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Current trends to green food sample preparation. A review

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ABSTRACT

Food analysis plays an important role in preserving the integrity and quality of food. Despite these noble goals, most official methods for the analysis of nutrients (vitamins, carotenoids, etc.) antioxidants (polyphenols, etc.), and contaminants (pesticides, veterinary drugs, mycotoxins etc.) still rely on time-consuming, complex, and polluting procedures of sample preparation. To solve this discrepancy, the scientific community has frantically been working to make extraction procedures faster and safer, resorting to miniaturization, automation, low-energy consumption, and solvents/sorbents from renewable resources. This review provides an overview of the most sustainable extraction methods in food analysis, developed over the last ten years (2014–2024), including relevant examples of both liquid phase and sorbent-based techniques. Particular emphasis is placed on solutions aimed at improving the method sustainability such as smart devices, neoteric solvents, and composite sorbents, discussing the latest advancements and future trends in this sector.

1. Introduction

Despite the high aim to preserve the quality of foods and to protect consumers' health, most methods applied for the analysis of nutrients (vitamins, carotenoids, polyphenols, etc.) or undesirable substances (i.e. pesticides, heavy metals, mycotoxins, etc.) are still based on procedures typical of Brown Chemistry (BC), which involves the use of harmful chemicals, long time of analysis, high energy consumption, and a general low attention towards the effects on analysts and the environment. For >30 years now, the scientific community started to create a bridge from the BC towards a Green Chemistry (GC). However, from a sustainable point of view, the weakest link in the analytical chain of these methods is sample preparation, being the most polluting and complex step. For these reasons, important measures have recently been taken to green traditional procedures [1–3]. In 2022, the ten principles of green sample preparation (GSP) were presented [1]. Among the proposed solutions there are the use of automated methodologies, the reduction of waste employing miniaturized techniques, and the use of non-hazardous solvents and sorbent materials. However, besides the need of improving the method sustainability, there is the parallel necessity to maintain high analytical standards (recovery, accuracy, precision, sensitivity, limit of detection, and limit of quantification). For this reason, the concept of White Analytical Chemistry (WAC) [2] and its twelve principles were proposed as an alternative to the twelve principles of Green Analytical Chemistry (GAC) [3]. The importance of both approaches emerges clearly when food matrices are studied since extraction performance cannot be overlooked in favor of the method sustainability. In fact, in food analysis, it is not always possible to conduct direct analyses, omitting the sample preparation as suggested by the first principle of GAC ("*Direct analytical techniques should be applied to avoid sample treatment*"). Biomolecules such as lipids, carbohydrates, and proteins, being the main components of food matrices, can hinder the extraction of other compounds and/or interfere with their detection and quantification. In addition, active constituents can accumulate in different food parts (i.e. peel, seeds, or pulps for fruit and vegetable samples) or be strongly linked with other biomolecules. Thus, it often happens that harsh conditions of extraction or strong solvents are applied to free a natural component from a food matrix. For example, the alkaline hydrolysis of milk or fatty food is often necessary to free fat-soluble vitamins entrapped in the lipidic fraction [4,5]. Sample treatment is also necessary to increase the analysis selectivity in case of complex matrices or when analytes are present in traces. Because of these limitations, depending on the sample nature, an extraction procedure mediated by a sorbent or a solvent is usually required to make analytes detectable and achieve satisfactory analytical performance [6].

In the last decade, the sensitivity of the scientific community towards the respect for the environment and the desire to contribute to a more sustainable society has been the germ that has triggered an explosion of

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solutions to make analytical methods more sustainable, also in food analysis. In the present review, an overview of some relevant applications published in this sector over the last ten years is discussed, examining how previous "brown" approaches have been greened. Examples of sustainable extraction methods are presented in separate sections for the analysis of both contaminants and nutrients, highlighting aspects related to analytical novelty, eco-compatibility, and recyclability/reuse of solvents and sorbents.

2. Solid phase extractions and its variants in food analysis

Solid phase extraction (SPE) is undoubtedly the most used technique for the treatment of food samples such as milk, wine, fruit juices, etc. [7]. Thanks to the use of specific sorbent materials, SPE can modulate the selectivity of the extraction process, unlike solvent-based techniques which do not guarantee high discriminating power. Moreover, SPE not only favors high enrichment factors (EFs) but also efficient clean-up, when coupled with other extraction techniques. For example, for protein- or fat-rich foods, a preliminary deproteination/defatting step with an organic solvent can be followed by an SPE clean-up step, by using sorbents such as alumina, primary-secondary amines (PSA), C18, OASIS HLB and Florisil [8]. Owing to the large use of SPE, this technique has gone through startling transformation with the aim of both improving its sustainability and overcoming some limitations inherent to in-cartridge modality. In the following sections, the intensive research conducted over the last decade is presented and critically discussed.

2.1. Solutions to green SPE in food analysis

2.1.1. Automation

Thus far, most of the SPE extraction methods applied in food analysis have focused on offline systems [9]. However, there has been an increasing trend in assembling automated devices to perform SPE, both offline and online [10,11]. The possibility of automating a process aligns with the 6th criterium of GSP (*maximize sample throughput*) because analyses are made with the additional benefit of reducing the analyst exposure to hazardous substances [1,12].

An example of fully automated off-line SPE configuration is the multi-well plate SPE which allows the simultaneous extraction of a significant number of samples [13]. A multiple entry pipettor can manage the simultaneous sampling and the elution of a large number of samples, offering numerous advantages in terms of cost, throughput, safety, precision and accuracy. Nevertheless, although this system has found many applications in the environmental field, it has not been tested in the food sector yet. An illustrative example of automated online SPE is from the work by Lhotská et al. [14]; in this case, online SPE on a C18 fused-core precolumn was coupled to high-performance liquid chromatography (HPLC) with fluorescence detection to analyze ochratoxin A and citrinin in beer samples. Filtered beer samples (100 μL) were directly injected into the on-line SPE–HPLC system and the analytes were back-flushed to a phenyl-hexyl chromatographic column, managing to realize the complete analysis in <6 min with quantitative recoveries.

Despite the advantages in terms of analysis time and reduced operator intervention, automated SPE systems suffer from some limitations. In general, such applications are restricted to filtered beverages such as beer, wine, tea, and soft drinks and less suitable to more complex liquid foods such as milk and smoothies (fresh fruit pureed with milk or yogurt). In such cases, to avoid the occlusion of the SPE cartridges or the HPLC system tubing, preliminary steps of filtration, protein/fat precipitation, and centrifugation are indispensable, but they decrease the automation degree and the number of samples processed per hour.

2.1.2. Miniaturization

Miniaturization (principle 5 of GSP) influences the greenness of sample preparation methods by minimizing the size/volume of samples and chemicals, and reducing the amount of waste generated [1]. Moreover, downscaled sample preparation methods have a higher potential to become an integral part of a portable device. In this sense, an excellent example of SPE miniaturization is solid-phase microextraction (SPME), developed by Pawliszyn in the early 90 s [15]. SPME consists of a solid retractable fiber, typically made of polymeric materials such as polydimethylsiloxane (PDMS) or polyacrylate, coated with a stationary phase for the simultaneous extraction and concentration of target compounds. From the analytical point of view, SPME can be applied to solid, liquid, and gaseous samples, which is a great advantage for food analysis. Furthermore, this technique offers the possibility to extract analytes with different polarity and physicochemical properties working both in infusion, in the case of liquid samples, or in headspace (HD), in the case of gaseous ones. In particular, the latter mode allows one to reduce drastically the matrix effect when volatile and semi-volatile compounds are extracted (for instance, aromas from food matrices). An interesting example is the work by Martínez et al. [16] who identified the formation of specific volatile compounds as a consequence of mechanical damage in apples by using SPME coupled to gas chromatography-mass spectrometry (GC–MS). After being mechanically damaged, the samples were placed inside jars with plastic lids to capture volatile compounds; a carboxen/PDMS fiber was then inserted through the jar lid at 25 °C for 40 min to adsorb analytes. A total of 83 volatile compounds including 41 esters, 11 hydrocarbons, 10 alcohols, and 7 terpenoids were identified, concluding that an increase of lower molecular weight esters and a decrease of higher molecular weight esters can be associated with mechanical damage of the fruits.

Recently, nanomaterial-based SPME has gained great attention due to its simplicity and the possibility to achieve high analytical standards. Among the several nanomaterials, hexagonal boron nitride (h-BN) is a layered lattice-structured material used for such aim. H-BN is analogous to graphite that, in the form of nanosheets (h-BNNs) is also known as "white graphene". This emerging coating sorbent is characterized by high chemical and thermal stability, high specific surface area and cost-efficiency [17]. This material is preparable via an ecofriendly method which is the ultrasound-assisted exfoliation of h-BN using various extracts of plants [18]. The B-N bonds in h-BN can provide strong polarity at N- or B- atom defected sites; introducing fluorine elements into such defected sites, the modified h-BN can adsorb fluorinated compounds very efficiently. Li et al. [19] fabricated SPME fibers coated with fluorinated BNNs for the LC-MS determination of perfluoroalkyl acids in milk and meat (Fig. 1). Milk samples were deproteinized and defatted before the extraction, while meat samples were first homogenized with acetonitrile, evaporated, reconstituted, and finally submitted to SPME reaching quantitative recoveries (77.7–110.5 %) and good repeatability (RSD% <13.5 %).

Among the plethora of microextraction techniques introduced after SPME, there is fabric phase sorptive extraction (FPSE) [20], whose further evolution is magnet-integrated fabric phase sorptive extraction (MI-FPSE). This state-of-the-art sample preparation technique foresees a magnet-integrated stand-alone sample preparation device consisting of two FPSE membranes sandwiched together with a cylindrical magnetic bar inside. MI-FPSE offers several advantages including simplicity in handling, high capacity, low cost, reduction of organic solvent consumption and high thermal and chemical stability. High extraction efficiency can be obtained due to the open, porous, permeable configuration of the membranes. As an example of application in food analysis, we report the use of a sol–gel poly(tetrahydrofuran) (PTHF) coated FPSE cellulose membrane for the extraction of six triazine herbicides from herbal infusions, such as chamomile (*Matricaria chamomilla*) and Greek mountain tea (*Sideritis scardica*) [21]. The ionic strength of the samples was adjusted by adding NaCl at a concentration of 10 % w/v. The triazine herbicides were adsorbed in 45 min under the device stirring at 1200 rpm. Then, the MI-FPSE membrane was removed, rinsed with water, and placed for 2 min in a glass vial where 250 μL of methanol was added for the analyte desorption. After filtering, the

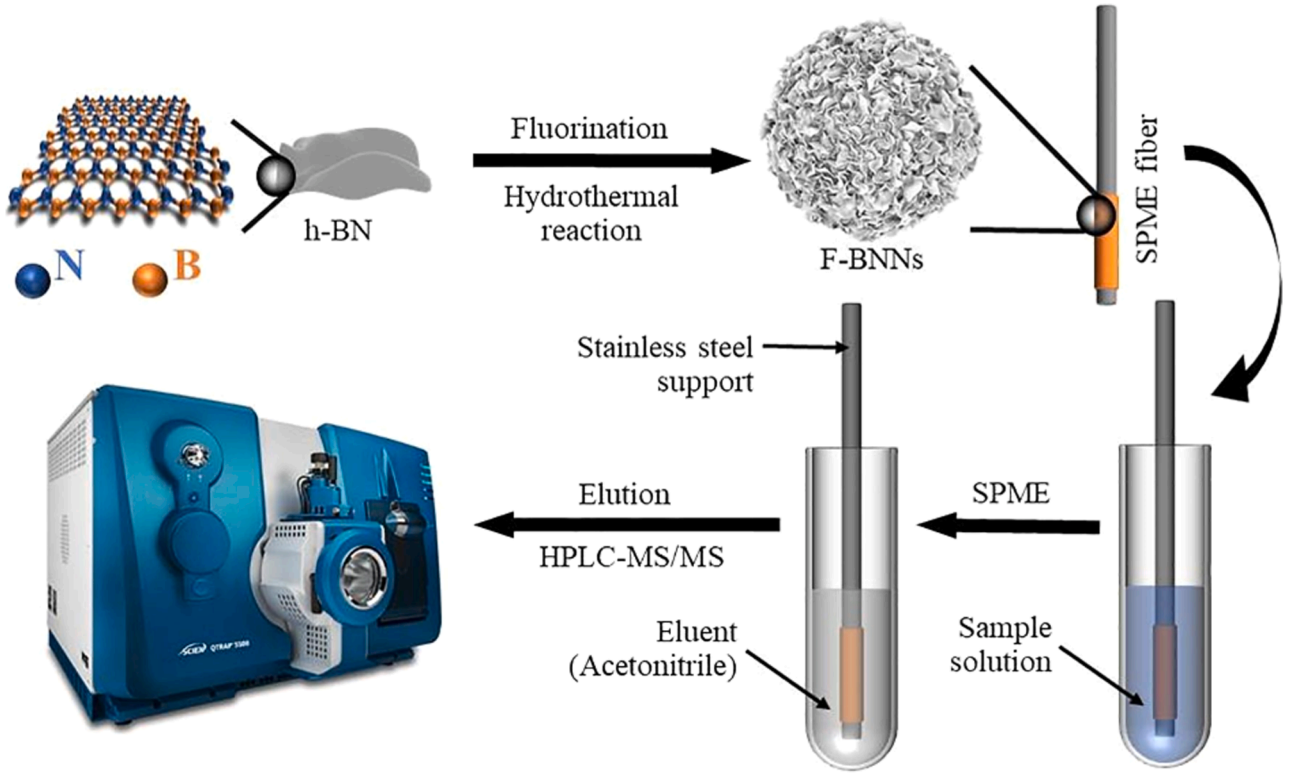

Fig. 1. Schematic representation of the fiber functionalization with boron nitride nanosheets synthetized by the authors. SPME fiber was used in infusion mode on the homogenized milk and meat samples (from [19]).

eluate was analyzed by HPLC-DAD. Recoveries ranged between 42 and 63 % with the inter-day precision was <8.5 %. Finally, a study of recycling showed that the sol–gel PTHF MI-FPSE membranes were reusable for at least five subsequent cycles of extraction.

Pipette-tip SPE (PT-SPE) is another miniaturized SPE technique where the sorbent material is packed or held inside plastic micropipette tips or syringe needles. The extraction of analytes and their subsequent elution are carried out by means of a pipettor (Fig. 2) [22].

The main advantages of this technique arise from its simplicity, the usage of very small volumes of sample and elution solvents, the capability to process multiple samples using a multichannel micropipette, shorter extraction time, high recovery efficiency, and easy automation. However, the EF is limited by the sample volume. Typically, PT-SPE is applied to biological samples, but recently its usage has been expanded to environmental and food analysis [23–25]. Lu et al. [25] developed a PT-SPE method to isolate four plant hormones from watermelon juice using only 5.0 mg of m-aminophenol–urea–glyoxal resin as the sorbent. The need of a low amount of sorbent was due the high specific surface area of the resin and the multiple functional groups (hydroxyl, amino, and imino, among others) on its surface responsible

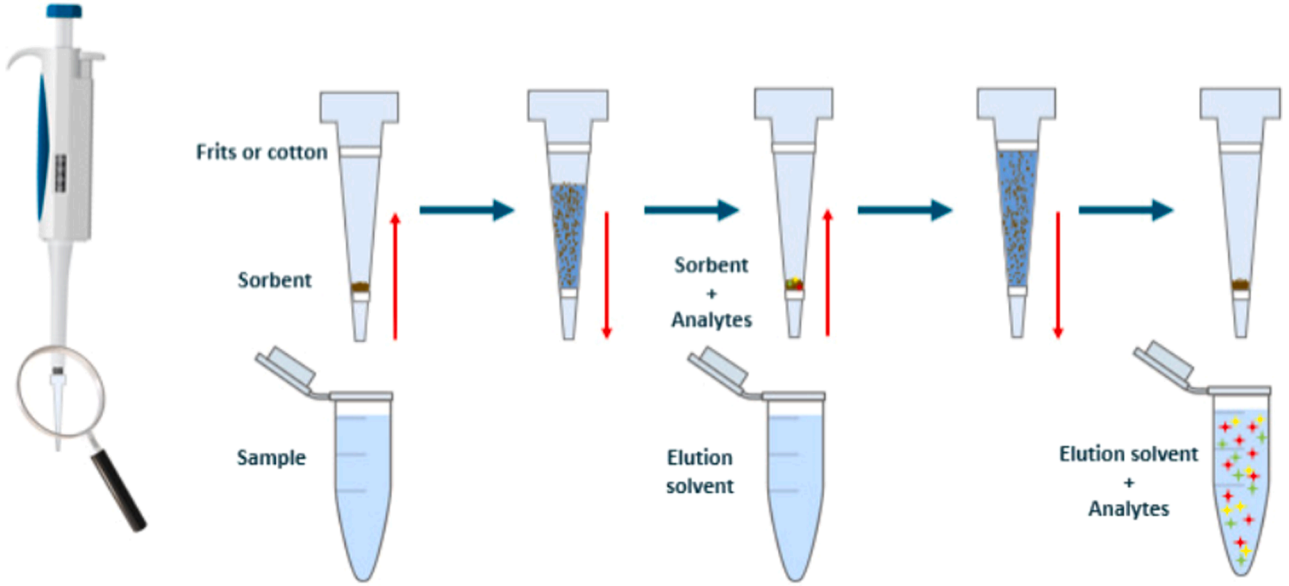

Fig. 2. Scheme of adsorption/desorption cycles performed during a pipette-tip SPE.

for high adsorption capacity. The recovery of four analytes at three spiking levels ranged from 87.2 % to 102.3 % with an RSD $\leq$ 7.2 %. The reusability of the sorbent was also investigated by performing several cycles of recovery experiments which showed yields higher than 92 % after 6 cycles.

Although miniaturized SPE techniques show several strong points in terms of sustainability, there are also some limitations that must be considered when such techniques are applied in food analysis. For instance, most applications use headspace-SPME since the direct immersion into a liquid sample can be difficult due to the complex nature of food matrices. The fibre can be damaged or proteins can adsorb irreversibly to it, modifying the fibre properties and making it unusable for more than one sample. A solution in case of complex samples is to protect the fibre by placing it inside a hollow cellulose membrane; in this case the membrane can also exhibit a size exclusion effect allowing only compounds with molecular weights <1000 Da to diffuse through it. Nevertheless, such an approach requires longer extraction times, and clogging of the membrane might be expected for many food matrices.

2.1.3. Sustainable, reusable, and renewable sorbents

Sample preparation is a hectic field of analytical chemistry, in which part of the research is devoted to the preparation of sorbent materials effective in achieving high figures of merit (high recovery yields associated with good precision and accuracy values). Nanoobjects (nanotubes, nanoparticles of different nature, nanofibers, etc.) and nanostructured materials (nanosponges, buckypaper, composite materials, etc.) are ideal candidates as SPE sorbents due to high specific surface area, selectivity, an enhanced mechanical or thermal stability. Reusability is a further property of such materials, especially shown off by the third principle of GSP which encourages the use of such sorbents over the disposable ones [1]. In the previous subsection, we have already seen some examples of reusable sorbents, which can be regenerated and applied more times reducing waste [21,22]. Carbon nanomaterial (CNMs) (fullerenes, graphene, carbon nanotubes, carbon nanocones, carbon nanohorns, nanodiamonds, quantum dots and carbon nanofibers, etc.) have aroused great interest within the sample preparation field [26]. The sp^2 carbon-based graphitic structure of these materials makes them particularly suitable for the extraction of aromatic compounds due to the strong π–π stacking interactions they can establish. Their polarity and selectivity can easily be modified through oxidizing treatments, often followed by covalent functionalization [27]. Other interesting materials are Metal–Organic Frameworks (MOFs), also known as porous coordination polymers [28,29]. MOFs are an emerging class of porous sorbents, whose two- or three-dimensional crystalline structure relies on inorganic metal species (nodes) and organic species (ligands). The wide structural and functional tunability makes them suitable materials for sample preparation even if their synthesis can be challenged from the point of view of sustainability. In fact, the use of energy-intensive reaction conditions, heavy and rare metals, and toxic solvents, as well as the lack of knowledge about their toxic effects make these materials not exactly safe for the operator and the environment [30]. Recently, covalent organic frameworks (COFs) synthetized by organic systems of light elements (C, B, O, Si, N) connected through strong covalent bonds and greener synthesis (low-toxicity solvents like water, ethanol and methanol and metals such as aluminum, zirconium and zinc) have solved these problems. CNMs and MOFs have been used alone or in combination in most sorbent-based microextraction techniques for the pretreatment of different food matrices such as vegetables [31,32], fruits [33], meat [34], eggs [35,36], and honey [37]. Very often, these micro- and nano-sorbents are used to perform dispersive solid-phase extraction (d-SPE) that, in the sector of food analysis, is especially useful to treat particularly complex samples. The sorbent is directly dispersed into a liquid sample (for instance, deproteinized milk), thus avoiding occlusion problems like those occurring with a sorbent packed in a cartridge and making the recovery process more rapid and simpler [38]. The sorbent, enriched with analytes, is then separated by means of centrifugation, filtration, or applying an external magnetic field (magnetic-SPE). This procedure is directly applicable to food liquid matrices (milk needs a preliminary step of deproteinization), while solid matrices (tissues, flour, etc.) require a preliminary liquid-solid extraction [39].

Du et al. [35] developed a method for the simultaneous determination of 11 macrolides in different tissues of swine, chicken, bovine, and sheep tissues, as well as eggs. Samples were extracted using a mixture of acetonitrile, ethyl acetate, and methanol containing 1 % ammonia; then, D-SPE was performed using multi-walled carbon nanotubes (MWCNTs) as the sorbent. The average recoveries ranged from 83.5 % to 111.4 % with an intra-day and inter-day precision <13.6 % and 16.4 %, respectively. OASIS-HLB and C18 provided lower performance in terms of recovery and gave problems of cartridge clogging limiting the sample throughput. However, since MWCNTs are quite light, high-speed centrifugation (10,000 rpm) is indispensable to achieve good separation of the extracts from the MWCNTs.

A magnetic composite sorbent based on MOF (MIL-100) and polyethyleneimine (PEI) was prepared by Senosy et al. [40] to extract triazole pesticide residues from vegetables and fruit samples (apple, orange, tomato, cabbage, and cucumber). After sample homogenization and solid-liquid extraction with acetonitrile, the supernatant was submitted to a magnetic-SPE clean-up with Fe_3O_4@MIL-100(Fe)/PEI, obtaining recoveries which spanned from 73.9 % to 109.4 %. The sorbent exhibited excellent stability and recovery through its regeneration in five successive cycles. The material was characterized with different techniques which revealed the presence of a high number of binding cavities and functionalities able to potentially establish several types of interactions (electrostatic interactions, hydrogen bonds, acid–base interactions, etc.) both to adsorb organic compounds and chelate metal species.

Another interesting example of hybrid nanomaterial is that prepared by Liu et al. [36] to extract polycyclic aromatic hydrocarbons (PAHs) and bisphenolic pollutants (BPs) from roasted meat. $NiFe_2O_4$ nanoparticles were the magnetic core of the nanohybrid composite, while graphene oxide (GO), NH_2–MIL-101(Al), and β-cyclodextrin (β-CD) were functional components. After homogenizing and hydrolyzing meat samples under alkaline conditions, the filtered digest was diluted with ultrapure water and submitted to magnetic SPE. The dispersion of the magnetic sorbent within the sample as well as the analyte adsorption were supported with the aid of effervescence whose duration was around 4 min. For the analyte desorption, a mixture of acetone and hexane (2:1, v/v) for a total time contact of 5 min was used. The method gave satisfactory recoveries (86.9–103.9 %) and high precision (RSD of 1.9–6.7 %). The procedure does not demand energy and it is quite rapid; however, long time it is necessary to prepare the several materials for the realization of the composite.

The third principle of GSP also supports the development of bio-based materials to replace petroleum-derived polymeric sorbents, which are less polluting due to their potential for biodegradability. Sorbents from renewable sources, such as cellulose, chitin, starch etc., are also highly recommended. They are often used in combination with nanomaterials (CNMs, MOFs, etc.), dispersed or coated on such nature-based supports, to prepare composite sorbents with similar or superior performance to the conventional ones (silica-based, carbon-based or polymeric) [41]. A telling example is the work by Abujaber et al. [42]. The authors synthesized magnetic cellulose nanoparticles (MCNPs) as sorbents for stir bar-sorptive dispersive microextraction of polychlorinated biphenyls from juice samples. After diluting a 5-mL aliquot of filtered sample with water to 50 mL into a beaker, this solution was poured out to a beaker containing 10 mg of MCNPs coating a stir bar. Under the action of the stirring (700 rpm for 10 min), the MCNPs were dispersed into the solution and the analytes adsorbed on them. Once the stirring was finished, the MCNPs rapidly returned to the stir bar under magnetic attraction. Then, the coated stir bar was transferred with tweezers to a vial containing 3 mL of n-hexane and stirred for 5 min at

700 rpm for back-extraction of the analytes. Fig. 3 shows the steps of this efficient process. Recoveries ranged from 70.4 to 108.0 % with precisions <9.3 %. The reported work is an illustrative example of how limitations of conventional stir bar sorptive extraction (SBSE) can be overcome. In fact, even if applications of SBSE in food analysis are increasing, due to the limitations of the PDMS phase, they are still currently limited to non-fatty food matrices and non-polar or semi-polar analytes.

Table 1 lists some selected SPE applications to food analyses.

3. Solvent-mediated extractions in food analysis

Solvent-mediated extractions, encompassing both liquid-liquid extractions (LLE) and solid-liquid extractions (SLE), are the most common procedures used in food analysis. Over the last decade, both LLE and SLE have undergone several improvements that concern two main aspects [55,56]: technological/applicative innovations arising from the development of new extraction techniques and identification of more sustainable extraction solvents [57].

3.1. Liquid-phase (micro)extractions

Liquid-phase extractions are among the techniques that have mostly transitioned towards environmental friendliness. Initially characterized by significant usage of hazardous solvents, long operational times, and low efficiency, LLE has undergone revitalization with the advent of miniaturized methods and neoteric solvents. Through miniaturization, now it is possible to talk about liquid-phase microextractions (LPME) which, among the major advantages, offer an enhanced mass transfer of analytes, increased extraction efficiencies, rapidity, and decreased risks for operators and the environment as the volumes of organic solvents have been reduced from milliliters to microliters. A large variety of LPME techniques have been developed over time, depending on how the extraction solvent is introduced into the donor solution [58]. Three main configurations are available: (i) single-drop microextraction (SDME), (ii) dispersive liquid-liquid microextraction (DLLME), and (iii) hollow-fiber liquid-phase microextraction (HF-LPME) [45]. SDME represents the easiest way to perform an LLE. It consists in putting in contact a single drop of extraction solvent with the sample through a syringe. It can be carried out through direct immersion (DI), drop-to-drop (DD), directly suspended droplet (DSD), continuous flow (CF), headspace (HS), or liquid-liquid-liquid (LLL) SDME [59]. The analyte transfer from the sample to the droplet is mainly regulated by diffusion as well as by partition coefficient (K_d). Solvent viscosity, temperature, and the thickness of the interface layer organic solvent/solvents can affect the analyte diffusion rate from the donor solution to the acceptor phase, so they should be controlled during an extraction. Ideally, an optimal extraction solvent suitable for SDME should have high boiling point, low volatility, compatibility with detection systems, immiscibility with donor solution, and a proper viscosity. The solvent viscosity should be sufficiently high to maintain the droplet stability, avoiding its spreading (especially in DSDME) but not so high to reduce the diffusion rate. The main advantages of these techniques are simplicity, the lack of carryover effect, the possibility to automate the procedure, and the high EFs due to the extremely low amount of solvent used (<200 μL). For instance, Chen S. et al. [60] extracted vanadium (IV and V) from some beverages by means of two-step direct immersion SDME. Theonyltrifluoroacetone (TTFA) and chloroform were used as the chelating reagent and extraction solvent, respectively. In the first step, only V(V)-TTFA complexes were separated and enriched in one organic solvent drop at pH 2.5, while V(IV) remained in the solution. Next, another organic solvent drop containing TTFA was immersed in the original solution to extract V(IV) complexes at pH 4.5. Compared with conventional and tedious pre-oxidation/pre-reduction operations, which may cause contamination and error, this procedure is very simple and effective allowing the achievement of an EF of 300. On the other hand, the drawbacks are the difficulty of detaching the drop especially when the solvent viscosity is not so high, the variability of its dimension, and the volatility of extraction solvent that can evaporate during an extraction.

DLLME consists in dispersing a small volume of extraction solvent (100–200 μL) in an aqueous sample (5–10 mL), often in the presence of a dispersant solvent (400–2000 μL), i.e. a solvent miscible with both the aqueous sample and the extractant (which instead is immiscible with water). Following mixing (manual, vortexing, ultrasonic or magnetic stirring), an emulsion of the three components, called "cloudy solution", is obtained. The fine dispersion of extractant and dispersant into the donor solution ensures (i) a higher contact surface between the two phases, (ii) a faster and more efficient mass transfer of analytes. These effects translate in greater extraction efficiencies, higher EFs, and in a faster and cheaper extraction procedure compared to the HF-LPME and SDME [60]. The extraction solvent is then recovered by centrifugation on the top of the aqueous sample with low-density solvents or on the bottom of the centrifuge tube with solvents having higher density than water; another solution is the solidification of the floating droplet (SFOD-DLLME) cooling the solution. Junza et al. [61] developed a

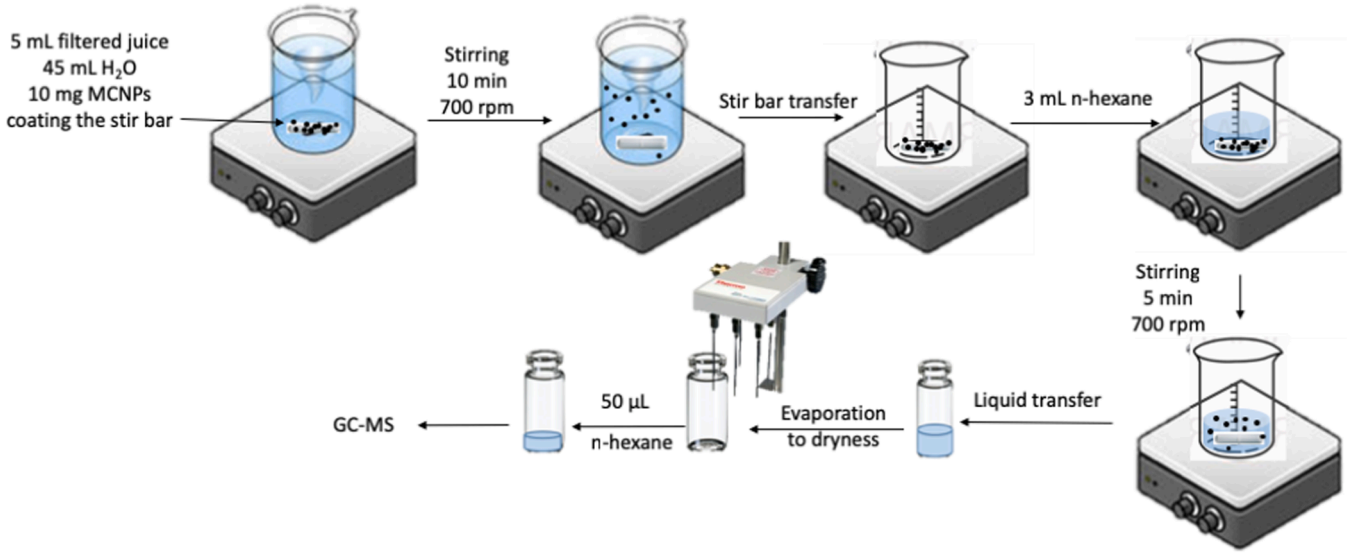

Fig. 3. Scheme of the SBSDME analytical method based on MCNPs (from [42]).

Table 1
Green SPE procedures applied to food analysis.

Analyte	Extraction technique	Type of sorbent	Food matrices	Instrumental technique	Analytical performance	Refs.
Lipidomics	d-SPE	Hybrid SPE-Phospholipid and C18 50/50 w/w	Oilseeds	LC-Q-TOF-MS	The identified lipid classes included lysophosphatidylcholines (LPC) and lysophosphatidylethanolamine (LPE), glycerophosphatidylcholines (PC) and glycerophosphatidylethanolamines (PE), diacylglycerols (DG), and triacylglycerols (TG).	[43]
Tetracyclines	d-SPE	MIL-101 (Cr), MIL-100 (Fe) and MIL-53 (Al) (7:1:2, w/w/w)	Honey	HPLC–MS/MS	LOD: 0.073–0.435 ng/g LOQ: 0.239–1.449 ng/g R = 88.1–126.2 %	[44]
Perfluorinated compounds	d-SPE	Perfluorotetradecanoic acid as dummy template (MIP)	Pork meat	HPLC-MS/MS	LOD: 0.011–0.08 ng/g LOQ: 0.037–0.27 ng/g R = 89.3–116.3 %	[45]
Organophosphate pesticides	d-m-SPE	Magnetic (Fe_3O_4) restricted access (bovine serum albumin) carbon nanotubes	Broccoli, eggplant, cauliflower, green pod, and soy milk	Flow injection analysis (detection at 560 nm)	LOD: 0.74 μg/L LOQ: 5 μg/L R = 95.5–108.9 % EF=164	[46]
Triazole fungicides	PT-SPE	Carbon aerogels from waste sources	Tomato, apple, cucumber and pear	GC-FID	LOD: 0.08–0.32 mg kg^{-1} LOQ:0.24–0.96 mg kg^{-1} R = 81–119 %	[47]
Sulfonamide residues	PT-SPE	Triazine-based porous organic polymer (TAPT-BPDA)	Meat, egg and milk	HPLC-DAD	LOD: 0.1–0.28 μg/L LOQ: 0.33–0.93 μg/L R = 76.1–114.0 %	[48]
Aflatoxins	UAE-MIP-μ SPE	DMC (5,7-dimethoxycoumarin) as dummy template for MIP particles synthesis, mixed with 115 μL of MAA and 25 mL of porogen (1:3 acetonitrile/toluene)	Fish feed	UHPLC-MS/MS	LOD: 0.42–1.15 μg/kg LOQ: 1.30–3.50 μg/kg R = 80–100 %	[49]
Phenylurea herbicides	SBSE	Carboxyl-enriched microporous organic network (MON-2COOH) as stir bar coating	Tomato and apple	HPLC-PDA	LOD: 0.025–0.070 μg/L LOQ: 0.085–0.230 R = 80–104.8 % EF=46–49	[50]
Allergen protein concanavalin A	SBSE	Aptamer as the stir bar coating	White beans, chickpea, lentils, and wheat flours	MALDI-TOF-MS	LOD: 0.5 μg/L LOQ: 1.5 μg/L R = 81–97 %	[51]
Pesticides	HF-SPME	Three-dimensional hydroxyl-functionalized covalent organic framework (COF)	Rice and apple	HPLC-DAD	LOD: 0.86–1.38 ng/g LOQ: 2.38–3.68 ng/g R = 79.3–106.8 %	[52]
Pesticides	HF-SPME	MIL-101 (Cr) @ graphene oxide (MIL-101@GO)	Tomato, cucumber	HPLC-UV	LOD: 0.21–0.27 μg/L LOQ: 0.72–0.91 μg/L R = 88–104 % EF=41–49	[53]
Aflatoxins	IS-D-μ-SPE	C_{18}	Cow milk	HPLC-FLD	LOD: 0.003–0.005 ng/mL LOQ: 0.01–0.02 ng/mL R = 73–109.6 %	[54]

d-m-SPE: Dispersive magnetic solid phase extraction; D-SPE: Dispersive solid phase extraction; HF-SPME: Hollow fiber-solid phase microextraction; IS-D-μ-SPE: In-syringe dispersive solid phase microextraction; PT-SPE: Pipette-tip solid phase extraction; SBSE: Stir bar sorptive extraction; UAE-MIP-μ SPE: Ultrasound-assisted molecular imprinted polymer micro solid phase extraction.

DLLME procedure to extract 17 quinolones and 14 β-lactams (penicillins and cephalosporins) from raw cow milk. For each sample, two parallel extractions, at two different pH values were necessary: at pH 3 for acidic quinolones and β-lactams, and at pH 8 for amphoteric quinolones. Prior to the DLLME, milk deproteinization was realized with acetonitrile (1:1, v/v). To determine acidic quinolones and β-lactams, the supernatant (about 2 mL) was diluted with acidified water with 0.1 M HCl at pH 3 to a final volume of 10 mL (solution A). In case of amphoteric quinolones, the supernatant was diluted to a final volume of 10 mL with 1 % (v/v) ammonia aqueous solution at pH 8 (solution B). Then, acetonitrile was used as the dispersant and trichloromethane as the extractant in the DLLME. The organic phases obtained in both extractions (A and B) were merged, evaporated to dryness, and the reconstituted residue analyzed by UHPLC-MS/MS. Recoveries between 72 and 110 % were obtained. This method is advantageous because it is quicker than the existing analytical procedures based on SPE, which is a more expensive and time-consuming technique.

Recently, the literature has reported several examples of QuEChERS (quick, easy, cheap, effective, rugged and safe) extraction followed by DLLME to treat both liquid and solid foodstuffs, such as vegetables [62, 63], meat and cheese [64], fish [65], and yogurt [66]. This combination takes advantage of both the exhaustive extraction of QuEChERS and the good EF provided by DLLME. A representative example is the work by Nagyova et al. [67]. For the determination of 15 PAHs in crustacean gammarids, a miniaturized QuEChERS-DLLME method was developed. After homogenization, 0.2 g of sample was submitted to the QuEChERS procedure: 2 mL of Milli-Q water and 2 mL of acetonitrile was added and vortexed; after the addition of 0.8 g of MgSO4 and 0.2 g of NaCl, the tube was shaken again. After centrifugation, the sorbent clean-up step was performed treating 1.5 mL of supernatant with 150 mg of MgSO4 and 50 mg C18. In the DLLME step, a 1-mL aliquot of supernatant was transferred to a centrifuge tube with 4 mL of 0.1 M NaHCO3 solution. Then, 50 μL of CHCl3 was rapidly added. Finally, the whole settled phase was treated with 1 mL of 0.1 M H2SO4. Then, 100 μL of hexane was added to the top of the solution and, after centrifugation, the upper phase was submitted to GC analysis. The recovery yields for all the analytes were in the range 72–104 % and repeatability was <10 %. Although the good figures of merit, the method involves several steps losing the main advantage of DLLME which is quickness.

Despite its simplicity DLLME suffers from poor automation. Another

crucial point is the choice of type and volume of dispersant, which can affect the extraction drastically: an excessive volume could lead to the solubilization of the extractant in the aqueous sample; conversely, volumes that are too low may not guarantee proper formation of the cloudy solution. Finally, even if good EFs can be achieved, it does not allow the same level on enrichment as SPE, which remains the gold standard to face trace and ultra-trace analyses.

In HF-LPME the extraction of analytes takes place exposing the extraction solvent, supported into a fiber, with the donor solution. The extractant device is composed of a porous (0.2 μm) hydrophobic fiber (polypropylene, polytetrafluoroethylene, and polyvinylidene fluoride) with a diameter lower than 1 mm with an empty lumen for housing the extraction solvent. Before its use, the membrane is immersed in an organic solvent (e.g. octanol) to create a liquid-supported membrane. This configuration is advantageous: (i) because the membrane prevents the dissolution of the acceptor phase in the aqueous sample and (ii) because the rate of the analyte diffusion between the donor and acceptor phases is faster due the greater contact surface between the two phases. The analyte extraction takes place thanks to the molecular diffusion from the aqueous sample through the organic layer to the acceptor phase. The latter is then extracted from the fiber lumen and analyzed [59]. Two different configurations of HF-PLME are available: "two--phase HF-LPME" and "three-phase HF-LPME". Fig. 4 shows the schematic representation of the two approaches.

The choice of HF-LPME method depends not only on the analyte nature but also on the available instrumental technique. In the first configuration, the pores and lumen of the fiber are filled with the same solvent having the characteristic to be immiscible with the donor solution. The use of this configuration is useful for subsequent GC and LC analyses in which non-polar solvents are used. Two-phase HF-LPME is suitable for the extraction of mid/low-polar compounds from aqueous samples. An example is the work by Yamini et al. [69] who developed a two-phase LPME based on polypropylene hollow fibers to extract amitraz, a formamide acaricide, from honey after dilution with buffered water at pH 6. The extraction lasted 45 min and was performed using 1-undecanol as the extractant. The EF was 75, and the recovery greater than 90 %. However, to maintain high reproducibility and repeatability, the hollow fiber should be discarded after each extraction to avoid carryover and cross contaminations, unlike what recommends the third principle of GSP.

In "three-phase HF-LPME" the lumen of the fiber is filled with a solvent miscible with the donor solution. The dissolution into the donor solution is prevented by the membrane socked with an apolar solvent that acts as a barrier between the acceptor and donor phases. This extraction mode is applied to isolate polar and ionizable compounds (e.g., acids, phenols, amines, and amino acids) from aqueous samples. The use of acetonitrile, methanol, ethanol and water as acceptor phases makes this technique compatible with capillary electrophoresis (CE) and LC analyses. The work by Moyo et al. [70] is just based on a three-phase HF-LPME to enrich tetracycline residues from honey samples, after its dilution with buffered water (pH = 9.5). Using 1-octanol as the extractant, and a solution of 0.1 M H_3PO_4 containing 1 M NaCl (pH = 1.0) as the acceptor, recoveries between 81.2 and 107.5 % and EFs between 58 and 105 were obtained.

In both the considered modes two different configurations are possible: rod configuration (static mode) with a closed bottom and U-configuration (dynamic mode) where both ends are connected to a guiding tube. In the latter configuration, the acceptor phase is flushed into the HF lumen through an external peristaltic pump. The U-configuration due to the higher diffusion rate which is established between the two phases can enhance the analyte enrichment and reduce the extraction time compared to the rod configuration; it also prevents solvent loss during the extraction process, with no need for a micro syringe. Overall, the HF-LPME procedure is simple, cheap, and provides for the possibility of automation; however, as in SDME, the main limits are the time consumption, and the limited contact surface area between the sample and the extractant.

Although LPME techniques has a great potential for liquid samples, food applications are still limited, but an increasing number of methods based on these techniques are expected, especially to extract polar

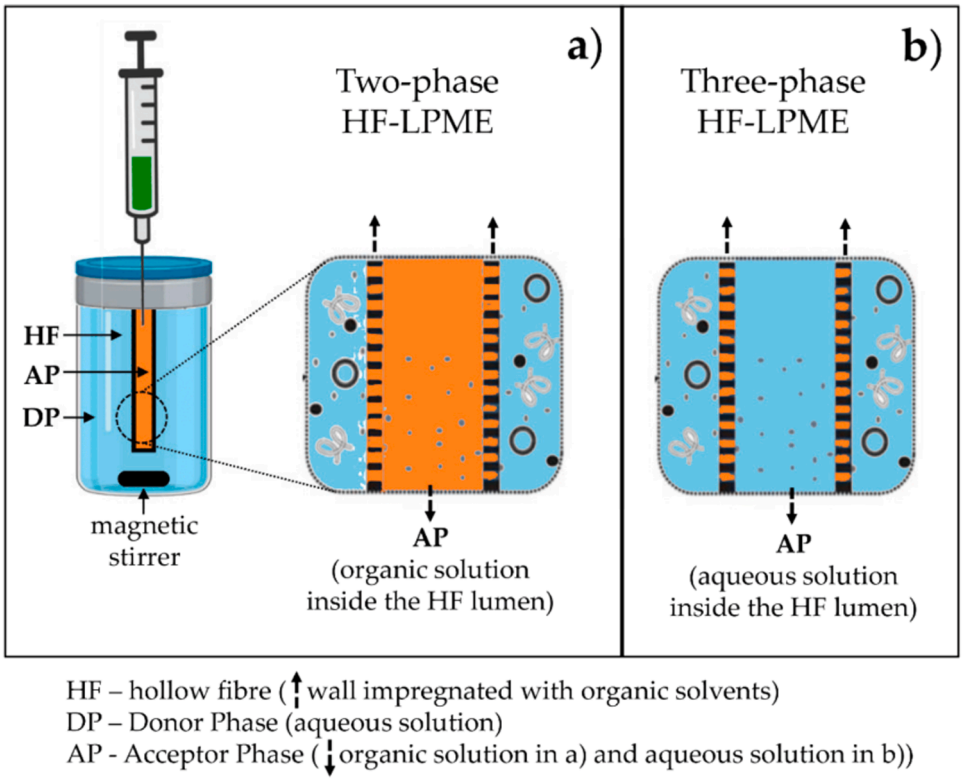

Fig. 4. Representation of the (a) two phases HF-LPME end (b) three phases HF-LPME configuration and solvents location into the fiber (from [68]).

micronutrients or contaminants from edible oils (olive oil, sunflower oil, fish oil, etc.) by working in a reverse mode.

3.2. Solid-liquid (micro)extractions

The latest SLE procedures, in addition to being geared toward the general miniaturization of apparatus, are also physically assisted by microwave, ultrasound, ultrasound-microwave, pulsed electric fields, pressure (pressurized liquid extraction (PLE), supercritical fluid extraction (SFE) and liquefied gas extraction (LGE)); however, the support can be also biological, such as the extraction assisted by enzymes (EAE). Conventional SLE procedures (manual SLE, Soxhlet, matrix solid phase dispersion (MSPD)) have almost totally been replaced with assisted techniques. The employment of such external forces is nowadays very common in sample preparation (especially in SLE) to improve the contact between the extraction solvent and the matrix, promoting a more efficient mass transfer of analytes. They can increase the wettability of matrices, favor the cellular lysis, improve the analyte diffusion or the solubility of target analytes in extraction solvents; they also act favoring a better dispersion of extraction solvents into a matrix and reducing the potential decomposition of analytes thanks to a faster extraction. Such assisted techniques comply with principles 6 and 7 of GSP, maximizing the sample throughput (6) and promoting automation (7), even if they require a certain energy consumption not completely respecting the principle 8. However, this last limitation is compensated by the high ratio productivity/application time that translates to be one of the most efficient approaches to improve the greenness of procedures.

The advantages of microwave-assisted extraction (MAE) on Soxhlet are clear in works by de la Fuente et al. [71], and by Hu et al. [72] where the two techniques are compared. Both papers describe the extraction of nutritional and bioactive compounds from salmon (Salmo Salar) and *Sapindus mukorossi* seed oil. The results indicate how, even if lipids are recovered with similar yields with both techniques, MAE shows a higher throughput: 15 min per sample was the extraction time necessary to perform MAE, while 360 min was required by Soxhlet [71]. Similar results were obtained by M. Hirondart et al. [73] for the extraction of rosemary antioxidants using PLE. Their results indicate how the PLE efficiency is comparable with that obtained with Soxhlet but with a faster and more environmentally friendly procedure. An extraction time reduction by about 8 h, and a reduction of the solvent volume and the sample amount by 6 and 3 times, respectively, were the significant advantages obtained.

Introduced in 2003, QuEChERS is among the extraction methodologies that most closely matches the requirements of safety and sustainability with those of high analytical performances. A generic QuEChERS procedure involves a first extraction step in which water and an organic solvent are added to the homogenized solid sample, obtaining a phase separation through the salting out effect due to the addition of inorganic salts (NaCl and $MgSO_4$); the salting out effect also favors the analyte transfer to the organic phase. The second step of the procedure is D-SPE, performed to remove the interfering compounds co-extracted with analytes in the first step. The principal benefits of the QuEChERS method are the high extraction efficiency and the employment of low amounts of toxic solvents. Moreover, the possibility of commercially available kits, in which the extraction procedure is explained step by step, has made their application very simple.

A representative example is reported by Ly et al. [74]. The authors determined 400 pesticide residues in green tea leaves by LC-MS/MS and GC–MS/MS. After grinding tea leaves, the analytes were extracted following a QuEChERS extraction procedure with 10 mL of ACN (1 % CH_3COOH), while the extract from the first step was purified employing graphitized carbon black/PSA sorbents in a mixed mode SPE. At 10 μg/kg, 373 pesticides showed recovery between 70 and 120 % and 390 pesticides an RSD <20 %. Surely, the combination of the sample preparation performance and the efficiency of LC/GC–MS apparatus offers very high throughput, allowing the analysis of a huge number of pesticides per sample in short time. Kecojevic et al. [75] reported the development of an analytical method for the determination of 179 pesticides in cabbage and rice by modified QuEChERS extraction. The clean-up step was avoided by diluting the extract from the first step; in this way, the process was simplified and the possible loss of analytes during sample preparation was minimized. The matric effect was controlled through an adequate dilution of the extract (acetonitrile: final extract 1:1, v/v). For all types of foods, recoveries ranged between 70 and 120 % with an RSD <17 %.

Several approaches aimed to make QuEChERS greener can be found in the literature. The miniaturization and the elimination of petrol-based solvents are the two main aspects involved in its evolution. Modified μ-QuEChERS, in which a reduced amount of extraction solvent is used (<10 mL), has been applied to treat different food matrices, such as juices, milk [76], raspberry [77], red pepper [78], and mussels [79]. El-Deen et al. [80] describe the application of μ-QuEChERS coupled to air-assisted DLLME for the determination of fifteen PAHs in coffee, using only 1 mL of acetonitrile for the QuEChERS step and diethyl carbonate for the DLLME, the latter being a green bio-based and biodegradable solvent. The method also showed good analytical performance with recoveries greater than 90 %.

Although QuEChERS offers excellent results for hundreds of different compounds in many food matrices, polar and low-molecular weight pesticides are difficult to extract with this technique (for example, glyphosate and its metabolites). Additionally, despite good results, other techniques such as PLE provide better yields even if resorting to more expensive apparatuses.

3.3. Neoteric extraction solvents

Together with the miniaturization and the application of assisted techniques, the development of new solvents represents the third key point in improving solvent-mediated extraction procedures. The selection of safer solvents meets the 2nd principle of GSP. Traditional petrol-derived solvents, characterized by high toxicity to humans and the environment, high flammability, and explosivity, are nowadays replaced by biocompatible and biodegradable solvent systems such as, deep eutectic solvents (DES), low transitions temperature mixtures (LTTM), supramolecular solvents (SUPRAS) and switchable solvents (SS). However, several classical and less classical organic solvents have recently been revaluated according to the CHEM21 guidelines [81] and ranked in recommended, problematic, and hazardous.

Neoteric solvents (DES, LTTM, SUPRAS, SS, etc.) represent the new frontiers in solvent-mediated extractions for their green/sustainable characteristics, biodegradability, and possibility of modulating their solvent properties [82]. However, some of them show problems of compatibility with the instrumental analysis conditions, as discussed in the following sections.

3.3.1. Deep eutectic solvents

DESs and LTTMs are mixtures with a transition (melting for DESs and glass transition for LTTMs) occurring at a temperature very much lower than the melting points of the individual starting components. Only mixtures that are liquid at room temperature are interesting within the analytical field. DESs are systematically described by the general formula $Cat^+X^-\cdot zY$, where Cat^+X^- is a salt, often composed by a quaternary ammonium cation and a Lewis base as the counterion (e.g. Cl^-); Y is a Lewis or Brønsted acid that acts as complexing agent and z is the number of Y molecules. Depending on the nature of Y, DESs have initially been classified in four main classes [83]. Recently, a fifth class has been added which include DESs based on non-ionic species with phenolic and aliphatic hydroxyl groups, such as the terpenoids thymol and menthol [84]. Among classes I-V, the most used ones in analytical chemistry are type-III and type-V DESs. Regardless the class, a DES is the result of a self-association mediated by hydrogen-bonds between an acceptor (HBA) and a donor (HBD). Depending on the polarity of HBA and HBD,

DESs can be hydrophilic (type-III DESs), quasi-hydrophobic (type-III DESs), and hydrophobic (type-III and type-V DESs) and so applied to treat matrices of different nature for extraction purposes [85–87]. Like ionic liquids, DESs exhibit low vapor pressure, low flammability, negligible toxicity and ease of preparation with high purity grade [88]. Natural deep eutectic solvents (NADESs) are DESs whose components HBA and HBD are obtained from natural sources, such as amino acids, organic acids, sugars and their derivatives characterized by non-toxicity and biodegradability [89].

Popovic et al. [90] synthesized three different types of NADES based on choline chloride (ChCl) as the HBA and malic acid, urea, and fructose (MalA, Ur, and Fru) as the HBD. The fast synthesis (30 s) and the rapid (<5 min) extraction procedure (MAE) allowed the authors to extract polyphenols from sour cherry pomace very quickly. Compared to conventional solvents, the extract based on the ChCl:MalA was 62.33 % more efficient.

Nia et al. [91] applied a NADES composed of serine (HBA)/lactic acid (HBD) (1:5 molar ratio) to perform two-phase HF-LPME of caffeic acid from coffee, green tea and tomato samples. The NADES was used to impregnate membrane and lumen of the hollow fiber. The tomato samples were peeled and squeezed to obtain the juice; coffee and green tea were diluted with hot distilled water and stirred for 1 h at 80 °C. Finally, all the prepared food samples were centrifuged, filtered and submitted to HF-LPME. For each experiment, U-shape HF was placed in 10 mL of sample solution and stirred at 840 rpm till the extraction was completed. The analyte-enriched acceptor solution was taken using a needle micro-syringe and analyzed by the HPLC-UV. The extraction procedure provided quantitative recoveries (> 92.0 %) with a high EF (>400). However, each piece of HF was utilized only once to avoid memory effects.

Another interesting application was the work by Dal Bosco et al. [92] who synthetized a hydrophobic eutectic solvent (ideal mixture, not deep) based on L-menthol and butylated hydroxytoluene (BHT) (3:1 molar ratio) with a strong antioxidant activity due to the presence of BHT into the mixture. The authors applied the ES for the DLLME of carotenoids and fat-soluble vitamins from fruit juices, providing a precise (4–8 %) and accurate (4–6 %) method with recoveries ≥70 %. The antioxidant power of the mixture was useful to preserve the photo-oxidable analytes during both the extraction and for the time before the HPLC-MS analysis.

Interesting applications are represented by switchable DESs in which the polarity of the solvent can be reversed instantly by varying temperature [93], bubbling a gas [94], changing the pH [95] or the ionic force of the sample.

Salamat et al. [96] prepared a pH-dependent switchable DES based on octylamine, succinic acid and water in a molar ratio 1:2:5 to be used for the DLLME of curcumin from food samples (herbal tea boiled and then hydrolyzed with HNO_3). After the DES addition to the digested tea sample, the addition of an alkaline solution (NaOH) promoted the conversion of the hydrophilic DES into a hydrophobic phase. After transferring the extract in another tube, the addition of a HCl solution allowed the recovery of the synthesized DES. As a result, the extracted analyte was separated from the DES phase and determined by a spectrophotometer. Fig. 5 shows the scheme of the DLLME procedure. The relative recovery of curcumin was 92.6 %–100.3 %, with a precision <6.4 and an EF of 38.68.

Despite the considerable advantages, DES and LTTM have also some limitations: (*i*) for hydrophobic and quasi-hydrophobic systems, it is difficult to find a compromise with chromatographic reversed phase conditions; (*ii*) such mixtures can interfere with the analyte detection; (*iii*) the high viscosity due to the dense network of hydrogen bonds requires dilution with water (in case of hydrophilic DES) or with an organic solvent (in case of quasi-hydrophobic DES); (*iv*) the separation of a DES from the extracted biomolecules is not a trivial issue. In the last case, an approach often experienced is the so-called back extraction which, however, requires the use of an additional solvent. To date, this solution does not appear to be the most suitable one because of its inner irreconcilability with the GAC principles and inevitable additional costs, which can represent a problem in industrial applications.

3.3.2. *Switchable solvents and supramolecular solvents*

Switchable hydrophilicity solvents (SHS) are essentially based on amidines (i.e. secondary/tertiary amines) and saturated fatty acids. Properties of switchable-hydrophilicity solvents have briefly been introduced above. The peculiar characteristics to change in situ the water solubility through an external agent (i.e. bubbling CO_2 into the donor solution) allows one increasing the dispersion and the analyte mass transfer in a similar way to DLLME, but with the advantage of avoiding both shaking techniques and centrifugation [97]. Anyway, aspects like the synthesis conditions and the component biodegradability can reduce the greenness of these solvents.

Abdullahi et al. [98] prepared an edible oil-based switchable-hydrophilicity solvent to perform the liquid–liquid microextraction of lead as its metal chelate with ammonium pyrrolidine dithiocarbamate (APDC) from food samples (canned tuna fish, carrot, onion, potato and yam), followed by determination with flame-atomic absorption spectrometry (FAAS). Edible oils are mostly triglycerides that can be easily converted into their corresponding hydrophilic salts of fatty acids (SFAs) through a simple saponification reaction. SFAs are thus promising solvents for switchable-hydrophilicity solvent liquid–liquid

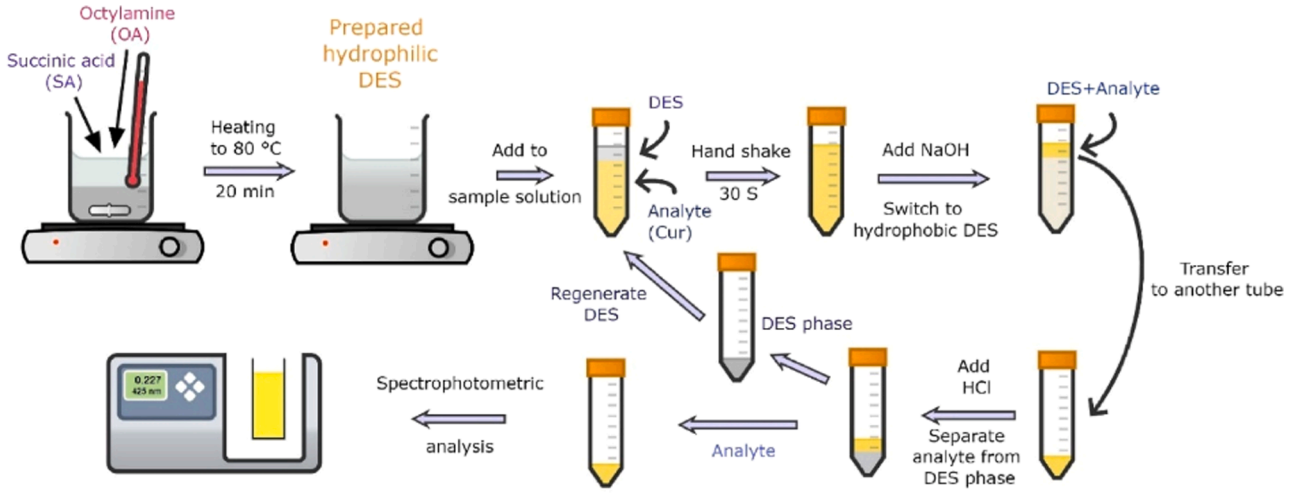

Fig. 5. Scheme of the DLLME procedure based on a switchable solvent to extract curcumin from food samples (from [96]).

microextractions, which form a stable emulsion in aqueous solution providing large surface area for the analyte extraction. After being ground, each sample was treated with a nitric acid/ hydrogen peroxide mixture (5:1, v/v) and digested at 120 °C for 2 h; then the pH of the sample digestate was adjusted to 4.50 with 1 M acetate buffer and added with 1.0 % (w/v) APDC for complexation of lead. Optimum extraction conditions were achieved using coconut oil as the extraction solvent and 2.0 M sulfuric acid as the hydrophilicity switching-off trigger. Finally, the analyte-rich extract was back-extracted with 8 M nitric acid, and the concentration of lead was determined via micro-injection in FAAS. Precision was <4.6 %, while accuracy within the range of 97.1–106.0 %.

The major advantages of SHS are their simple recovery after the analyte pre-concentration and isolation. The challenge associated with their use is that chemicals used during their synthesis, such as amines, amides and amidines, are not always green.

SUPRAS have been defined as nanostructured liquids produced in colloidal solutions of water-immiscible amphiphilic compounds, such as surfactants and long-chain carboxylic acids, through spontaneous and sequential phenomena of self-assembly and coacervation [99]. The SUPRAS formation process occurs initially on a molecular scale by the self-aggregation of amphiphilic species in solution into three-dimensional molecular structures above the critical aggregation

Table 2
Selected applications in food analyses in which solid-liquid, liquid-liquid extractions were used.

Analyte	Extraction technique	Type of solvent	Food matrices	Instrumental technique	Analytical performance	Refs.
Pesticides	SFO-DLLME	DES: 1) Choline chloride: ethylene glycol (ChCl: EG) 2) Menthol: decanoic acid	Milk	GC-FID	LODs = 0.90–3.9 ng/mL LOQs = 3.1–13 ng/mL R = 64–89 % EFs = 320–445	[105]
Fluoroquinolones	SO-DLLME-BE	DES: *n*-decanoic acid (DecA): methyltrioctyl ammonium bromide (N_{8881}-Br) 2:1	Milk, honey, tap water, yogurt	MECC-UV	LODs = 0.006–0.010 μg/mL LOQs = 3.1–13 ng/mL R = 87.8–114.1 % EF = 531–858	[106]
Heavy metals: cadmium (Cd) and arsenic (As)	UAE-DLLME	DES: DL-lactic acid/ trioctylmethylammonium chloride 1:3	Wine	FAAS	LOD: 0.08 μg/L and 0.30 μg/L for Cd and As, respectively LOQ: 0.25 μg/L and 1.00 μg/L for Cd and As, respectively R = 90.6–103.6 %	[107]
Free L- tryptophan	RP-DLLME	DES: Choline chloride: urea 1:2	Vegetable oils	HPLC-DAD	LOD: 11 mg kg^{-1} R = 93 %	[108]
Antibiotics	HF-LPME	HCl 0.1 M	Eggs	SERS	LOD: 10 ng/g	[109]
Terpenes	HS-SDME	DES: N_{4444}Br and dodecanol 1:2	Spices: cinnamon, cumin, fennel, clove, thyme, and nutmeg	GC–MS	LOQs: 0.47–86.40 μg/g	[110]
Thallium: Tl(III) and Tl (I)	DI-SDME	1) PAN-1-dodecanol 2) DCH-18-C-6-nitrobenzene	Soft Beverage	GFAAS	LODs: 1.9 ng $L-1$ and 2.5 ng/L for Tl (III) and Tl(I) LOQs: 6.3 ng/L and 8.3 ng/L for Tl(III) and Tl(I), respectively ER=300 R = 90.0–110 %	[111]
Manganese ethylene-bisdithiocarbamate (maneb)	SUPRAS	(1-(2-pyridylazo)−2-naphthol complex at pH 12.0) (PAN) (750 μL) 1-decanol and tetrahydrofuran	Potato, cracked wheat, and rice	HPLC-DAD	LOD: 2.22 μg/L LOQ:7.32 μg/L R: 89–109 %	[112]
Neonicotinoid insecticides	SUPRAS	1-decanol and tetrahydrofuran	Fruit juice samples (watermelon, and rose apple)	HPLC-DAD	LOD: 0.01 μg/L LOQ: 0.025 μg/L R = 81–119 % ER=33	[113]
Organophosphorus and pyrethroid pesticides	QuEChERS-SFO- DLLME	*n*-hexadecane	Lettuce, long bean, broccoli, tomato, carrot, pumpkin, siew pak-choy, sweet choy sum, sweet pak choy, celery, amaranth, spinach, cabbage, mushroom, and cucumber	GC–MS	LOD:0.3–1.5 μg/kg LOQ: 0.9–4.7 μg/kg R = 61.6–119.4 %	[62]
Fenazaquin	QuEChERS SS-LPME	N,N-Dimethylbenzylamine	Tomato	GC–MS	LOD: 0.05 ng/mL LOQ: 0.18 ng/mL R = 97.4–105.9 % ER=800	[114]
Lead (Pb)	SS	Coconut oil	Carrot, fish, onion, potato and yam	FAAS	LOD: 2.8 μg/g LOQ: 9.4 μg/g R = 97.1–106 %	[98]

DI-SDME: Direct immersion single-drop microextraction; HF-LPME: Hollow fiber liquid-phase micro-extraction; HS-SDME: Headspace single-drop microextraction; QuEChERS-SFO- DLLME: Quechers- Solidification of a floating organic drop-dispersive liquid-liquid microextraction; QuEChERS-SS-LPME: Quechers-switchable solvent liquid phase microextraction; RP-DLLME: Reversed phase dispersive liquid-liquid microextraction; SFO-DLLME: Solidification of a floating organic drop-dispersive liquid-liquid microextraction; SO-DLLME-BE: Salting out-assisted dispersive liquid-liquid microextraction-back extraction; SS: Switchable solvent; SUPRAS: Supramolecular solvent liquid phase microextraction; UAE-DLLME: Ultrasound-assisted dispersive liquid-liquid microextraction; MECC-UV: Micellar electrokinetic capillary chromatography-ultraviolet detection; FAAS: flame atomic absorption spectroscopy.

concentration (CAC). Over the few last years, SUPRAS have become a viable alternative to organic solvents for sample preparation due to their peculiar properties. The ordered structure provides microenvironments of different polarities, multiple binding sites which can establish different interactions with analytes (ionic interactions, hydrogen bonding, π-cation, and hydrophobic interactions), and the possibility of customizing their properties through appropriate selection of amphiphiles [100].

Although SUPRAS have been applied to different food matrices such as milk, honey, eggs [101], wine, vegetables, tea, and infant food, [102, 103], adjustments are still required to make SUPRAS-based methods analytically robust. An interesting comparison between extraction procedures based on SUPRAS, alkaline hydrolysis, sonication, and QuEChERS was reported by Singh et al. [104] who validated a method for analyzing PAHs in cooked chicken and roasted coffee. In this work, the authors compare the performance of these extraction techniques taking in consideration the process efficiency, the environmental burden, and the greenness. The recoveries obtained through sonication and alkaline hydrolysis were significantly lower; on the other hand, SUPRAS displayed satisfactory recoveries for high-weight PAHs in chicken samples (ranging from 71.33 % to 112.23 %), even if notable interferences from the sample matrix were observed. QuEChERS was identified as the most effective extraction method in terms of recovery (ranging from 52.63 % to 103.85 %) and selectivity. The results of a quantitative green chemistry evaluation demonstrated that QuEChERS is the least time- and energy-consuming process. However, the SUPRAS method holds an equivalent value as it generates minimal waste residues and requires a smaller amount of solvent/chemical. Table 2 lists some selected applications based on solvent-mediated extractions.

4. Conclusions and perspectives

Green extraction techniques are “mature” but “underused” in food analysis, where conventional extraction techniques are still largely applied especially to treat complex food samples. However, in this review, we have seen that, beyond the sustainability aspect, conventional procedures can also have limitations in terms of analytical performance as, for instance, the analyte extraction from animal and plant tissues. For such matrices, the diffusion of solvents into the sample matrix is limited due to the structures of cell walls. The use of physically assisted techniques (examined in Section 3.2) can enhance the diffusion of solvents, and disrupt cell walls. Thus, PLE and MAE overcome Soxhlet performance because they allow solvents to penetrate the matrix and accelerate the analyte mass transfer, increasing recoveries and decreasing the extraction time. We have also highlighted how one of the main trends is the development of miniaturized techniques. Nevertheless, their applicability for the analysis of contaminants or minor components present at trace levels in foods is still in question and researchers must ensure that a representative sample is taken from such naturally inhomogeneous samples. We have discussed the necessity for automation to allow fast on-line extraction and analysis, even if attention should be paid to increase the robustness of such methods. With complex samples such as foods, the reproducibility is often matrix dependent and, therefore, a combination of different techniques can be required to extensively remove interfering compounds, trying to achieve the required analytical performance in as few steps as possible.

All of the discussed extraction techniques have their advantages and disadvantages. What they all have in common is that they are part of a sustainable development towards the use of less (or no) organic solvents and biodegradable sorbents from renewable sources; moreover, they are quicker, less toxic, more automated, sensitive and easier to use than classical extraction techniques. It is important not to forget that sustainability should not overshadow the analytical request you are trying to fulfil. A critical point is that of many of these methods have been tested on a restricted number of analytes or based on lab-made devices. That being so, major efforts in this sector should be invested in the design and commercialization of accessible technologies and cheap devices to extend their applicability as much as possible.

In general, the matrix complexity and the foodstuff heterogeneity guide the choice of the extraction approach, and some appear to be more recommended or practicable than others. Last but not least, green metrics turn out to be useful tools to compare new green methods with the classic ones to highlight the real improvements produced [115].

CRediT authorship contribution statement

Massimo Giuseppe De Cesaris: Writing – original draft, Conceptualization, Visualization. **Lorenzo Antonelli:** Writing – original draft, Conceptualization. **Elena Lucci:** Writing – original draft. **Nina Felli:** Writing – original draft, Data curation, Formal analysis. **Chiara Dal Bosco:** Data curation, Methodology. **Alessandra Gentili:** Writing – review & editing, Supervision, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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