Review Article

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Extraction approaches for the isolation of some POPs from lipid-based environmental and food matrices: A review

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Abstract: This review examined various analytical approaches for extracting some persistent organic pollutants (POPs) from environmental and food matrices containing lipid components. The impact of the lipid component on the extraction of such hazardous chemicals from fatty matrices is well-known due to their lipophilicity. The analysis of the scientific literature revealed different approaches, typically characterized by the use of a solvent mixture that leads to the co-extraction of lipid components, followed by one or more laborious clean-up steps to remove the interferents from the matrix. Despite the differences in the approaches used, the observed recoveries are high, >80%. Additionally, it was found that the same technique could extract different contaminants from various matrices, resulting in a loss of selectivity of the method used. The uncertainties suggested in this review consider (i) the actual extraction of POPs with polar solvents (e.g., acetonitrile) from lipid component, for which POPs may have higher retention; (ii) the use of laborious, long cleaning steps (e.g., polar and non-polar adsorbent phases) could affect recoveries; (iii) the absence of studies investigating the concrete and constant distribution of POPs between extractive solvent/lipid component and solvent/adsorbent phase. Further, the recent application of eutectic solvents was discussed as a promising approach towards a green chemistry procedure.

Keywords: extraction, lipids, persistent organic pollutants, food, environment

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1 Introduction

The terms “Persistent Organic Pollutants” (i.e., POPs) include a wide range of organic contaminants present in the environmental ecosystems. They originate from several anthropogenic and natural sources, posing a global concern since the Second World War [1,2]. POPs could be classified into three groups: (i) POPs resulting from chemical synthesis for agricultural use (e.g., organochlorine pesticides [OCPs] such as aldrin, dieldrin, dichloro-diphenyl-tetrachloroethane); (ii) POPs synthesized by the industry for industrial applications (e.g., hexachlorobenzene, polychlorinated biphenyls [PCBs], perfluorinated compounds or brominated compounds [BFRs]); and (iii) POPs resulting from the incomplete combustion of organic matter (e.g., polycyclic aromatic hydrocarbons [PAHs] polychlorinated, dioxins/dibenzo-dioxins, polychlorinated furans/dibenzofurans) [3]. POPs have specific chemical characteristics that make them capable of exhibiting toxic effects, environmental persistence, and accumulability in fat-rich tissues (animal-derived foods, olive oil, leaves), causing biomagnification in the trophic level [2,4]. Due to their lipophilic nature, these pollutants are challenging to extract and further isolate from lipids in complex matrices. Indeed, during extraction, lipids can be co-extracted with POPs causing interferences and reduction of sensitivity and reproducibility of the analytical method [5]. Conversely, POPs are present in ultra-trace levels in food and environmental matrices, and their affinity with lipidic macromolecules may lead to underestimation of their concentration. Based on such assumption, the most relevant part for the determination of POPs is the extraction and purification of the sample. The extraction techniques used, so far, are generally time-consuming, and they use a significant number of organic solvents or, more frequently, mixtures of them. Based on the scientific literature, the extraction methods more frequently applied for fatty matrices are solid phase extraction (SPE) [6–8],

liquid–liquid extraction (LLE) [9,10], dispersive liquid–liquid micro-extraction (DLLME) [11], accelerated solvent extraction (ASE) [12], quick, easy, cheap effective, rugged, and safe (QuEChERS) extraction [13,14]. Frequently, the extraction techniques follow a pre-treatment step, which can involve a lipid separation [15] or saponification using an ethanolic solution [9,16]. Further, after the extraction, a cleaning-up is required because of the cloudy supernatant. For instance, several clean-up procedures have been proposed. More often, various adsorbent phases are used both in SPE cartridges [17] as well as in dispersion solid phase extraction (d-SPE) [18,19]. All the techniques discussed seem to yield high recovery rates for all investigated POPs in the food and environmental matrices studied.

This review aims to underline the differences between extraction techniques to clarify which are the most affordable and effective ones based on the matrix and the analyte of interest. From scientific literature, research studies emerged that some of the most common extraction approaches are suitable for different compounds and matrices. Therefore, in the reviewed methods, the discussion about the type of solvent, adsorbent phases, and the methodological approach is reiterated.

2 Methodology for the literature research

For the collection of scientific studies, Google Scholar and Scopus databases were used. The search was conducted using different combinations of the following search terms: POPs, PAHs, PCBs, BFRs, pesticides, extraction, extraction technique, milk, meat, olive oil, fish, and leaves. The studies that emerged were first analyzed by reading the titles and abstracts. Therefore, studies that matched the aim of the present review were read in the full-text. However, due to the significant number of studies available in the scientific literature, the most representative studies for each extraction approach were selected. Therefore, a comparison of the proposed extraction approaches was conducted.

3 Results

The results obtained from the present literature review are reported below. Precisely, each extraction approach for each POP was discussed in a dedicated section for each food and environmental matrix selected.

3.1 Extraction of PAHs from bovine and human milk

The extraction of PAHs from both human and bovine (commercial) milk has been found to require sample preparation prior to extraction. The chemical composition of bovine milk is highly complex; the main fat component is triacylglycerol (95%) [20]. Bovine milk contains 400 different fatty acids, where approximately 70% are saturated fatty acids, 11% are short-chain fatty acids, 25% are monounsaturated, and 2.3% are polyunsaturated [21]. Approximately 85% of fats (3.8–3.9 g·100 mL^{-1}) of human milk are saturated and monounsaturated fatty acids – the rest are polyunsaturated ones. The main fat component of human milk is triacylglycerol (98%) [22].

The complexity of the fat fraction in bovine (commercial) and human milk necessitates matrix preparation prior to extraction. Saponification of the sample has emerged as one of the most commonly employed approaches [16,23–27]. It has been carried out using both sodium hydroxide (NaOH) and potassium hydroxide (KOH) (Table S1). Saponification is a preliminary step in milk analysis targeting non-polar/medium-polar POPs. This process converts fats into sodium or potassium salts of fatty acids, aiding in the separation of POPs from lipids and enabling sample purification [28]. Following saponification, LLE is utilized with various solvent combinations, notably, *n*-hexane and dichloromethane (1:2) [24,25] and cyclohexane and *n*-hexane (1:1) [16]. Subsequently, clean-up procedures are performed, involving both filtration with polytetrafluorethylene filters (0.45 μm) and SPE using a silica gel (C18) and amino adsorbent phases [16,25,26]. However, it is worth noting that high percentage recoveries can also be achieved without clean-up [24], reporting percentage recoveries of 80–120% [25], 85–110% [24], 90–93% [26], and 40–130% [16]. More recent approaches involve the use of direct immersion solid-phase extraction (DI-SPME) following a pretreatment involving sample homogenization with water (H_2O), with recoveries between 73–94% and ~100% [29,30]. Such recoveries were obtained without any cleaning-up. The pre-treatment with saponification was also carried out in combination with treatment using Carrez I (potassium hexaferrocyanide) and Carrez II (zinc acetate). Extraction with DLLME without clean-up recovered between 88% and 100% [31]. The described techniques did not show significant differences in percentage recoveries; however, DI-SPME emerged as the fastest technique, achieving percentage recoveries >70%, bypassing both the pre-treatment phase (only H_2O addition) and any clean-up.

From a green chemistry perspective, a recent method has proposed the use of eutectic solvents for the extraction

of PAHs from commercial milk. Triglycerides hydrolyzed by alkalis into water-soluble glycerol and fatty acid salts can produce *in situ* deep eutectic solvent (DES) formation and DLLME. Therefore, the natural deep eutectic solvents from *in situ* hydrolyzed triglycerides in animal or vegetable food samples have successfully extracted PAHs (i.e., 70–89%) [32].

From the literature analysis, it emerged that conventional LLE for isolating PAHs from milk requires a clean-up step before instrumental qualitative and quantitative analysis. It is well known that traditional LLE involves the use of harmful organic solvents for the operator, long analysis times, and a considerable number of steps (at least three details like pre-treatment, extraction, and cleaning-up). Despite the modeling techniques applied to improve LLE, this extraction method still presents significant limitations. In particular, since the extraction relies on the relative ability of solutes to distribute themselves between immiscible (or only partially miscible) liquid phases in contact, the process sometimes leads to the formation of emulsions, particularly in the case of milk [33,34]. Furthermore, the formation of a cloudy supernatant could affect the extraction. For example, for milk, the formation of cloudy supernatants occurs when an extraction solvent with a polarity index greater than 5 (i.e., ethanol, 5.2) is used, where the fatty acids of milk are not soluble [35]. Theoretically, for effective extraction of PAHs, it is necessary to use a nonpolar or moderately nonpolar solvent. Scientific literature indicates that an efficient extraction is achieved using solvents/mixtures of solvents with a low polarity index (e.g., *n*-hexane, 0.0; dichloromethane, 3.1; cyclohexane, 0.2) (Table S1). The use of nonpolar or moderately nonpolar solvents to recover fatty acids from milk (post-saponification) is necessary based on the distribution of PAHs in milk (both human and commercial bovine). The less polar compounds (i.e., PAHs) are, in fact, primarily distributed in the fat component of the milk [36]. The use of solvents with a high polarity index (e.g., acetonitrile, 5.8; methanol, 5.1) for the recovery of analytes post-evaporation is common. This could be justified by the fact that, after evaporation of the extracting solvent, the solutes remain inside the container. The use of a solvent with a polarity index >5 might only promote the redissolution of the analytes, but not that of the fatty acids, thereby facilitating their chemical analysis. Therefore, LLE requires a considerable number of steps; faster extraction techniques, such as DI-SPME ensure satisfactory extraction efficiencies while reducing the number of steps and the volumes of organic solvent used. However, complex matrices could interfere with the absorption properties of coatings as well as time and temperatures required for the extraction [37]. From scientific studies considered in this review, it resulted that fiber coating mostly used was diethoxydiphenylsilane (PDMS). It has recently been reported that to avoid variations in the adsorption kinetics of PAHs from the PDMS fiber, the optimal extraction time and temperature were investigated considering the coefficient distribution of PAHs between milk and coating. At 85°C, the distribution coefficient favored the fiber, whereas the optimal extraction time was 10 min. This extraction approach would allow for percentage recoveries of 75–110% [37]. This is in contrast with what was previously reported; satisfactory percentage recoveries (73–100%) were reported using different experimental conditions (60 min at 55°C). In terms of green chemistry, the use of eutectic solvents should be encouraged. Compared to LLE, extraction using eutectic solvents requires the same number of steps, with necessary pre-treatment and clean-up of the solution. However, these techniques would ensure the reduction in the use of hazardous organic solvents, both for the environment and for the operator, while achieving a satisfactory recovery percentage.

3.1.1 Extraction of pesticides from bovine milk

Over the years, pesticide extraction has been optimized and summarized in Table S2. For instance, the use of solid phase micro-extraction (SPME) through the development of innovative fiber coatings was investigated. This extraction technique is very rapid and requires only brief sample preparation consisting of the addition of acetonitrile, agitation, and filtration [38]. Similarly, DI-SPME has achieved satisfactory recovery rates (82–112%) through the use of innovative multi-walled carbon nanotubes with minimal sample pre-treatment (sonication and centrifugation) [39]. The QuEChERS extraction was primarily conducted using acetonitrile. The acidification of acetonitrile has been investigated in several studies, as acetonitrile alone, due to its polarity, may not efficiently extract pesticides from fatty matrices. Acidification facilitates sample clean up and enhances the effective extraction of pesticides. Acetonitrile was generally combined with magnesium sulfate ($MgSO_4$). $MgSO_4$ is generally added to the acetonitrile extract as, due to its high-polarity level, water residual may be present [40]. Post-extraction, a clean-up step was conducted. This step was performed using both the hydrophilic-lipophilic balance Oasis sorbent phase and primary secondary amine (PSA) and Z-Sep (zirconium oxide coating on silica) mixture. The recovery rates obtained in both cases ranged from 30% to 131%, due to the selectivity of both adsorbent phases [41,42]. The concurrent use of PSA with Z-Sep should be underscored. PSA, as a weak anion exchanger, typically cannot retain pesticides but efficiently eliminates fats. Combining it with the

Z-Sep adsorbent phase ensures improved pesticide retention [40].

The QuEChERS technique is widely employed for pesticide extraction due to its versatility in extracting compounds with different polarities. However, what stands out is the use of acetonitrile in the extraction phase of pesticides from milk. Specifically, the use of acetonitrile could be functional for the extraction of more polar pesticides due to its high polarity index. The range of percentage recoveries when acetonitrile is used is indeed wide (35–131%). This hypothesis could be confirmed by the different percentage recoveries obtained for two pesticides with different polarity indices; for example, Lufenuron, a more polar pesticide due to the presence of amino and aromatic groups, showed a percentage recovery of 112% using acetonitrile, compared to Bitertanol, which was only extracted at 35% [42]. The use of a moderately polar solvent could likely optimize pesticide extraction; for instance, as demonstrated by Shamsipur et al. [43], the use of chlorobenzene reduced the range of percentage recoveries, with a more satisfactory lower limit (66–98%) [43].

3.1.2 Extraction of flame retardants (FRs) from bovine and human milk

The extraction of FRs from human milk was conducted using various approaches. A common point found among different studies is the use of formic acid in the pre-treatment phase. At higher concentrations (>70% v/v), formic acid solubilizes the casein protein of milk [44] and at 2% in acetonitrile induces protein precipitation, reducing the matrix effects in the chemical analysis [45]. Another common aspect among various approaches is the use of acetonitrile as the extraction solvent. The polarity of FRs is quite broad; however, polarity influences their behavior in the milk system and, consequently, during the extraction process. An investigation into the distribution of ß-HBCD FR in milk showed that 80% of it was distributed in the fat phase, while the remaining 20% was in the aqueous phase [46]. The use of acetonitrile for extraction lacks specific justification in the scientific literature; the studies reviewed do not specify or justify the choice of acetonitrile as the extracting solvent. A possible hypothesis is that acetonitrile's ability to reduce the percentage of milk fats extracted along with the target analytes could be a likely reason. Extraction performed by means of acetonitrile (5.8 as polarity index) yielded percentage recoveries between 75% and 125% [14,47], whereas ethanol, with a polarity index of 5.2, yielded recoveries ~60% [48]. Even though the high polarity of the solvents should have reduced the presence of interfering compounds (e.g., fats), post-extraction clean-up of the solution was necessary. As shown in Table S3, clean-up procedures were carried out using different approaches. Notably, the use of silica acidified with sulfuric acid (i.e., 98%) [49–51] stands out. Acidified silica helps reduce emulsifications that occur during extractions, thereby increasing extraction efficiencies [52]. The most interesting use of acidified silica for clean-up is post-extraction of FRs with an acetone:hexane mixture. Hexane, being relatively nonpolar, could facilitate the recovery of fats from milk. Clean-up with acidified silica allowed for recovery percentages ranging from 63% to 135% [51].

3.1.3 Extraction of PCBs from bovine and human milk

The technique to extract PCBs from milk varied relevantly among studies, as reported in Table S4. Among the different extraction techniques, head space solid phase micro-extraction (HS-SPME) represents an effective and simplified methodology, eliminating the need for complex clean-up steps and enhancing the accuracy of the analysis. The reliability of HS-SPME appears to be confirmed by satisfactory recovery percentages (75–122%) achieved [53,54]. HS-SPME for the extraction of PCBs involved the use of PDMS; however, studies have investigated alternative coatings for HS-SPME fibers. For example, Joshi et al. [54] synthesized and evaluated the use of an IL crosslinker coating ($[(DVBIM)_2C_{12}]_2[NTf2]$). In particular, this coating provides increased selectivity towards PCBs due to π–π interactions, which are attributed to the introduction of aromatic moieties to the IL monomer and IL crosslinker. However, unlike PDMS, the IL coating exhibited a wider range of recovery percentages, although higher (i.e., 131%), with a range of 69–131%, indicating greater variability in extraction efficiency [54]. HS-SPME relies on the partitioning of analytes between the matrix and the stationary phase. Therefore, to increase its extraction efficiency, analytes should exhibit greater affinity for the fiber coating than for the matrix. Salting out has been proposed to enhance extraction efficiency. The addition of salt to the medium reduces the solubility of analytes in the medium, thereby improving the extraction capacity of the fiber coating [55]. Indeed, the addition of sodium chloride (NaCl) in the study by Joshi et al. [54] resulted in higher recovery percentages (94–122%) compared to that of Llompart et al. [53] (75–102%), where pretreatment involved saponification with NaOH [53]. Soxhlet extraction has been successfully employed for the extraction of PCBs [15]. However, despite achieving optimal recovery percentages, Soxhlet extraction requires long extraction times (e.g., 20 h) as well as large volumes of extracting solvent [56]. Therefore, modern extraction techniques are strongly suggested compared to more traditional ones.

3.2 Extraction of PAHs from meat

The extraction of PAHs (Table S5) from various types of meat samples is performed using the QuEChERS method. Similar to milk, the most commonly used extracting solvent is acetonitrile [9,13,17,18,57]. In terms of fatty acid composition, meat is, on average, similar to milk, containing saturated fatty acids (i.e., palmitic acid, stearic acid), monounsaturated fatty acids (i.e., oleic acid), and polyunsaturated fatty acids (i.e., linoleic acid). The lipid content percentage in meat varies significantly depending on the type of cut (10–40%). Consequently, the difficulty of analytical extraction approaches is reasonably comparable. The literature review indicates the utilization of the QuEChERS method consistently without any pre-treatment of the sample, or, at most, simple grinding. This extraction approach invariably used acetonitrile as the extracting solvent and $MgSO_4$ during the clean-up phase to remove water likely present in the extract due to the high polarity of acetonitrile itself [40]. The high polarity of acetonitrile (polarity index 5.8) could theoretically reduce its efficiency in extracting PAHs from the lipid component of meat, to which these compounds are likely more closely associated [58]. Lai et al. [18] conducted the extraction using acidified acetonitrile, which appears to enhance the extraction efficiency of the target compounds [40]. The application of acidified acetonitrile using acetic acid narrowed the range of percentage recoveries, significantly increasing the lower limit (80.1% vs 63.6%, 68.5% with and without prior acidification of acetonitrile, respectively) [9,13,18].

For the clean-up phase of QuEChERS, various adsorbent phases were employed, details like EMR Lipid Tube, PSA, and C18, only C18, PSA, graphitized black carbon (GBC), Z-Sep, and PSA [9,13,17,18,57]. The best results were yielded using Z-Sep and PSA phases (72.5–110%); the simultaneous application of PSA with Z-Sep is, in fact, noteworthy. While PSA, functioning as a weak anion exchanger, typically cannot capture PAHs, it effectively removes fats. Its combination with the Z-Sep adsorbent phase (comprising zirconium oxide coating on silica) enhanced PAH retention [40]. Similar to the extraction approaches used for milk, pretreatments of the sample were considered necessary in the case of meat. The saponification of the lipid component with an ethanolic solution (1 $mol \cdot L^{-1}$ KOH) was performed [9,59]. Post-saponification, the sample is typically subjected to LLE using cyclohexane [9] or methanol [59]. Different approaches to the clean-up phase with C18 [9] and multiwalled carbon nanotube-magnetic nanoparticle (MWCNT-MNP) composite [59] have not shown significant differences in percentage recoveries (85.6–90.1% vs 81.3–96.7%). However, due to the nanometric size of MWCNTs, they possess high surface areas and short diffusion paths, which were expected to result in higher extraction capacities and efficiencies [60] compared to the more traditional C18 adsorbent phase.

3.2.1 Extraction of pesticides and PCBs from meat

From the analysis of scientific literature, various extraction approaches have emerged for isolating pesticides from meat samples (Table S6). The most traditional approach involves LLE using acetonitrile as the extraction solvent. The protocol entails the use of acetonitrile combined with $Mg\ SO_4$ to absorb the aqueous component, followed by cold clean-up through immersion in liquid nitrogen [19]. The cooling of the sample system – target analyte – solvent is based on the assumption that lowering the temperature leads to a change in the state of the fat in the solvent, resulting in a faster removal of the fat [19,61]. However, the discrepancy that arises is that the extraction is conducted directly on the fatty component. Therefore, the cooling of the sample system – target analyte – solvent should facilitate an initial and selective separation between the solvent, the matrix, and the target analytes. This way, the subsequent SPME clean-up phase would be improved and streamlined. Other approaches involve the traditional use of QuEChERS, with and without acidification of acetonitrile. Similar to PAHs, the use of acetic acid appears to increase the solvent extraction efficiency, with a significant reduction in the amplitude of the percentage recovery range, by increasing the lower limit (2–112% vs 81.6–116%) [17,62]. Traditional approaches involve direct extraction of the lipid component. The use of a mixture of polar/apolar solvents facilitates lipid dissolution and extraction of target analytes (as described in Section 3.1.2). The use of sulfuric acid in the clean-up phase reduces emulsion formation, increasing extraction yields [10].

However, in a Green Chemistry scenario, the use of eutectic solvents is strongly recommended. Similar to milk, the extraction of pesticides from meat has also been investigated using eutectic solvents associated with DLLME [63].

The extraction approaches described for pesticides are also valid for the extraction of PCBs (Table S7). The extraction with acidified acetonitrile was also employed for the extraction of PCBs, achieving recovery rates between 99.8% and 112% [62]. QuEChERS [17,64] followed by a clean-up with Z-Sep and PSA adsorbent phases [57] and a mixture of C18, PSA, and GBC [17,57,64] has been widely used. However, it has been found that different extraction solvents other than acetonitrile have also been used for the extraction of PCBs from meat. For instance, Ostadgholami et al. [57] used a

mixture of ethyl acetate, acetone, and isooctane (2:2:1). While acetone and ethyl acetate are polar molecules (polarity indices 5.1 and 4.3), isooctane is a non-polar hydrocarbon, miscible with the first two. This approach yielded to percentage recovery rate ranging within 81% and 116% [57]. The use of acetone alone in the QuEChERS method conducted by Kuzukiran and Filazi [64] achieved a high percentage of recoveries (95.7–102.0%), whereas lower recoveries were observed when acetonitrile was used as the extraction solvent (41–99%) [17]. These results, therefore, seem to suggest (as also reported in Section 3.1.2) that the use of a mixture of solvents with different polarities can make the extraction of the analytes under examination more efficient, reducing emulsion formation due to the use of more polar solvents.

Recent extraction approaches involve the use of a combination of poly (diallyldimethylammonium chloride) (PDDA) and MWCNTs. Specifically, PDDA enhances the dispersion of MWCNTs in polar solutions. This innovative clean-up system was employed after an acetonitrile extraction of PCBs from meat, achieving recovery rates between 93.4% and 102% [65]. The extraction of PCBs from the PDDA/MWCNTs was subsequently carried out using a mixture of nonpolar solvents (dichloromethane:*n*-hexane, 60:40). The use of a strongly nonpolar solvent mixture facilitates the re-dissolution of PCBs in the solvent mixture. A potential issue with the method concerns the initial extraction phase: Is the use of acetonitrile sufficient to separate the PCBs from the fatty components of the meat?

Advances in the use of eutectic solvents have also been made for meat. Ganneru et al. [11] suggest the extraction of PCBs using DLLME with thymol–camphor (1:1), slightly diluted in acetonitrile. The achieved recovery rates range from 80.5% to 94.5%. Further development and expansion of research in the field of eutectic solvents is strongly recommended.

3.2.2 Extraction of FRs from meat

The extraction of FRs from meat can be conducted through several methods. Table S8 shows some of the methods reported in scientific literature. A common point to the different methods reported is the use of a mix of polar/medium polar and apolar solvents such as acetonitrile:toluene [66], *n*-hexane:acetone [67–69], and *n*-hexane:dichloromethane [70,71]. The lyophilized sample is placed in contact with the solvent mixture for a solid–liquid extraction [70,71] in some cases assisted by ultrasound [66], ASE [67], or by the Soxhlet apparatus [68,69]. This extraction also determines the extraction of the lipid component, and for this, it requires one or more clean-up steps. The clean-up is carried out by passing the extract through a column packed with Florisil [66], alumina [70], or acidified silica [67,69,71], in some cases followed by sulfuric acid treatment [68] to remove lipid components and other co-extracts. These methods report recoveries ranging from 50% [70] to 130% [68].

However, recently, QuEChERS methods have been used as an effective method for the extraction of POPs in different food matrices [72]. In their work, Poma et al. [73] used acetonitrile as the solvent and QuE Z-Sep sorbent for d-SPE. After extraction, the samples were cleaned up and fractionated by loading the solution onto Florisil cartridges. Fractionation was achieved with 12 mL of *n*-hexane:dichloromethane (1:1) and 10 mL of ethyl acetate. The first fraction was discarded, while the second fraction was concentrated and reconstituted with a solvent mixture of 50 µL of iso-octane:toluene (9:1) and 50 µL of iso-octane:ethyl acetate (8:2). The sample was then stored at −20°C for 30 min to precipitate residual lipids before injection. The recoveries obtained ranged from 53% to 71% [73]. The presence of the sample and other chemicals used during the QuEChERS extraction, which occupies space within the extraction tube, resulting in a substantial portion of the extract remaining untransferred. This results in a reduction in the method's sensitivity [72]. Xu et al. [72] developed a novel method combining ultrasonication and vacuum-assisted extraction (UVAE), using elements of QuEChERS methods, but involving modification in the clean-up step for the analysis of various groups of FRs in lipid-rich foods. The homogenized and lyophilized sample was extracted using 5 mL of a 9:1 mixture of acetonitrile:toluene without the addition of $MgSO_4$ or other salts. Consequently, lower amounts of lipids were extracted using less solvent, while less time was consumed for solvent concentration. The addition of a small percentage of toluene was justified by the need to increase the recovery of highly brominated compounds. Regarding the clean-up, usually a d-SPE is performed using Z-SEP as sorbents, which proved to be more effective in the clean-up for many FRs and other organic pollutants. However, large quantities of these sorbents are required for samples with high lipid content. For this reason, authors fractionated the UVAE extract using Florisil cartridges with *n*-hexane (Fraction 1) and acetonitrile (Fraction 2). Fraction 1 allows the elution of polybrominated diphenyl ether (PBDE) and most EFRs but also of most lipids, so the clean-up was performed using 10% H_2SO_4. While Fraction 2 was cleaned-up with a d-SPE using Z-SEP and C18 for the removing of the remaining lipids. After the two fractions were combined (Fraction 3) and fractionated again with an advanced polymer stationary phase cartridge and eluted with *n*-hexane (Fraction 4) and *n*-hexane:dichloromethane (1:1) (Fraction 5), allowing the removal of all the interferents. This method efficiently removes lipids and

other interferences, achieving recoveries that vary between 66% and 135% and better sensitivity and selectivity for FRs compared to previously published methods [72].

3.3 Extraction of pesticides from olive oil

Olive oil is a complex matrix to be analyzed because of the relevant fatty acid composition (98–99%). The most prevalent lipids in olive oil are the monounsaturated fatty acids (oleic acid, 18:1, *n*-9), with percentages ranging from 56% to 84%, while the polyunsaturated fatty acid (linoleic acid, 18:2, *n*-6) found at percentages between 3% and 21% [74]. This matrix can be affected by POP contamination during the processing and production stages or through environmental exposure of olive trees to several compounds. Pesticides are the common chemicals applied for protecting olive trees from pests and disease. The residual fraction of pesticides remaining in the olive may persist and be released in the final product [75].

The evaluation of pesticides in olive oil represents a relevant issue because of their difficult separation from the high fat content. The affinity and solubility of some lipophilic pesticides (organochlorine, organophosphorus, and carbamates) for lipids can lead to the retention and adsorption in the oil during the production and extraction phases from the olive fruit. To avoid the matrix interferences affecting the analysis as well as the co-elution of several contaminants, a preliminary step of sample treatment is conducted. In most cases, olive oil is diluted, mixed, and homogenized with *n*-hexane solvent, which removes the high-molecular-mass fat from the sample (Table S9). However, the liquid/liquid partition using different solvent combinations (e.g., acetonitrile saturated with petroleum ether or *n*-hexane) can also be used as a purification stage before the gel permeation (GPC), matrix solid-phase dispersion (MSPD) or SPE [76–78]. GPC sample preparation shows good properties in removing the high molecular weight of fat components of oil (triglycerides) from the low molecular weight of pesticides [79]. The separation of pesticides occurs through the columns made from polymeric porous microspheres able to isolate the compounds according to their molecular weight and the pore size of porous material [76]. The procedure of SPE is an alternative to GPC because of its cheapness, convenience, and less solvent-consuming. In the case of fat-containing matrices, it is used in the clean-up step for the purification of the extracts previously separated.

For the selective retention of pesticide residues in olive oil, several types of SPE adsorbents are necessary to be tested. N-Alumina, Florisil, C18, and ENVI-Carb sorbents are used for the isolation of different classes of pesticides (organophosphate, triazine, pyrethroid, organochlorine, pyridine, triadiazine, and trifluoromethyl) [80]. Alumina can be particularly useful for the isolation of polar pesticides, whereas Florisil is suitable for the clean-up of extracts containing nonpolar pesticides [81]. The recoveries reported for these two sorbents are in the range from 36.3% to 69.3% and from 58.0% to 78.0% [80]. Clean-up through the ENVI-Carb cartridge showed the high performance in removing olive oil residues from the final extract; the highest mean recoveries from 96.4% to 105.3% confirm its greater selectivity in the fractionation of target pesticides from high molecular mass lipid [82]. Moreover, the use of aminopropyl sorbent together with a Florisil cartridge suggests the usefulness of MSPD to achieve a better removal of matrix interferences due to the additional “co-column” clean-up in a small volume of an appropriate solvent [77,78,83]. The QuEChERS method, developed for the extraction of pesticides from fruits and vegetables, has been also applied for the pesticide’s determination in fatty matrices such as olive and olive oil. The classic method involves the extraction with acetonitrile solvent followed by the purification of the extracts by d-SPE using PSA (effective in the removal of fatty acids), GBC (effective in the removal of chlorophyll), and C18 (effective for the removal of non-polar matrix components) sorbents can be modified using new alternative sorbents. It was observed that Z-Sep sorbents enhance the sample clean-up than traditional phases of QuEChERS, showing recoveries between 72% and 107% in combination with other sorbents tested [84]. The efficiency of pesticide extraction is attributed to the Z-Sep composition made with C18 and zirconium bound to silica; the first binds the fats by means of hydrophobic interaction, while the second acts as a Lewis acid, attracting the compounds with electron donating groups.

Furthermore, the enhanced matrix removal (EMR-Lipid) sorbents show high selectivity for lipid removal through the combination of size-exclusion and hydrophobic interactions providing better recoveries (70–113%) and lower RSD value (<10%) for most pesticides’ residues [84].

3.3.1 Extraction of PAHs from olive oil

The lipophilic properties of PAHs promote their high solubility and accumulation in the fat molecules of olive oil. The complex nature of this fatty matrix requires accurate extraction and purification stages before the analytical determination of PAH (Table S10). The SPE is the most widespread approach used for cleaning and extracting lipophilic compounds from fat. The use of silica phase

packed into SPE cartridge shows the highest capacity to retain triglycerides while retaining the analytes in a small volume of elution solvent. However, it can be used as a dual-layer cartridge containing two separated sorbents selected for their ability to retain various constituent of fat. For example, the SupercleanTM EZ-POP NP is an efficient dual-layer cartridge containing Florisil, which retains polar functional groups and a lower layer of Z-Sep and C18 sorbents, which retain electron donors' compounds (phospholipids, fatty acids, and mono- and diacylglycerol) by hydrophobic interaction [85].

Moreover, due to the complexity of separating PAHs from the oil, the partition coefficient should be carefully investigated. The high percentage recovery rate reported in the studies considered suggested that a simple separation of a wide range of PAHs from the fat matrix is obtained by combining polar and non-polar solvents. Specifically, high recoveries are observed for acetonitrile:acetone (6:4) (70–120%) [86,87] and *n*-hexane/dichloromethane mixture (70:30) (32–152%) [88].

The LLE approach combined with the SPE clean-up of the extracts also shows good properties for the PAE extraction from olive oil. The limits of these techniques related to the expensive use of solvents have been passed by means of the HS-SPME technique, which allows the extraction of volatile and semi-volatile PAHs in the recoveries range from 74% to 115% [89–91]. However, the matrix effects caused by the lipid portion of the sample could decrease the SPME efficiency, requiring the optimization of several parameters, such as the type of fiber coating, temperature, and time of extraction [92].

3.3.2 Extraction of PCBs from olive oil

The presence of PCBs in olive oil is due to the environmental exposure of olive trees to several anthropogenic pollutants. The lipophilic and non-polar character of PCBs facilitates their solubilization in the lipid part of oil, requiring accurate isolation of fat before their analysis (Table S11). The preparation of the olive oil sample is generally carried out by the dissolution and mixing of the sample with *n*-hexane solvent, which preliminary removes the lipid part of the matrix [93–95]. For the isolation of PCBs from the sample, a lot of extraction methodologies are reported. Specifically, the SPE approach is used for extraction and clean-up stages before the PCB determination. To ensure the efficiency of extraction, it can be done first partitioning of the analyte from fat through the passage of lipid extract into a mini-column (e.g., Extrelut-QE) before the clean-up with SPE sorbents [93]. Moreover, the extraction of PCBs can be conducted also by the digestion of olive samples. The use of KOH/ethanol solution aids in breaking down the organic matter and solubilizing the PCB from the portion they are bound to [96]. All the extraction techniques adopted are combined with a clean-up phase developed using columns packed with specific sorbents selected since their densities and ability to retain the interferences and to elute the analytes. Particularly, silica gel acidified with sulfuric acid, alumina, and C18 shows great capability to minimize the interferences, ensuring an accurate analysis of PCBs in olive samples [93–95].

3.3.3 Extraction of FRs from olive oil

Halogenated flame retardants (HFRs) such as dechlorane plus, brominated phthalates, and PBDEs can be added to different commercial foods to improve their fire resistance. Due to their lipophilic nature, they can easily solubilize in fatty matrices and persist inside at low trace levels. The analysis of FRs in olive oil is documented (Table S12). Scientific research reported only two studies on the determination of HFRs in food items, including virgin olive oil, which are carried out by the same research group. The extraction of analytes was conducted using different solvents combined in different volumes. In detail, the acetonitrile solvent added with 10% of toluene (9:1) was used to improve the extraction of the lipophilic and highly brominated compounds, followed by a two-step clean-up with Florisil and silica sorbent slightly acidified with sulfuric acid (to 5%, w/W) to avoid the degradation of TBPH [66]. The QuEChERS-based extraction with acetonitrile solvent showed good performances of separation and purification of phases, requiring the further addition of 10% formic acid and *n*-hexane to the extraction solvent to improve the recovery of TBBPS and HBCDs, respectively. The following d-SPE clean-up reported satisfactory results using C18 and EMR-Lipid sorbent. However, the carbon and silica acidified (44%, p/p) were also applied for the purification extracts of TBBPS and BFR analysis [71].

3.4 Extraction of PAHs from fish

Since most POPs are apolar, they preferentially dissolve in fat- and lipid-rich tissues. Therefore, their extraction often results in an extract rich in lipid co-extractives. Therefore, the high lipid content of certain fish species interferes with the detection and quantification of the POPs under examination [97]. The extraction procedure often entails the non-selective extraction of the lipids fraction, and consequently

of the present POPs, from the samples through a simple extraction with a combination of solvents, both non-polar and polar, or through hydrolysis/digestion. This is followed by diverse clean-up steps to remove the lipid component, which is crucial for minimizing interferences and ensuring the proper maintenance status of the equipment used for analysis. These clean-up steps may employ either destructive techniques (such as sulfuric acid treatment) or non-destructive methods (such as GPC or SPE employing various stationary phases). The polar phases most utilized in SPE include alumina, Florisil, silica, or their combinations [98].

The half-lives of PAHs in organisms, including fish, are relatively short because they can be rapidly metabolized and excreted. However, some studies use fish as bioindicators to assess the level of water pollution concerning PAHs [99]. In the extraction of PAHs from fish samples, lipid digestion can be performed as a preliminary step [100]. Recabarren-Villalón et al. [99] used methanol and KOH ($0.7\,mol{\cdot}L^{-1}$) for the digestion of the lipid components, and then a non-saponifiable fraction was extracted with *n*-hexane [99]. However, combining digestion with extraction in a single step reduces the time and handling of the samples, thereby lowering costs and the risk of errors while increasing sample throughput. In their study, Pena et al. [100] used 4 mL of methanolic KOH for the digestion of the lipids during the microwave-assisted extraction with *n*-hexane. The authors evaluated the required amounts of KOH and concluded that using an excess of alkali eliminates the need to assess the fat content in samples, providing satisfactory results across all types of samples tested [100]. As an alternative to digestion, Cloutier et al. [101] proposed a modification of the classical QuEChERS extraction method for the analysis of PAHs along with other POPs. Typically, QuEChERS extraction is performed, and after centrifugation, 50–67% of the extract is collected and subjected to clean-up. In their work, the authors fully collected the extract after centrifugation and subjected it to a second extraction. The second extract was then combined with the first one and further purified before instrumental analysis. Ethyl acetate was used as an extraction solvent that showed good recoveries, but high variability was observed. Regarding the salts, the commonly used $MgSO_4$ was replaced with sodium sulfate (Na_2SO_4), thereby preventing the exothermic reaction that could have resulted in the loss of some more volatile PAHs [101]. Chatterjee et al. [97], instead, utilized QuEChERS extraction methods, employing a based on a triple partition extraction method involving water, acetonitrile, and *n*-hexane. During method optimization, the authors explored the use of ethyl acetate as well, which demonstrated recoveries similar to those achieved with acetonitrile but exhibited a higher matrix effect. Consequently, acetonitrile was selected as the extraction solvent [97]. Following the extraction, further purification is required to avoid interferences. Among the various purification procedures developed, the most used are chromatographic columns filled with alumina and silica gel [99,101,102] or Florisil [100]. To remove co-extracted fatty acids, Chatterjee et al. [97] performed a d-SPE. The acetonitrile extract clean-up involved a two-step process: first using calcium chloride ($CaCl_2$), followed by another clean-up step with PSA, Florisil, and C18. Florisil and PSA, due to their basic surface, remove fatty acids, whereas C18 removes nonpolar lipid co-extractives. It has often been observed that these sorbents are more effective at removing co-extractives when used in combination rather than individually [97]. The recoveries related to PAHs reported by various studies range from 60% to 120% [97] (Table S13).

3.4.1 Extraction of PCB, BFRs, and pesticides from fish

Extracting PCBs, BFRs, and pesticides, particularly OCPs, from fatty fish tissues can be carried out using various methods (Tables S14–S16). Soxhlet [103–105], ultrasonic bath [106], and ASE [107] are the most reported extraction techniques in the literature. Soxhlet extraction is usually performed using acetone: *n*-hexane mixture [103,104] or *n*-hexane: dichloromethane mixture [105]. The use of a combination of solvents with different polarities can be explained by the fact that it could increase extraction efficiency. However, following the extraction, the removal of the lipid component is necessary, which is carried out using sulfuric acid [104] or columns packed with silica acidified with sulfuric acid [103,105]. Sulfuric acid is an effective and cost-effective agent for removing lipids, but it requires a lengthy process, and its residues in the final extract can potentially damage the gas chromatography columns [98]. Also, further clean-up is performed using Florisil column [104,105]. GPC has also been utilized and demonstrated as an efficient clean-up procedure, but, like other techniques, the addition of a second clean-up step has often been found to be necessary. For instance, GPC has been combined with SPE [101,105]. The recovery reported by the different studies for this extraction techniques ranges from 80.5% to 106.5% [105]. In ASE extraction, instead, the extraction cell is packed with a cellulose filter, and neutral silica is used as a fat retainer. This enables the extraction of analytes without additional clean-up using a chromatography column, allowing for recovery rates ranging from 90% to 105% [107]. Removal of lipids can also be achieved by freezing the extract to below −20°C and then quickly filtering it before the lipids dissolve. These techniques, known as freezing lipid filtration, relies on the

difference in melting point and solubility between the target organic substances and the co-extracts. It is a simple and cost-effective procedure, but the clean-up may not be complete, and furthermore, it is not optimal for processing a large number of samples [108]. Norli et al. [108] demonstrate a new and easy method to perform the freeze-out step. After a QuEChERS extraction, the supernatant was drawn into disposable syringes equipped with a polyethylene frit. These syringes were then placed into a freezing device and stored in a freezer at −24°C for 2 h. Subsequently, the contents of the syringes were transferred into the tube filled with calcium chloride, shaken, and centrifuged. The resulting supernatant was additionally cleaned-up pouring it into a new tube containing magnesium sulphate and PSA for the removing of fatty acids. Thanks to this two lipids removal step, up to 86% of lipids contents was removed and many samples was easily processed [108].

3.5 Extraction of POPs from leaves

The detection of POPs in leaf samples requires multistep strategies, including sample preparation, selective and sensitive extraction methods, and clean-up procedures for the removal of the waxes as completely possible. Concerning the sample preparation, among the methods reported in the literature for the analysis of all the classes of POPs, leaf shredding was mainly found [109–118]. The shredding is often followed or preceded by a lyophilization of the sample [109,110,112,113,118–121] to remove water. Other studies, however, do not perform any pre-treatment of the sample [122,123].

The commonly used analytical methods for the extraction and clean-up of PAHs, PCBs, pesticides, and BFRs in different leaf samples are summarized in Tables S17–S20. As can be seen from the tables, leaves of conifer species, such as pine needles, due to their evergreen nature, widespread distribution, and high lipid content, are the plant leaves most studied in the literature for determining different classes of POPs [124,125]. Mukhopadhyay et al. [114] provided a comparative analysis of different extraction methods, such as mechanical stirring, sonication, Soxhlet and microwave-assisted Soxhlet extraction (MASE), for the optimization of extraction factors (solvent and extraction time) for isolation of PAHs from *Murraya paniculata* leaves. Both the Soxhlet (272.07 ± 26.15 $\mu g \cdot g^{-1}$) and MASE (280.17 ± 15.46 $\mu g \cdot g^{-1}$) techniques yielded higher amounts of total PAHs compared to sonication (173.61 ± 13.02 $\mu g \cdot g^{-1}$) and mechanical stirring (122.06 ± 5.19 $\mu g \cdot g^{-1}$). Authors affirmed that in the Soxhlet method, achieving complete extraction of the desired PAHs was made possible through multiple siphoning cycles. This was facilitated by the solvent's enhanced ability to reach the active sites of the matrix more effectively at elevated temperatures. Moreover, the rapid rate of diffusion promoted the mass transfer of PAHs, consequently boosting the extraction efficiency. For those reasons, the method selected for real samples was Soxhlet extraction with 120 mL toluene for 6 h. The extraction ensured excellent selectivity, yielding the highest number and quantity of non-polar PAHs [114]. Similarly, Yang et al. [117] utilized three different extraction methods, ultrasonic extraction, Soxhlet extraction, and ASE using an *n*-hexane:dichloromethane mixture (1:1) to determine PAHs in plant leaves. Results illustrate no significant differences in extraction efficiencies of low-molecular-weight PAHs, such as naphthalene, due to its superior sealing performance, minimizing naphthalene loss during extraction. Considering its suitability for processing large batches of leaf samples simultaneously, ultrasonic extraction was chosen for their study [117]. Considering this, the analysis of the works found in the literature has shown that ultrasound-assisted extraction and ASE are the most used and rapid techniques for PAHs extraction.

Different solvents, such as acetonitrile [126], dichloromethane [110,116], acetone [118,127], toluene [114,119], and *n*-hexane [128], or a mixture of solvent such as dichloromethane:*n*-hexane [111,113,117,120,121,129], dichloromethane:acetone [122], dichloromethane:petroleum ether [115,123], *n*-hexane:acetone [112], and acetone:acetonitrile [109], are used for the extraction of PAHs from the leave samples. Solvent extraction operates on the fundamental principle of "like dissolves like" (the law of similarity and miscibility), which suggests that a solute dissolves more effectively in a solvent with a closely matched polarity. The plant cell membrane is composed of non-polar lipid tails that restrict the transmembrane permeation of polar molecules to a certain extent, thereby hindering the diffusion pathway through the plasma membrane for the extraction of PAHs. This indicates that non-polar solvents are more effective for the extraction of PAHs from leaf samples [114]. For the clean-up procedure, different approached were used among the different. Extract clean-up is usually performed by column chromatography or SPE cartridges with different sorbents such as silica [110,112,114,118,123], alumina [111,120,121,129], or both [113,117,127]. This sorbent exhibits apolar behavior, effectively retaining the lipid fraction during elution with low-polarity organic solvents. This implies that these sorbents are best suited for apolar analytes, as more polar analytes are likely to co-elute with the lipid fraction [128]. In some cases, SPE is followed by GPC [110,128,129]. These double-cleaning show the best removal of the fatty components (lipids and waxes) from the leaves [128]. Clearly,

as the number of steps increases, so does the complexity of the operation, and the likelihood of analyte loss rises significantly. The recovery reported in the different studies varied between 40% [122] and 120% [113] for PAHs, 52% [115] and 108% [127] for PCBs, and 52–117% [113] for pesticides and 50% [110] and 113% [127] for PBDEs and OCPs.

3.6 Application of green chemistry for the extraction of contaminants from lipid-rich matrices

Contemporary scientific research emphasizes the development of alternative green extraction solvents, including supercritical fluids, ionic liquids, DES, and supramolecular solvents. These approaches aim to reduce energy consumption and waste generation, addressing the challenges associated with the complex preliminary extraction steps from intricate matrices. A review of the scientific literature reveals that these green extraction methods are being applied across a diverse range of matrices. While the application of ionic liquids in extraction within a green chemistry framework remains limited, their use in extracting PAHs from crude caraway oil has emerged. Among the available ionic liquids, 1-butyl-3-methylimidazolium tetrafluoroborate demonstrated the highest efficiency in removing benzene (73.1 ± 0.1%), anthracene (42.5 ± 1.0%), phenanthrene (33.1 ± 1.4%), and benzo[*a*]fluoranthene (38.8 ± 2.9%) [130]. In the context of green chemistry, DES have found application in the extraction of pesticides from fatty matrices. A water-immiscible DES, made of choline chloride and decanoic acid has been effectively used to extract various pesticides–such as carbaryl, hexythiazox, pretilachlor, iprodione, famoxadone, sethoxydim, and fenazaquin–from milk samples. Dispersive liquid–liquid microextraction (DLLME) using this DES yielded extraction efficiencies between 64% and 89% [131]. Similarly, DES-based DLLME enabled pesticide extraction efficiencies ranging from 74% to 87% [132]. Microextraction with DES, utilizing the hydrolysis of milk fatty acids as precursors, yielded extraction efficiencies of 70–91% for isopropyl alcohol (IPA), with a relative standard deviation (RSD) of less than 5.2%. Additionally, quantitative recovery (100%) of 13 elements (Ag, Al, Ba, Cd, Cr, Cu, Fe, K, Li, Mg, Mn, Ni, and Pb) from animal fats and oils was achieved using hydrophilic DES extraction with a choline chloride:ethylene glycol mixture (1:2 molar ratio). The dispersive liquid-liquid microextraction with air-assisted liquid-liquid microextraction technique effectively isolated the target analytes [133]. Among several green chemistry approaches, a novel bio-supramolecular solvent (bio-SUPRAS) based on rhamnolipids was developed for the efficient extraction of pyrethroid insecticides from water and food matrices. The method exhibited desirable limits of detection (5–10 $\mu g \cdot L^{-1}$), good precision (RSDs < 16.9%), and satisfactory recoveries (75.2–94.3%) [134].

The literature review demonstrates that traditional extraction methods, relying on solvent mixtures, yield high recovery rates exceeding 80%. However, these traditional solvent-based methods often suffer from limited selectivity, while innovative approaches still require further development to improve selectivity.

3.7 Nanomaterial-based extraction techniques

Nanomaterial-based extractions, such as nano-SPE, offer a promising approach to improve the selectivity of extraction processes. These techniques are particularly well-suited for lipid-rich matrices, where the affinity of lipids for the extraction solvent can be exploited. An example of such applications is solid-phase extraction using PEGylated multi-walled carbon nanotubes; this extraction technique has enabled an increase in the selectivity of aflatoxin extraction from liquid milk samples, with recovery percentages ranging from 82% to 106% [135]. While these applications show promise, they are still in the early stages of development and have not been extensively investigated in scientific literature. Future studies should focus on minimizing the use of organic solvents and optimizing extraction procedures to enhance efficiency and speed, particularly for complex lipid-rich matrices.

4 Potential harmful effects of POPs and industrial application

The identification of sensitive, rapid, and routine extraction techniques for POPs is critical due to their potentially harmful effects on living organisms. Therefore, a brief overview of the harmful effects on organisms and some industrial applications of POPs is provided below. It has been demonstrated that both aquatic and terrestrial species, including humans, can be significantly impacted by POPs through specific pathways. Aquatic flora and fauna, in particular, predominantly accumulate POPs in adipose tissue, and LC50 values for the analytes of interest have been determined. For example, industrially significant POPs, such as penta- and octa-brominated diphenyl ethers, commonly used in construction materials, electronics, motor

vehicles, airplanes, and the plastics industry, have been shown to exert toxic effects on aquatic species, such as the grass shrimp, with an LC50 value of 2.46×10^6 ng·L^{-1} [136]. It is important to note that analyte-molecule binding mechanisms vary and influence different metabolic pathways depending on the specific characteristics of the target molecule. The scientific literature indicates that xenobiotic substances can induce initial cellular damage, which may become persistent if detoxification and repair processes do not act promptly. Endocrine disruptors, in contrast, interfere with metabolic pathways involved in growth, development, and reproduction, primarily affecting the thyroid and gonads [137].

5 Conclusion

The efficient extraction of POPs from fatty matrices has been of significant interest to the scientific community for several years. A comprehensive analysis of the scientific literature reveals a wide variety of extraction approaches. One of the common points of the extraction of different classes of POPs is the necessity of sample preparation prior to extraction. The most employed pre-treatment methods include saponification with NaOH and KOH (milk and meat), lyophilization (meat, fish, leaves), sample dilution in solvent, and homogenization (olive oil).

For the POPs separation, LLE, DLLME, SPE, ASE, and QuEChERS methods are mainly applied. Another common aspect of the extraction approaches includes the clean-up and purification of samples essential for the removal of lipid components, which could be co-eluted with the POPs investigated. For this step, Florisil, Alumina, C18, PSA, and EMR-lipid are the frequent sorbents selected. Among the extracting solvents, acetonitrile is the best solvent used alone or in combination with other solvents (e.g., acetone, *n*-hexane, dichloromethane). The selection of this solvent could be attributed to the ability to reduce the formation of emulsions and the opacity of the supernatant, enhancing the quality of the analysis. Recently, innovative approaches have been developed for the efficient extraction of POPs. DI-SPME has been successfully applied for the extraction of PAHs, while HS-SPME has proven efficient for the extraction of pesticides and PCBs.

Additionally, the development of innovative coatings for SPME fibers appears to be a promising approach, reducing the need for extensive sample preparation. However, from a green chemistry perspective, the use and development of extraction techniques employing eutectic solvents is suggested as a promising solution.

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