acetone/dichloromethane (3:1, v/v)	110/1500 psi	Static cycles 2	SPE	GC–FPD	>70%; LOQ 0.0019–0.14 μg/g	[109]
130 multiclass pesticides	Fruits, vegetables	Ethyl acetate	70/10.34 MPa	Static time 3 min Static cycles 2	GPC	GC–MS/MS	70–120%; LOQ 0.01 mg/kg	[110]
405 pesticide residues	Grain	ACN	80/1500 psi	Static time 3 min Static cycles 2	SPE	GC–MS LC–MS–MS	60–120%; LOD 0.5–300 μg/kg	[111]
12 organochlorine pesticides; 29 pesticides and herbicides	Potato, banana; wheat grains	n-Hexane/10% acetone or ACN	100/–	Static time 5 min Static cycles 1–2		GC–ECD		[113]
Organochlorine residues	Fruits, vegetables	n-Hexane/acetone (1:10, v/v)	100/10 MPa	Static time 5 min Static cycles 2		CGC–ECD	85.7–108.5%; 1.1–20 μg/kg	[114]
Organochlorine, chlorobenzenes	Strawberries	Water/acetone (90:10, v/v)	120/–	Static time 10 min Static cycles 2	SPME or SBSE	GC–MS	42–132%;LOD 0.0005–0.3000 mg/kg	[115]
Organochlorine, chlorobenzenes	Fruit, vegetables	Water/acetone (90:10, v/v)	120/–	Static time 10 min Static cycles 2	SPME or SBSE	GC–MS		[116]
Hexachlorocyclon-hexanes (HCHs), DDX compounds, chlorobenzenes	Strawberries	Water/acetone (90:10, v/v)	120/10 MPa	Static time 10 min Static cycles 2	SPME or SBSE	GC–MS	LOD: 40 μg/kg for p, p N-DDT and p, p N-DDE; 1–10 μg/kg for the others	[117]
20 organochlorine pesticides	Vegetables	n-Hexane/acetone (50:50, v/v)	110/10 MPa	Static time 5 min Static cycles 1	SPE	GC–MS	About 1005%; LOQ 1.2–5.5 ng/g	[118]
14 organochlorine pesticides	Cereal crops	n-Hexane/acetone (1:1, v/v)	110/1500psi	Static time 5 min Static cycles 2	SPE	GC–ECD	78–116%; LOQ 4.6–12.5 μg/kg	[119]
19 organophosphorus pesticides	Flour, grapefruit, orange juice	Cyclohexane/acetone (1:1, v/v)	100/1500 psi	Static time 5 min Static cycles 1	GPC	GC–FPD	83–115% for most analytes	[120]
26 organophosphorus pesticides	Apple, carrot puree	EtAC/cyclohexane or DCM/acetone	100/–	Static time 5 min Static cycles 1–2	GPC	GC–FPD		[121]
26 organophosphorus pesticides	Carrot, apple baby foods	Ethyl acetate/cyclohexane	100/10 MPa		GPC	GC	91–89.7%	[122]
Organophosphorous insecticides	Polished, cookedrice	Acetone	Ambient temperature/1500 psi	Static time 3 min Static cycles 3	D-SPE	GC–FTD	73–124%; LOQ 77.6 ng/mL for polished rice, 2.6–18.6 ng/mL for cooked rice	[123]
58 pesticides	Tomatoes	ACN	60/2000 psi	Static time 2 min Static cycles 1		GC–ITD	>80%	[124]
7 carbamates	Fruit, vegetables	Water	50/–	Dynamic mode at 1 mL/min[1]		LC–MS	84–110%; LOQ 2–10 ppb	[125]
Diazinon, isoprothiolane and EPN	Polished rice (*Oryza sativa* L.)	Acetone/n-hexane (25:75, v/v)	100/1500 atm	Static time 5 min Static cycles 2		LC–MS	82.7–126.4%; LOQ 0.04–0.08 ppm	[126]
Benzoylurea insecticides	Food, lettuce, avocado, lemon,	Ethyl acetate	80/1500 psi	Static time 5 min Static cycles 2		LC–MS/MS	58–97%; LOQ 0.002–0.01 mg/kg	[127]
6 pesticides:	Grapes skin	Water	120/–	Dynamic at 1.0 mL/min for 40 min	Microporous membrane	GC–MS	LOQ 0.3–1.8 μg/kg	[128]
N-methyl-carbamates (namely, oxamyl, dioxacarb, metholcarb, carbofuran and carbaryl)	Fruits, vegetables	Water	75/15 bar	Static extraction time 20 min	SPE	HPLC–FLD	80–104%; LOQ 0.5 mg/kg	[129]
17 *N*-methylcarbamate pesticides	Banana, green beans, broccoli, melon, carrot	DCM/acetone (1:1, v/v)	100/2000 psi	Static time 5 min	SPE	HPLC–FLD	70–100%	[130]

Table 2 (*Continued*)

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
8 acetanilide herbicides	Cereal crops	n-Hexane/acetone (1:1, v/v)	110/1500 psi	Static time 5 min Static cycles 2	SPE	GC–ECD	82.3–115.8%; LOQ <12.5 µg/kg	[131]
Herbicides (chlormequat and mepiqua)	Wheat flours, flour-based baby foods	Water	120/100 atm	Static time 5 min Static cycles 3		LC–MS/MS	83–99%; LOD 0.1 ppb	[132]
16 polycyclic aromatic hydrocarbons	Tea	n-Hexane	100/100 bar	Static time 5 min Static cycles 2	SPE	GC–HRMS	LOQ 0.03 – 0.09 µg/kg	[133]
14 polycyclic aromatic hydrocarbons	Plant matrices	n-Hexane	40, 120/–	Static time 3 min Static cycles 10	GPC	GC–MS	LOD 10 – 50 pg/g	[134]
Polyphenols	Peel, pulp of 15 Basque cider apple varieties	MeOH	40/1000 psi	Static time 5 min Static cycles 2		RP–HPLC–DAD		[135]
Organotin compounds, tributyltin, triphenyltin, tri-cyclohexyltin, trioctyltin	Vegetable	MeOH/ethyl acetate	100/100 bars	Several 3 min	Ethylation with NaBEt4	GC–PFPD	About100% for TBT; LOD 1–2 ng (Sn)/g	[136]
Seven banned azo-dyes	Chilli, hot chilli food	Acetone	95/1000 psi	Static time 5 min Static cycles 2	GPC	LC–MS/MS	94–105%; LOQ 0.006–0.036 ng/g	[137]
Zearalenone	Wheat, corn	MeOH/ACN (1:1, v/v)	80/–	Static time 5 min Static cycles 2		LC–MS	93–103%	[138]
Ochratoxin A	Rice	MeOH	40/1500 psi	Static time 5 min Static cycles 1		LC–FLD	94.0%	[139]
Zearalenone	Wheat, corn	MeOH/ACN	80/–	Static time 5 min Static cycles 2		LC–MS	118%; LOQ 15 ng/g	[140]
Zearalenone	Corn	MeOH/ACN	80/–	Static time 5 min Static cycles 2		LC–MS	101.4%; LOQ 15 ng/g	[141]
Zearalenone	Flour, corn, bread, pasta	CAN/water (85:15, v/v)	40/–	Static time 20 min Static cycles 3	IAC	HPLC–FLD	1 ng/g	[142]
Zearalenone	Corn	Water/isopropanol	80/–	Static time 5 min Static cycles 2		LC–MS	Above 100%	[143]
Deoxynivalenol, fumonisin B1, zearalenone	Maize, wheat	PBS then with MeOH/water (80:20, v/v)	40/–		SPE	LC–MS/MS	>79%; LOD 0.3–4.2 mg/kg	[144]
Zearalenone, α-zearalenol	Wheat, corn, rye, barley, rice, swine feed	MeOH/ACN (50:50, v/v)	50/1500 psi	Static time 5 min Static cycles 1		LC–FLD	98.4% for α-ZOL, 96% for ZON;6 ng/g for ZON, 3 ng/g for α-ZOL	[145]
Carotenoid food additives	Matrices beverages, pudding mixes, breakfast cereals, cookies, sausage	MeOH/ethyl acetate/light petroleum (1:1:1, v/v/v)	40/70 bar	Static time 2 min Static cycles 3		LC–DAD LC–MS	91.0–99.6%; LOQ 0.53–0.79 mg/L	[146]
Deoxynivalenol (DON), fumonisin B1 (FB1), zearalenone (ZEN)	Maize	ACN/water (75/25, v/v)	40/2000 psi		SPE	LC–MS/MS	l70% for DON, 40% for FB1, ZEN; LOQs: 10–50 mg/kg	[144]
Trans-resveratrol	Grapes	Water then with MeOH	40/40 atm 150/40 atm	Water:3 cycles of 5 min, and then MeOH: 3 cycles of 5 min.	SPE	HPLC–UV	104.2 ± 4.5% (50 °C), 106.6 ± 4.3% (100 °C) and 99.5 ± 5.7% (150 °C; LOQ 0.004 mg/L	[147]
Monacolin K	Red yeast rice	Ethyl acetate	120/1500 psi	Static time 7 min Static cycles 3		HSCCC, UV, ESI-MS and ^{1}H NMR.		[148]
Isoflavones	Soy farina, soy meat granulate, soy meat laminae, soy meat bits, Protmix and EKO-B1	90% aqueous MeOH	145/–	Static time 5 min Static cycles 1		LC–MS	103–106%; LOD 1.2/1.6 fmol for daidzin/genistin	[149]

Table 2 (*Continued*)

Analytes	Matrix	ASE conditions			Cleanup	Final method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
Cholesterol	Solid food	Water	135/20 bar	Flow-rate 3.0 mL/min and 5 min of static extraction	SPE	UV	85.71%	[150]
6-Gingerol 8-gingerol 10-gingerol 6-shogaol	Ginger (*Zingiber officinale* Roscoe)	70% ethanolaqueous solution	100/1500 psi	Static time 5 min Static cycles 2		HPLC–MS/MS	106.8–109.3%	[151]
Fat, oil	Bread, derivatives products	n-Hexane/isopropanol (3:2, v/v)	175/1500 psi	Static time 5 min Static cycles 1		Gravimetrics	LOQ 2 g/100 g dry weight	[152]
Oil content	Oilseeds	Petroleum benzene	105/6.67 MPa	Static time 10 min Static cycles 4		Standard method B-I 5		[153]
Polar and nonpolar lipids	Corn, oats	N-hexane, methylene chloride	40 or 100/1000 psi	Static time 10 min Static cycles 3		HPLC–DAD		[154]
Total sugars, proteins	Defatted rice bran	Subcritical water	200/–			Anti-oxidant study		[155]
Isoflavones	Soybeans	EtOH/H_2O/DMSO (70:25:5, v/v/v)	100/1000 psi			HPLC		[156]
Lignans, proteins and carbohydrates	Defatted flaxseed meal	Water	130, 160, 190/750 psi	Dynamic		HPLC		[157]
Flavonoids	Knotwood of aspen	Water	150/220 bar			GC–FID, GC–MS		[158]
Catechins, proanthocyanidins	Grape seed	75% MeOH	150/1500 psi			HPLC	70%	[159]
Capsaicin, dihydrocapsaicin	Peppers	MeOH	50–200/100 atm	Static time 5 min Static cycles 1		LC–MS	≤100%	[160]
Anthocyanins, phenolics	Dried red grape skin	Water	100–160/–			HPLC		[161]
Catechin, epicatechin	Tea leaves, grape seeds	MeOH	130/100 atm	Static time 10 min		HPLC	Below 95%	[162]
Isoflavones	Defatted soybean flakes	Water	110/641 psi		SPE	HPLC	49.0%	[163]
Fumonisins B1 and B2	Corn, rice	Ethanol/water (30:70, v/v)	80/–	Static time 10 min	SPE	LC–FLD		[164]
Total phenolic content	Citrus pomaces	Water	200/1.4 MPa			Anti-oxidant study		[165]

Note: D-SPE – dispersive-solid phase extraction and SBSE – stir bar sorptive extraction. Other abbreviations and acronyms are same with those in Table 1.

10%. A multi-residue method has been developed and validated for the simultaneous quantification and confirmation of around 130 multi-class residues including insecticides, herbicides, fungicides and acaricides in orange, nectarine and spinach samples by ASE–GC–MS/MS with a triple quadrupole analyzer [110]. To improve accurate quantification the authors used three isotopically labeled standards as surrogates. The selection of two SRM transitions, one for quantification and one for confirmation, gave excellent selectivity, sensitivity and the possibility of safe identification, using *Q*/*q* intensity ratio as a confirmatory parameter. Although the use of labeled I.S. helped to minimize matrix effects for some pesticide/matrix combinations, matrix-matched standard calibration was required in order to perform a correct quantification in samples. A new multi-residue method has been established for simultaneous determination of 405 pesticide residues in grain, using ASE, SPE, and GC–MS and LC–MS/MS [111]. The method was based on appraisal of the GC–MS and LC–MS–MS characteristics of 660 pesticides, their efficiency of extraction from grain, and their purification. For the 362 pesticides determined by GC–MS, half of the extracts were cleaned with an Envi-18 cartridge and then further cleaned up with Envi-Carb and Sep-Pak NH_2 cartridges in series. For the 43 pesticides determined by LC–MS/MS the other half of the extracts were cleaned with Sep-Pak Alumina N cartridge and further cleaned with Envi-Carb and Sep-Pak NH_2 cartridges. After evaporation to dryness the eluates were diluted with acetonitrile–water, 3:2, and used for analysis. The proposed method is suitable for the determination of 405 pesticide residues in grain such as maize, wheat, oat, rice, and barley.

Brown rice powder certified reference material, NMIJ CRM 7504-a, for the analysis of pesticide residues was developed. Brown rice sample was harvested to contain the pesticides such as etofenprox and fenitrothion. The certification was carried out using ASE–isotope dilution mass spectrometry [112].

4.1.2. Organochlorine pesticides

By using ASE technique several methods have reported for the determination of organochlorine pesticide residues in foods of plant origin by GC [113,114] or GC–MS [115,116]. An analytical scheme for the determination of several OCPs like hexachlorocyclon-hexanes, DDX and chlorobenzenes in strawberries has been developed by ASE–GC–MS with solid-phase micro extraction (SPME) or stir bar sorptive extraction (SBSE) cleanup [117]. Using SPME, LODs were 40 μg/kg for p, p N-DDT and p, p N-DDE, and 1–10 μg/kg for the others. Using SBSE, the LOD of these compounds could be improved A GC–ECD method with ASE and SPE cleanup to determine OCPs in horticultural samples (lettuce, tomato, spinach, potato, turnip leaf and green bean) was described [118]. The methods provide simple and rapid procedures for the determination of pesticides in vegetables with good reproducibility and low quantification limits (1.2–5.5 ng/g), in the requirements of European Union Legislation. A procedure based on ASE with n-hexane/acetone and SPE clean up on graphitized carbon black/primary–secondary amine has been developed for analysis of 14 OCPs in cereals by GC–ECD with high extraction efficiency, satisfactory recovery, and clean chromatograms [119].

4.1.3. Organophosphorus pesticides

Residual organophosphorus pesticides (OPPs) in foods were determined by ASE, GPC and GC–FPD [120]. Pesticides were extracted at 100 °C under 1500 psi pressure in less than 20 min. Wet samples were extracted after mixing with Extrelut drying agent. Four foods were spiked with 19 pesticides at 0.1 ppm or less. The average recoveries of these pesticides were 80–90% with RSD < 10%. However for both methamidophos and acephate, recoveries and precision were low, i.e., 37–50%, 6–40%, respectively. This ASE method has been used for extraction of 26 OPPs from apple and carrot puree with EtAC–cyclohexane or DCM–acetone [121].

ASE operated at 100 °C and 10 MPa with ethyl acetate/cyclonhexane as solvent was used for the extraction of OPPs from large sizes sample (30 g) of carrot and apple baby foods. The extracts were cleaned up by GPC before GC determination of 26 OPPs with FPD. Recoveries were 91 and 89.7% from apple and carrot, respectively, RSDs were 11.8% (n = 12) and 8.7% (n = 12), respectively [122]. Quick, simple and efficient multi-residue analytical method was developed and validated for the determination of organophosphorous insecticides from polished and cooked rice [123]. Polished rice was extracted using ASE with dichloromethane. Cooked rice was extracted with acetone and cleaned up using dispersive-solid phase extraction (D-SPE) technique. The total uncertainty was evaluated, taking four main independent sources viz., weighing and purity of the standard, GC calibration curve and repeatability under consideration. The expanded uncertainty was found to be in the range of 5–20%.

4.1.4. Other pesticides

A fibrous cellulose powder (CF-1) was used as a drying agent for ASE. Of fifty-eight diverse pesticides, recoveries >80% were achieved for nearly all pesticides [124]. An analytical method for determining seven largely used carbamate insecticides in tomato, spinach, lettuce, zucchini, pear, and apple was presented. This simple, specific, and rapid method is based on the MSPD technique, with heated water as extractant followed by LC–MS equipped with a single quadrupole and an electrospray ion source [125]. The residue of two insecticides (diazinon and EPN) and one fungicide (isoprothiolane) in polished rice was determined simultaneously by an ASE–GC–ECD method. The optimized procedure has been applied for the determination of diazinon, isoprothiolane and EPN in real rice samples. This method was confirmed by GC–MS [126].

Benzoylureas (BUs) constitute an important group of pesticides with herbicide, insecticide, or acaricide activity that act as insect growth regulators. A method based on pressurized liquid extraction and LC–MS/MS has been developed for determining nine BUs in fruit, vegetable, cereals, and animal products [127]. LOQs (0.002–0.01 mg/kg) are equal or lower than maximum residue limits established by the Codex Alimentarius. Validation of the total method was performed by analyzing in quintuplicate seven different commodities. This study provides a sensitive and selective method for the determination of BUs in food.

The residue of procymidone and tetradifon pesticides in green grapes was analyzed using pressurized hot water extraction–microporous membrane liquid–liquid extraction and GC–MS [128]. Procymidone and tetradifon were found in the skins of the grapes. The results were in good agreement with those obtained by liquid–solid and ultrasonic extractions. The method could suitably be applied to the determination of pesticides in other plant material.

A combination of static–dynamic modes of pressurized hot water extraction has been used for the extraction of N-methylcarbamates from different fruits and vegetables [129]. The selection of water as leaching agent provides a clean approach which avoids the use of organic solvents. The use of water as leaching agent at a relatively low temperature (75 °C) and in a combination of static–dynamic extraction modes provides a clean alternative for the extraction of N-methylcarbamate pesticides without degradation of the compounds. Lower concentrations than 0.5 mg/kg can be determined using the proposed method, thus, allowing determination levels of the pesticides lower than those required by the Food and Agriculture Organization (FAO) of the United Nations.

Residual N-methylcarbamate pesticides in food were determined by ASE and HPLC with post-column fluorescence [130]. Pesticides were extracted with acetonitrile at 100 °C under 2000 psi

pressure in less than 20 min. Extracts were cleaned-up with a carboxylic acid mini-column eluted with 10% or 30% acetone in n-hexane. Eight foods were spiked with 17 pesticides at 0.2 ppm. The average recoveries of these pesticides were 70–100% and the RSDs were <10%. These results suggested that ASE can be used to extract residues of N-methylcarbamate pesticides in foods.

4.2. Herbicides

Acetanilide herbicides are the most commonly used herbicides, mainly used in corn, soybean and many other cereal crops which are staple foods of some countries. Eight acetanilide herbicides from cereal crops were analyzed based on ASE and SPE followed by GC–ECD [131]. After extraction with ASE, four SPE tubes were assayed for comparison to obtain the best clean up efficiency. The results show that graphitic carbon black/primary secondary amine cartridge gave the best recoveries and cleanest chromatograms. The proposed analytical methodology was applied for the analysis of the targets in samples; only three herbicides, propyzamid, metolachlor and diflufenican, were detected in two samples. It was demonstrated that the developed method is suitable for the analysis of acetanilide herbicides in cereal products. Marchese et al. [132] developed a new ASE–LC–ESI-MS/MS method for the rapid extraction and unequivocal confirmation of herbicides chlormequat and mepiquat in wheat flours and various flours utilized in infant foods. Typical recoveries from flours and baby food samples ranged from 83% to 99% with RSD less than 10% at a fortification level of 10 ppb, corresponding to the maximum residue limits established by the European Union. Applying the method traces of the selected herbicides have been detected in about 50% of baby foods. Of specific interest is the class of weed herbicides known as triazine pesticides, atrazine is the most widely used of all the triazines. Curren et al. [60] have developed a novel extraction method that utilizes ethanol-modified subcritical water in combination with SPME for the removal of atrazine from beef kidney. The total time of analysis for a single kidney sample is 90 min. The average recoveries from samples spiked with 2 and 0.2 μg/g were 104 and 111%, with the average RSD of 10% and 9%, respectively. The method limit of detection for beef kidney spiked with atrazine was found to be 20 ng/g.

4.3. Other organic contaminations

For the analysis of the 16 PAHs, the sample preparation included ASE and the highly automated clean up steps, GPC and SPE [133]. The LOQ (0.03–0.06 μg/kg) was determined. The repeatability (RSD, $n = 3$) of different PAHs in fruit tea ranged from 0.1% to 11%. It was observed that the total contents of the 16 PAHs in tea samples ranged from 14 to 2662 μg/kg.

Polyphenols in the peel and pulp of 15 Basque cider apple varieties were determined by ASE followed by RP–HPLC–DAD [135]. It was observed that the polyphenolic composition in apple peel depended on varieties, whereas the main classes of phenolic compounds in apple pulp were flavan-3-ols and hydroxycinnamic acids in all cases, representing both together between 86% and 95% of total polyphenols assayed.

Organotin compounds (OTC) are widely used in many fields of activity. They have become a ubiquitous environmental presence. The presence of organotins in the environment impacts upon food safety, making it important to monitor the levels of organotin pesticides in fruits and vegetables. Nevertheless, only a few studies have been published on organotin speciation in plants. Marcic et al. [136] described an ASE–GC analysis procedure for the extraction of four trisubstituted organotins: tributyltin (TBT), triphenyltin (TPhT), tricyclohexyltin (TcHexT) and trioctyltin (TOcT) from vegetable samples. Ethylation was carried out using $NaBEt_4$. The optimized ASE allowed LOD to 1–2 ng (Sn)/g to be reached. Comparison with usually employed solid/liquid extraction (SLE) confirms that ASE is an interesting tool for vegetable analysis.

An automated, confirmatory and sensitive procedure has been developed and validated for the determination of 7 banned Sudan (I–IV), Sudan Orange G, Sudan Red 7B and Para Red in hot chilli food samples based on ASE with acetone and GPC followed by LC–ESI(+)-MS/MS [137]. Linear calibrations were obtained with correlation coefficients $R^2 > 0.999$. The LOQ was in the ranges of 0.006–0.036 ng/g. The method has applied to the determination of azo-dyes in 46 spice samples.

4.4. Natural toxins

The contamination of cereal crops by naturally occurring mycotoxins caused by moulds is a common phenomenon. The determination of mycotoxins in food and feeds is of general interest because of their different toxic effects on humans and animals. Among such compounds, zearalenone (ZON) is a non-steroidal estrogenic mycotoxin that is stable even at high temperatures and that has been detected in certain cereal-based foods and feedstuffs. Thus, the extraction and determination of this compound have been addressed by several authors. CAN–water, MeOH–water and ACN/MeOH are the three mixtures most commonly used in the extraction of ZON from cereals by other extraction techniques, such as conventional liquid shaking or MAE. Thus, they are also the mixtures most used in ASE as extraction solvents.

Pallaroni et al. [138] investigated the possibility of using ASE as extraction technique for zearalenone (ZON). Afterward, ASE with different solvents has been used for the determination of ZON in many kinds of plant origin foodstuffs [139–145]. Pallaroni and von Holst [140,141] have described the application of ASE to the analysis of ZON in corn and wheat by LC–MS without any additional clean up step. A statistical design approach was applied to optimize the ASE parameters. In the optimized procedure, a mixture of acetonitrile–methanol was selected as the extraction solvent, applying a temperature of 80 °C. Extraction recoveries of ZON of over 100% were obtained under these conditions. Recently, those authors have developed an alternative extraction method using a less toxic extraction solvent mixture 1% triethylamine (TEA) in water–isopropanol (1:1, v/v) instead of the ACN/MeOH (1:1, v/v) mixture [143]. ZON is almost insoluble in water but its solubility increases in alkaline aqueous solution. However, since ZON is not stable in alkaline conditions, those authors had to find a compromise and therefore tested various solvent mixtures. The mixture of 1% TEA in water–isopropanol (1:1, v/v) fulfilled these criteria. Urraca et al. [145] have developed a method for the determination of ZON and its metabolite (α-zearalenol) using LC with FID. Recoveries between 94% and 104% were obtained for these two compounds in all the matrices tested using a methanol–acetonitrile mixture as extraction solvent.

4.5. Bioactive and nutritional compounds

4.5.1. Carotenoid, ochratoxin A and mycotoxins

For the determination of the carotenoid food additives (CFA), Breithaupt [146] has developed a sensitive HPLC multi-method using an RP C30 column for analysis of norbixin, bixin, capsanthin, lutein, canthaxanthin, b-apo-80-carotenal, b-apo-80-carotenoic acid ethyl ester, b-carotene, and lycopene in processed food. For unequivocal identification, the mass spectra of all analytes were recorded using LC–APCI–MS. ASE was used for the first time to extract CFA from various food matrices. The presented ASE method can be used to monitor both, forbidden application of CFA or the compliance of food with legal limits.

ASE is applied for the extraction of ochratoxin A (OTA) from rice samples [108]. The total extraction time was 15 min. OTA was determined by LC–FLD and confirmed by methyl ester derivatization. The method was used to evaluate 12 rice samples, 1 of which was positive with an OTA content of 4.17 ng/g. The proposed method offers the possibility of a fast and simple process to obtain a quantitative extraction of OTA. Royer et al. [144] described a method for the simultaneous quantitative determination of deoxynivalenol (DON), fumonisin B1 (FB1) and zearalenone (ZEN) in maize by LC–APCI–MS/MS, using stable isotopically labeled and structural analogues internal standards. The procedure involves ASE followed by a tandem strong anion exchange and Mycosep SPE cartridges. Analytes confirmation and quantization were realized using LC–APCI–MS/MS in alternative positive/negative polarity switching mode. The analyses provided a high degree of selectivity and sensitivity, enabled LOQ for DON, FB1 and ZEN at 50, 50 and 10 μg/kg, respectively.

4.5.2. Trans-resveratrol and monacolin K

Trans-resveratrol is a natural compound present in many vegetables and in related foods. A study has been made of the extraction of trans-resveratrol from grapes using pressurized liquids, without the necessity of a cleaning stage [147]. This method enables trans-resveratrol to be determined extremely fast (in around 2 min) and simply, and with FID, an increase has been achieved in the analysis sensitivity by a factor of 250 times, compared with detection by UV–vis spectroscopy. Monacolin K is a cholesterol-lowering agent and is able to reduce the risk of colon cancer. Monacolin K from red yeast rice was extracted by ASE [148]. Under the optimum extraction conditions obtained by an orthogonal test design $L_9(3)^3$. The yield of ASE extract and monacolin K was 5.35% and 9.26 mg/g of dry red yeast rice, respectively. A separation and purification method of monacolin K was then established using HSCCC with a two-phase solvent system composed of n-hexane–ethyl acetate–methanol–water (8:2:5:5, v/v/v/v). From 300 mg of crude extract, 51.2 mg of monacolin K was obtained with the purity of 98.7%. The chemical structure of isolated compound was identified by UV, ESI-MS and ^{1}H NMR. It is demonstrated that the combination of ASE with HSCCC is an efficient method for the extraction, separation and purification of monacolin K from red rice yeast.

4.5.3. Isoflavones and cholesterol

It is well known that the impact of dietary isoflavones, daidzein and genistein, upon the health of adults and infants. An ASE procedure allowed more accurate (<2%) and precise (<5–8%rel.) HPLC–UV–MS determination of isoflavones in different kinds of food made from soybean food samples [149]. Final concentrations of daidzin in soybean foods fluctuated between 30 and 60 μg/g of dry matter (DM). Significantly higher concentrations of genistin (between 60 and 130 μg/g DM) were found in the soybean foods.

Cholesterol is the most important steroid alcohols among animal sterols, being the most abundant component of the cell membranes of the higher species of organisms and a precursor to a whole series of steroid hormones. Cholesterol is mainly found in all animal fats, so it is present in food from animal origin, such as eggs, meat, fish and dairy products.

A host of methods have been proposed for the removal of sterols from food samples including extraction with organic solvents, Soxhlet extraction, microwave-assisted saponification and CO_2–supercritical fluid extraction. Fernández-Pérez and de Castro [150] have developed a method based on superheated water extraction for the removal of cholesterol from solid food. The method was validated using a certified reference material (NIST–CRM1845) and was used to analyze food samples within a wide range of cholesterol concentrations.

4.5.4. Gingerol-related compounds

To develop an efficient green extraction approach for recovery of bioactive compounds from natural plants, recently, Hu et al. [151] examined the potential of ASE of ginger with bioethanol–water as solvents. The advantages of ASE over other extraction approaches, in addition to reduced time/solvent cost, the extract of ASE showed a distinct constituent profile from that of Soxhlet extraction, with significantly improved recovery of diarylheptanoids, etc.

An ASE method for extraction and quantification of total fat and oil in bread and derivatives products has been proposed [152]. ASE parameters were optimized using a formal methodology based on statistical experimental design. A mixture of n-hexane-isopropanol (3:2, v/v) was selected as solvent. The extraction method has been validated, and the expanded uncertainty for the analytical method has been calculated with a value of 4.1% and the LOQ is established to be 2 g/100 g dry weight. The investigation and assessment of the oil content of oilseeds are important criteria, especially for the oil milling trade. Standard methods for the determination of the oil content of oilseeds are very time consuming, with extraction periods of 4–8 h. Matthäus and Brüh [153] compared ASE, SFE, MAE, solid fluid vortex extraction and Soxtherm extraction for three different oilseeds. The results of the determination of the oil content under optimal conditions are comparable with the results of the German Fat Science Society (DGF) standard method B-I 5. There are no significant differences between the different methods. The content of tocopherols is dependent upon the extraction method and the type of oilseed. The highest content is obtained by SFE. The content of diglycerides and free fatty acids varied according to the oilseed.

ASE is a common method to extract compounds from food materials [154–165]. The stability of these compounds at elevated temperature and their extraction efficiencies compared with other methods of extraction were studied. The total sugar present in defatted rice bean was determined to be the highest using ASE with water at 200 °C [155]. The extraction of catechins and proanthocyanidins from dried grape seeds was found to be comparable to conventional extraction with 75% methanol [159]. Using ASE with water, five different capsaicinoids present in peppers were successfully isolated at 200 °C and quantified by HPLC before the extraction yield decreased at higher applied temperatures [160]. The feasibility of ASE with water as a green method to extract natural compounds from food materials was also validated with reference to other methods such as Soxhlet extraction, ultrasonic extraction and heating under reflux with pure or aqueous mixture of alcohols.

5. Application of ASE in analysis of feed

The conditions of ASE and final analytical methods for the determination of persistent halogenated hydrocarbons, antimicrobials and other contaminations in animal feed are summarized in Table 3.

5.1. Persistent halogenated hydrocarbons

ASE has been used for the extraction of OCPs from animal feeds [166]. Clean up of the extracts was performed by a two-step procedure including silica gel adsorption and GPC. Finally, the target compounds were analyzed by GC–MS. In addition, the complete analytical procedure was validated by parallel analysis of the certified reference material BCR 115. ASE and MAE provided significantly better extraction efficiency than Soxhlet extraction for the analysis of OCPs in animal feed [167]. Under the investigated operation conditions the ultrasonic extraction was not efficient, with the recoveries of target compounds being about 50% less than Soxhlet. The performances of ASE were validated by determination of

Table 3
Application of ASE in analysis of animal feed.

Analytes	Matrix	ASE conditions			Cleanup	Analysis method	Recovery; LOD/LOQ	Ref.
		Solvent	Tem (°C)/pres	Mode				
Organochlorine pesticides	Animal feed	n-Hexane/acetone (1:1, v/v)	100/1700 psi	Static time 5 min Static cycles 2	Silica gel adsorption then GPC	GC–MS	1.6–9.2 pg/μL	[166]
Antibacterial (lasalocid)	Feed	MeOH/0.3% acetic acid	80/10 MPa	Static time 5 min Static cycles 1		HPLC–UV	96–105%	[167]
Robenidine	Animal feeds: chicken, rabbit and chinchilla feeds	Methanol acidified using 1% (v/v) acetic acid	100/1500 psi	Static time 3 min Static cycles 3		HPLC–DAD HPLC–MS	85–95%; LOQ 0.1 mg/kg for DAD and 0.02 mg/kg for MS	[168]
Polychlorinated biphenyls	Fish meal and animal feed	n-Heptane	100/–	Static time 5 min Static cycles 2		GC–ECD	90–93	[31]
7 Polychlorinated biphenyls,	Fish meal and feed samples	Heptane	100/–	Static time 5 min Static cycles 2		GC–MS	89–103%	[68]
Chlorinated pesticides	Animal feed	n-Hexane/acetone (3:2, v/v)	100/–	Static time 9 min Static cycles 2	Adsortion + GPC	GC/MS	LOD 1.6–9.2 pg/μL	[169]
Chlorinated pesticides	Animal feed	DCM/hexane (3:1, v/v)	180/–	Static time 10 min Static cycles 3		HRGC/HRMS		[170]
Persistent halogenated hydrocarbons	Fish feeds containing fish oil and other alternative lipid sources	Dichloromethane/acetone (1:1, v/v)	100/2000 psi	Static time 5 min Static cycles 2	GPC	GC–ECD	63–144%	[171]
Antimicrobial feed additives	Animal feeding stuffs	65% acetone/water at pH 2.0	80/–	The initial heat cycle was 5 min, followed by two 5-min static cycles		Single–plate detection system	From 57 ± 1.5% for avoparcin to 96 ± 4% for virginiamycin	[172]
13 quinolones	Feeds	Metaphosphoric acid/ACN mixture at pH 2.6			SPE	LC–DAD	51–103%; LOQ 5 mg/kg	[173]
β-Lactams and sulfonamides	Animal feed	MeOH	55/1500 psi.	Static time 5 min Static cycles 3	SPE	LC–QLIT-MS/MS	71–115%; LOQ 0.25–13.32 ng/g	[174]
Selenocysteine, selenomethionine, selenoethionine, selenite (Se(IV)), and selenate (Se(VI))	Yeasts	Water/MeOH (1:1, v/v)	160/1600 psi	Static time 10 min Static cycles 1		HG–AFS	70% of the selenium present in the yeas; LODs 0.01–0.04 μg/g	[175]
Zearalenone (ZON) and α-zearalenol (α-ZOL)	Cereals and swine feed	MeOH/acetonitrile	50/1500 psi	Static time 5 min Static cycles 1		LC–FLD	98.4% for α-ZOL, 96% for ZON; LODs3–6 ng/g for ZON, 2–6 ng/g for α-ZOL	[145]
5 antibiotics (avoparcin, bacitracin, spiramycin, tylosin, virginiamycin)	Feed	Acetone/water (65:35, v/v) pH 2.0	80/–	Static time 5 min Static cycles 2		Microbial growth inhibition screening	78 ± 4.5–98.6 ± 5.3% for virginiamycin, 96 ± 4.0–94 ± 3.0% for tylosin, 94 ± 4.4% for whilst spiramycin	[176]

Note: Abbreviations and acronyms are same with those in Table 1.

the certified reference material BCR-115. The results were in good agreement with the certified values. A rapid and effective analytical procedure for the determination of robenidine in animal feeds was developed [168]. Robenidine was extracted from samples with acidified methanol using ASE. Extracts were dried and subjected to clean up with aluminium oxide. Robenidine was eluted with methanol and determined by HPLC using UV-DAD and MS detectors. Sulfuric acid impregnated silica can be used for the lipid free extraction of PCBs from fat containing food and feed matrices using ASE with n-pentane, n-hexane or heptane as extraction solvent [31]. ASE was utilized for the extraction of seven selected PCBs from a naturally contaminated fish meal and two feed samples fortified with a naturally contaminated fish oil sample. For the feed samples high extraction efficiencies were obtained at temperatures above 100 °C using heptane as extraction solvent [68]. Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofu-rans (PCDFs) and PCBs were extracted by ASE from animal feed samples and analyzed by HRGC–HRMS [169,170]. Recently, a multi-residue analytical method was developed for toxic persistent halogenated hydrocarbons including nine OCPs, twenty six PCBs and seven polybrominated diphenyl ethers in fish feeds with differing proportions of fish oils and alternative lipid sources by GC–ECD after ASE, GPC and sulfuric acid clean up. The GPC removed the majority of the neutral lipids and sulfuric acid treatment effectively destroyed the polar lipids [171].

5.2. Antimicrobials

ASE is a versatile technique suitable for the automated extraction of a range of antimicrobials from animal feedstuffs. Employing ASE with a single-plate detection system permits the rapid antimicrobial screening of animal feeding stuffs and allows the detection of the banned additives [172]. The feed samples were extracted with a metaphosphoric acid–acetonitrile mixture at pH 2.6 and automatically purified onto OASIS HLB cartridges. Thirteen quinolones from feeds were determined by LC with photodiode-array or FID [173]. Kantiani et al. [174] have described the development and validation of a sensitive and fast (30 min extraction time and 10 min chromatographic run) method for the detection of penicillins, cephalosporins and sulfonamides in animal feed using ASE and SPE procedures, followed by liquid chromatography–quadrupole-linear ion-trap mass spectrometry. The results showed 10 out of 18 analytes to be present in at least one sample and all 14 samples to contain at least one analyte. This method is capable of detecting the low concentrations that could result from failure to comply with the regulations or on-site contamination.

5.3. Other contaminations

The extraction of selenocysteine, selenomethionine, selenoethionine, selenite (Se(IV)) and selenate (Se(VI)) from spiked yeast was presented by ASE with 1:1 (v:v) H_2O:MeOH at 1600 psi and 160 °C. The authors pointed that the experimental conditions should be different for spiked and native yeast. The extracted selenium compounds were analyzed by LC–microwave-assisted digestion–hydride generation-atomic fluorescence spectrometry (HGAFS) [175]. Urraca et al. [145] have developed a method for the determination of zearalenone and its metabolite (α-zearalenol) in swine feed using LC with FID. Recoveries between 94% and 104% were obtained for these two compounds in all the matrices tested using amethanol–acetonitrile mixture as extraction solvent. The use of LC with FLD in combination with ASE allows the analysis for the selected analytes at the appropriate concentration in a broad variety of cereal samples and in swine feed.

6. Conclusion

Almost all papers have compared the performance of ASE with other extraction methods, such as Soxhlet extraction, MAE, and/or SFE. A most of test results have shown that ASE has the advantages of good recoveries, rapidity, adequate precision and less solvent use, but it has some disadvantages. ASE allows to reduce the extraction time, but many laboratories will not be able to purchase the equipment because of its high cost. Also, it is difficult to achieve selectivity in the ASE process. Although the extraction time of one sample using the ASE technique is short, the preparation of the extraction cells is time-consuming, tedious, and uses large volumes of solvents (e.g., for rinsing). Due to low selectivity of the process, the obtained extracts should be cleaned up and reconcentrated before the final analysis.

Various methods for determining different veterinary drugs, pesticides, natural toxins compounds as well as bioactive and nutritional compounds in animal origin foods, plant origin foods and feedstuffs have been developed. With some modifications, ASE with water as an extraction solvent could be scaled-up to extract high volume of desirable compounds. ASE as a fully automated technique could be useful especially for routine analyses of pollutants in food and feed. More research needs to be done in order make ASE more popular and useful. For food safety new methods still need to be developed to achieve lower LODs, to control and to quantify these contaminants and their main degradation products, and to identify new contaminants.

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