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Review

Exploring the Potential of Microextraction in the Survey of Food Fruits and Vegetable Safety

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Abstract: The increasing demand for food to feed an exponentially growing population, the fast evolution of climate changes, how global warming affects soil productivity, and the erosion of arable lands, create enormous pressure on the food chain. This problem is particularly evident for fresh fruits and vegetables that have a short shelf life. For this reason, food safety precautions are not always a priority and they are often overused to increase the productivity and shelf life of these food commodities, causing concerns among consumers and public authorities. In this context, this review discusses the potential of microextraction in comparison to conventional extraction approaches as a strategy to improve the survey of food safety requirements. Accordingly, selected examples reported in the literature in the last five years will focus on the detection and quantification of pesticides, antibiotics, hormones, and preservatives in fresh fruits and vegetables using different extraction approaches. Overall, the use of microextraction techniques to survey the presence of contaminants in the food chain is very advantageous, involving simpler and faster protocols, reduced amounts of solvents and samples, and consequently, reduced waste produced during analysis while conserving a high potential for automation. Additionally, this higher greener profile of the microextraction techniques will boost a progressive substitution of conventional extraction approaches by microextraction processes in most analytical applications, including the survey of food chain safety.

Keywords: microextraction; food safety; food analysis; fruit; vegetables; pesticides; antibiotics; hormones; food preservatives

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Citation: Berenguer, C.V.; García-Cansino, L.; García, M.Á.; Marina, M.L.; Câmara, J.S.; Pereira, J.A.M. Exploring the Potential of Microextraction in the Survey of Food Fruits and Vegetable Safety. *Appl. Sci.* **2023**, *13*, 7117. https://doi.org/10.3390/app13127117

Academic Editor: Monika Gibis

Received: 16 May 2023
Revised: 7 June 2023
Accepted: 12 June 2023
Published: 14 June 2023

1. Introduction

Today's consumers are increasingly concerned about agriculture, nutrition, and sustainability, and they want to know where food comes from, how it was grown, what kind of industrial processes it suffered, and if it contains natural/synthetic food additives or not [1]. While fresh fruits and vegetables are important sources of phytonutrients such as polyphenols, vitamins, minerals, and fibres, they may also contain contaminants such as pesticides, antibiotics, or food preservatives [2]. Farmers use these contaminants to protect their crops and promote growth. Without suitable pest control measures, farmers could lose up to 40% of their yield, requiring more land, water, seed, tractor fuel, labour hours, and pest-control products to continue their activities [3,4]. However, the passive consumption of these molecules can have serious consequences for human health.

To address these concerns, many countries have strict regulations concerning the Maximum Residue Limits (MRLs) for pesticides in food [5]. The European Union (EU), for example, has established MRLs for 315 pesticides, with a default limit of 0.01 mg kg^{-1} for new pesticides [5] and the European Food Safety Authority (EFSA) prepares annual reports on pesticide residues in foodstuffs to control these MRLs [6]. The most recent report, approved in 2021 for the year 2019, found that pesticides exceeding their MRLs were present in almost 4% of the samples analysed, highlighting the importance of controlling pesticide presence in food for human health [6]. Another major concern is the presence of antibiotics in fruits and vegetables, which can promote antibiotic resistance and compromise food safety and the consumer's trust in the food chain [7–9]. Antibiotics can enter these samples using natural fertilizers derived from human or animal faeces processing.

The use of food preservatives can also impact human health [10]. Sulphites, for example, are marketed as preservatives and can be classified as antioxidants, antimicrobials, and antibrowning agents [11]. However, they can also have anti-nutritional consequences by promoting the degradation of vitamin B1 [10].

Different extraction techniques can be employed to assess food safety. This selection depends on several factors, with the nature of the target analytes as one of the most important. Regardless of the target analytes, most methods currently developed still rely on conventional techniques, requiring large sample volumes and organic solvents along with laborious, time-consuming, and complex protocols. However, the growing concerns with the environment and planet sustainability are boosting the interest in the development of microextraction approaches based on green analytical chemistry principles.

Most microextraction techniques employ the same preparation principles as conventional methods with enhanced analytical performance. Additionally, these approaches possess simple and faster extraction procedures, in which lower sample and solvent volumes are used [12].

In this context, this review will discuss the advantages of moving from conventional extraction techniques to modern microextraction approaches to survey the presence of pesticides, antibiotics, and preservatives in fresh fruit and vegetables, taking into consideration the works reported in the literature in the last five years.

1.1. Food Safety—Major Contaminants of Fresh Fruits and Vegetables and Their Toxicity

1.1.1. Pesticides

Pesticides are applied to protect plants from harmful organisms and pests, including insects (insecticides), weeds (herbicides), rodents, or fungi (fungicides), and to help control diseases [4]. However, their use can lead to long-term hazards for the environment and biodiversity due to their inherent toxicity [13,14]. Therefore, in recent years, great efforts have been made to develop pesticides that degrade faster, do not accumulate, and have less toxicity to humans and wildlife [4]. Pesticides can be very diverse and constitute a broad family of compounds, such as organochlorines, carbamates, and synthetic pyrethroids.

Organochlorines, also known as chlorinated hydrocarbons, are organic pesticides that contain at least five chlorine atoms. Examples of these include dichloro-diphenyl-trichloroethane (DDTm), aldrin, hexachlorocyclohexane (HCH), heptachlor, chlordane, and endosulfan [15] (Figure 1). Organochlorines are effective insecticides due to their ability to harm a wide range of insects. They are structurally related to steroid hormones and act on the respective hormone receptors. For example, DDT and chlordane can cause convulsions and paralysis by disrupting the nervous system of the target pest, ultimately leading to death [13,16]. These pesticides are volatile and resistant to environmental degradation [17], belonging to the class of persistent organic pollutants with high persistence in the environment [13,16]. Therefore, these pesticides can accumulate in the food chain and tissues, resulting in chronic exposure to animals and humans [16].

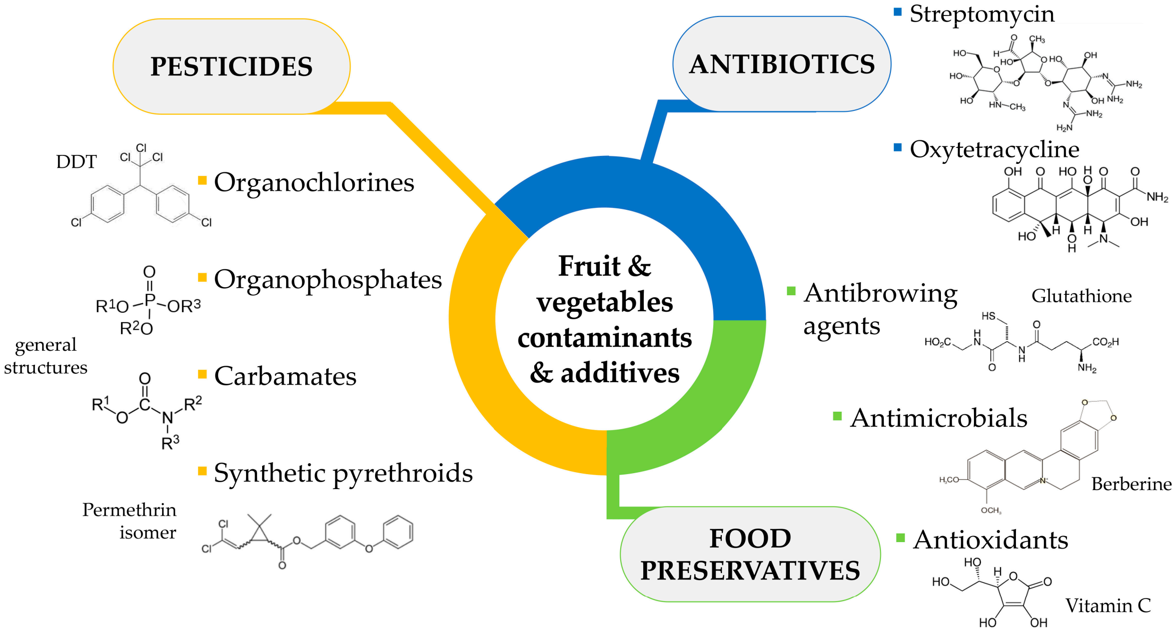

Figure 1. Major types of fruit and vegetables contaminants and additives.

Organophosphorus pesticides contain thiophosphoryl functional groups and are commonly found in the soil, atmosphere, groundwater, and agricultural products. They have moderate effectiveness and low persistence [18]. This group of pesticides is biodegradable and rapidly degrades by hydrolysis when exposed to light, air, and soil, minimizing environmental pollution [17,19]. However, they pose significant concerns for the environment, health, and food safety, and are detected in small amounts in food and drinking water [17].

Humans can absorb organophosphates through inhalation, ingestion, and dermal penetration [20]. This group of pesticides tends to phosphorylate the acetylcholinesterase enzyme (AChE) [20], thus, acting as AChE inhibitors with implications in the transport of nerve impulses [13]. Chlorpyrifos, diazinon, and dichlorvos are examples of organophosphates, along with parathion and malathion (Figure 1), which are commonly associated with stomach and contact poison, including fumigant infection that results in nerve poisons [13,15].

Carbamates and organophosphates share similar structures and working principles. Both pesticide groups disrupt nerve impulse transmission at the synaptic level through AChE inhibition, effectively killing target pests. Carbamates (Figure 1) are derived from carbamic acid and naturally degrade within weeks or months, minimizing environmental pollution [17]. They are commonly used as herbicides and fungicides, with examples including carbaryl, aldicarb, carbofuran, ethienocarb, fenobucarb, methomyl, and aminocarb [13,15]. However, these pesticides may adversely affect renal, hepatic, neurological, reproductive, immune, and metabolic functions in both humans and animals. Additionally, carbamate pesticides are classified as endocrine-disrupting chemicals, as they can interfere with the synthesis, secretion, transport, metabolism, and elimination of a wide range of hormones [21].

Synthetic pyrethroids are a combination of organic pesticides that are manufactured by duplicating natural pyrethrins. They act on the voltage-gated sodium channels in cell membranes, disrupting the sodium ion flux, which leads to the paralysis of the organism [17]. This group of pesticides is mostly used against insects and includes deltamethrin, esfenvalerate, fenvalerate, cypermethrin, or permethrin [13,16]. Synthetic pyrethroids are non-persistent and easily break down when exposed to light, as they have a fast biodegradation capacity. They have a comparatively low level of mammalian toxicity [17], making them one of the safest insecticides that can be applied to food products. Exposure to very high levels in the air, food, or water may cause giddiness, headache, vomiting, muscle twitching, low energy, convulsions, and loss of consciousness [17,22].

1.1.2. Antibiotics

Antibiotics are widely used around the world to control plant diseases. Agricultural antibiotics are applied at very low concentrations, and their quantity per unit area is much lower than that of other conventional pesticide chemicals [23]. However, antibiotics can exert continuous selective pressure on soil microbiomes for extended periods of time, leading to the selection of microorganisms with antibiotic-resistance genes [24]. These genes can be transmitted to potential pathogens through horizontal gene transfer mechanisms, which prolongs the dissemination of antibiotic resistance in the environment [23,25]. Additionally, fresh edible vegetables could potentially serve as reservoirs of antibiotic resistance [26,27]. Humans can also be exposed to antibiotics through the potential prevalence of antibiotic resistance, due to selective pressure on bacteria of clinical importance [27,28]. The most commonly used antibiotics in plant agriculture are streptomycin and oxytetracycline (Figure 1).

Streptomycin is an aminoglycoside antibiotic that is naturally produced by soil actinomycetes. It is used in the United States of America (USA) to control fire blight, which is an important disease in Rosaceae members. Minor uses of streptomycin include controlling plant bacterial diseases in floriculture as well as on potato tubers, tobacco seedlings, and other vegetable seedlings in the field or greenhouse [23,29]. This antibiotic is bactericidal and acts by irreversibly binding to the bacterial ribosome, thereby blocking protein synthesis [30,31].

Oxytetracycline, a tetracycline antibiotic produced naturally by *Streptomyces rimosus* [32], is primarily used to manage fire blight and other serious diseases in fruits (pears and apples as well as stone fruits such as peach and nectarine) and vegetable crops [23,31]. In rare instances, it can be used internally in plants to treat lethal yellowing diseases on palm and elm trees, as well as other diseases caused by phytoplasmas. This antibiotic is bacteriostatic and inhibits the multiplication of bacterial cells by binding reversibly to the bacterial ribosome, thus, blocking protein synthesis [31,32].

1.1.3. Food Preservatives

Food and food products are susceptible to deterioration due to microbiological, enzymatic, physical, and chemical changes. These changes may reduce their quality, nutritional value, and safety [33]. To mitigate these deleterious effects, food additives are added to foodstuffs to perform specific functions, such as preserving food, adding colour, taste, sweetening, and texture, among others. Additives are added during the food's manufacture and their amount is determined for each foodstuff. To ensure that the overall daily consumption by an individual does not exceed the Admissible Daily Intake (ADI) [11,33]. Preservatives are one of the most important groups of additives [33] and are subdivided into three smaller functional groups, which are antioxidants, antimicrobials, and antibrowning agents (Figure 1) [11].

Antioxidants prevent or inhibit lipid oxidation in food and the autoxidation of pigments, flavours, lipids, and vitamins [34]. They are classified as natural or synthetic and both have been reported to delay and prevent the cell damage caused by oxidative stress. The functional antioxidant groups of additives approved by EFSA have been reviewed by Carocho et al. [11].

Synthetic antioxidants are created from chemical processes [35]. Examples of synthetic antioxidants include terbutylhydroxyanisol (BHA, E320), butylhydroxytoluene (BHT, E221), tert-butylhydroquinone (TBHQ, E319), and propyl gallate (PG, E310) [11,35,36]. However, these have been associated with harmful health effects. BHA and BHT have shown carcinogenic and toxicological effects. TBHQ induces toxicity at cellular and molecular levels through reactive oxygen species (ROS) [36,37], which results in detrimental impacts on deoxyribonucleic acid (DNA) and some types of genotoxicity [38]. Concerning PG, it has been reported to contribute to mitochondrial impairment and inhibition of cellular respiration [39] as well as affect both cancer and normal cells, potentially leading to DNA fragmentation, genotoxicity, and cytotoxicity [36,40]. Given the harmful health effects of synthetic antioxidants, there is a demand for new and more efficient natural antioxidant agents. Natural antioxidants are obtained entirely from natural sources and consumers believe in their safety and non-toxic impacts on health. Moreover, it has been demonstrated that natural non-enzymatic antioxidants can be beneficial in preventing a range of chronic diseases, such as cancer, diabetes, and cardiovascular diseases [33]. These compounds are natural food antioxidants and include polyphenols, phenolic acids, and carotenoids [11].

Antimicrobials are added to control and prevent natural spoilage and contamination by microorganisms [11,34]. These compounds delay the proliferation and growth of pathogenic microorganisms (bacteria, yeasts, and moulds), ensuring food safety and quality [41,42]. Generally, two types of antimicrobials are applied: natural and artificial types [33].

Artificial antimicrobials are substances of chemical origin, including salts and organic acids (e.g., propionates, benzoates, sulfites, nitrites, chlorides, potassium sorbate, lactate, sorbic, citric, tartaric, and ascorbic acids). However, some of these substances are still subject to discussion and have acknowledged controversy due to research inconsistency. For instance, sorbates, sulfites, and nitrates have been associated with cancer and allergies. Sulfites can induce deterioration of thiamine (vitamin B1) in foodstuffs [43] and their use can lead to allergic reactions (e.g., nausea, urticaria, or asthma) in consumers with hypersensitivity to this compound [33]. Therefore, there is an increased interest in antimicrobials of natural origin.

Plant extracts can be used as natural antimicrobials and they can protect fresh food while providing health benefits. Antimicrobial compounds in plants include essential oils, polyphenolic compounds, polypeptides, lectins, and alkaloids, along with polyamines, organic acids, glucosides, and glucosinolates. Polyphenolic compounds modify microbial cellular permeability, inducing damage to cellular components and the penetration of other substances inside the cell [33]. Plant essential oils have been introduced as a way to improve the stability of fresh-cut fruit, due to their antimicrobial activity against microorganisms and pathogens [44].

Antibrowning agents are used to prevent browning, which typically occurs during the handling, processing, and storage of fruits and fruit products. There are two types of this phenomenon, enzymatic [44] and non-enzymatic browning [11,45]. The food industry uses anti-browning techniques to stop the enzymatic browning of fresh fruits and vegetables and extend their shelf life by inhibiting the activity of polyphenol oxidase. Some of these compounds include benzoic acid, cinnamic acid, ferulic acid, and kojic acid, among others, owing to the similarity of their chemical structure to the substrates of enzymatic reactions [45–47]. Sulfiting agents are also widely used by the food industry to inhibit enzymatic browning [47]. Although, their use is restricted in many countries due to safety issues, as sulfites have been linked to off-flavours and allergic reactions [48]. Several sulfite substitutes have been developed, such as sulfhydryl compounds (glutathione, N-(2-mercaptopropiony) glycine, l-cysteine methylester, and N-acetyl-cysteine) [47,49], as well as ascorbic and citric acids [50,51]. However, none of these have been able to replace sulfite due to its effectiveness [45,47]. Hence, it is important to develop inhibitors from natural sources free of harmful side effects in order to substitute synthetic compounds. Compounds found in honey, onion, pineapple, and chilli peppers such as β-carotene, thiols, bromelain, and other antioxidants have been shown to inhibit the activity of polyphenol oxidase [51].

Overall, the list of compounds that can be found in fruits and vegetables and are considered contaminants or additives with the potential to cause adverse effects on human health (Figure 1) is very long and is subjected to continuous monitoring and updates by competent regulatory authorities.

1.2. The Current Food Safety Regulatory Framework

Europe is the largest consumer of pesticides, followed by China and the USA [52]. Uncontrolled pesticide application leaves residues in the environment, which may persist and lead to pollution and adverse human health effects [52,53]. Furthermore, given the nature of the contamination, such as varying exposure to pesticides, differences in plant uptake mechanisms from the environment, or contaminants from food packaging, some food products may be more contaminated than others [53].

Monitoring programs worldwide aim to assess food safety. However, it is important to note that such monitoring cannot completely prevent the supply of contaminated food to consumers, since pesticides are tested on their active ingredients and may additionally contain highly toxic and carcinogenic substances declared as inert in the formulation [52,53]. Food regulations are in place at both national and international levels to restrict contaminated food from entering the human food chain. The Joint Food and Agriculture Organization (JECFA) and the Codex Alimentarius Commission (Codex), both play an important role in ensuring fair practices in the food trade to protect the consumers' health [11].

National authorities and regulatory bodies control and enforce MRLs by regularly checking pesticide residues in food [52,54]. In Europe, the European Commission (EC) is responsible for the approval of pesticide-active substances in the EU. Since 2006, the EC has implemented new legislation, the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH), EC regulation 1907/2006, to identify properties of chemicals, protecting both the environment and human health [53]. The EC regulation 396/2005 provides a coherent system of setting MRLs for all food treated with pesticides [55]. Moreover, in the EU document SANCO12571/2013, the EC states the methods of sampling for pesticide residues [52,56,57]. The EFSA is also responsible for legislating and regulating food additives in the EU by working with regulatory bodies worldwide to refine methodologies and provide risk assessors to determine possible combined effects derived from multiple pesticide exposure through food [58].

In the USA, the Environmental Protection Agency (EPA) oversees a registration process for pesticides to comply with federal laws, which enforce regulations and establish MRLs in food and feed. The Food and Drug Administration (FDA) enforces MRLs for plant commodities, while the Occupational Safety and Health Administration (OSHA) ensures the safety of people working with pesticides [59]. In Canada, the Pest Management Regulatory Agency (PMRA) is responsible for regulating pest control products, while in Russia federal law No. 107 FL regulates pesticide application [52,55]. In Australia, pesticides regulation is shared by the Commonwealth, state, and territories through the national registration scheme of the Australian Pesticides and Veterinary Medicines Authority (APVMA) and Food Standards Australia New Zealand (FSANZ), which establish pesticide MRLs in food [52,60].

In China, the Institute for Control of Agrochemicals regulates pesticides, and most MRLs do not defer to Codex [61,62]. In India, pesticides are regulated under the Central Insecticides Board and Registration Committee (CIB&RC), while the Food Safety and Standard Authority of India (FSSAI) sets the MRLs of registered pesticides [63].

However, some countries in Southeast Asia do not have pesticide legislation and regulations. The same situation occurs in some African countries, which do not have a pesticide registry system, leading to a high frequency of toxic illegal pesticides [64]. Nonetheless, most African countries have adopted pesticide MRLs from the Codex limits or that of the importing country, or have even developed their pesticide laws and regulatory authorities [52,55]. Nevertheless, policymakers need to review and enforce pesticide regulations and product traceability policies to ensure farmers' commitment to safe food production [65]. Developing countries lack the expertise, commitment, resources, and readiness to enforce legislation on pesticide residues [64]. Some of these countries even report low incidences of pesticides due to weak or inadequate control systems, and in most cases, farmers are aware of counterfeit and illegal pesticides and use them to produce food for the public market [52,65,66]. Another problem is the global harmonization of pesticide

MRLs. The Codex and JECFA have attempted to set and review these limits, but they remain variable [52,67–69].

Regulations and relevant laws regarding residual antibiotics in food have only recently been established to ensure food safety [70,71]. Regarding antioxidants, their importance and safety need to be further acknowledged. Furthermore, the harmonization of antioxidant legislation worldwide is still a challenge [11,72]. Given the growing concerns about food safety, society should be educated about safer crop cultivation and livestock rearing, choosing balanced diets, and safer cooking methods. Governments should also seek to reduce urban disparities in environmental exposures since some contaminants can be transported globally. Therefore, nations worldwide should ensure the trade of safer food products on a global scale by reducing environmental and food contamination through the adoption of common food safety laws [53].

2. Extraction Approaches Used to Assess Food Safety

Different analytical approaches are employed to assess food safety. The experimental layout most frequently used is briefly represented in Figure 2. As can be depicted, sample treatment is a very important step of the procedure. An inappropriate sample preparation or target analytes extraction will prevent the obtainment of good analytical performance for those analytes independent of the analytical power and sophistication of the instruments involved in the following steps. Regardless of the extraction procedure, high-performance liquid chromatography (HPLC), the use of ultraviolet (UV) or mass spectrometry (MS) as detection modes, or gas chromatography (GC) coupled with MS are the analytical separation techniques most often reported (Figure 2).

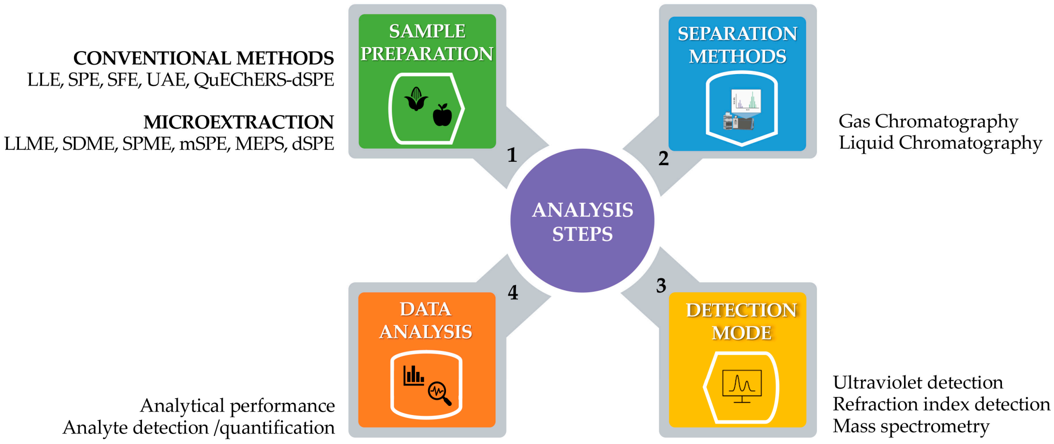

Figure 2. Scheme showing the steps to follow for the determination of pesticides, antibiotics, or preservatives in fruit and vegetable samples.

Depending on the nature of the target analytes, specific extraction techniques should be chosen for their determination. Considering solid samples such as fresh fruits and vegetables, if we are interested in volatile analytes, lyophilization or grinding of the sample for homogenization may be sufficient to obtain the analytes in the headspace. The volatile analytes can be then collected using an appropriate extraction procedure, such as solid-phase microextraction (SPME), followed by GC analysis [73]. On the other hand, if the analytes are not volatile, a solid–liquid extraction (solid–liquid extraction (SLE), ultrasound-assisted extraction (UAE) or supercritical-fluid extraction (SFE)) should be performed in advance to transfer the selected analytes from the fruits and vegetables matrices to a suitable organic phase. A second extraction step, using, for instance, liquid–liquid extraction (LLE), can be then employed before eluting the target analytes in a solvent compatible with the succeeding chromatographic separation [74–77]. Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) is particularly tailored for these applications, just involving an initial salting-out extraction step followed by a dispersive solid-phase extraction (dSPE) clean-up [78].

In the last few decades, alternatives to these conventional techniques have been developed. Most of them are known as green extraction techniques (GreETs) and have very attractive features such as simplifying or automating the extraction procedure, reducing extraction times as well as the volumes of samples and solvents used, and making them more environmentally friendly [12]. These alternatives are often reported as microextraction techniques and most of them employ the same separation principles of conventional extraction downscaled to a microextraction size. It is therefore very relevant to discuss the advantages and bottlenecks of migrating from conventional extraction procedures to microextraction techniques or GreETs in the survey of food safety. Accordingly, the next sections will discuss works found in the literature.

2.1. Conventional Extraction Approaches

Table 1 shows works found in the literature since 2018 using conventional extraction techniques such as SLE, LLE, magnetic solid-phase extraction (MSPE), QuEChERS, salting-out assisted liquid–liquid extraction (SALLE), SFE, UAE, and ultra-high pressure supercritical-fluid extraction (UHPSFE). Overall, the methods proposed showed high sensitivity, with low limits of detection (LODs) reported in most of them.

Pesticides were the most frequently reported contaminant in the articles discussed (Table 1). Akram et al. [74] extracted thiacloprid, a neonicotinoid insecticide, from 5 g of different fruit and vegetable samples, using SLE/SALLE/dSPE as the extraction approach. Good recovery values were retrieved (78.3–92%), as well as acceptable repeatability and reproducibility (reported values below 4.74%). Similarly, Heleno et al. [77] developed an extraction method for azoxystrobin, difenoconazole, and chlorothalonil employing SLE with a low-temperature partition (LTP). The determination of these pesticides was carried out in bell pepper samples and residual concentrations of 0.12, 0.18, and 1.73 mg kg^{-1} were obtained, respectively.

Malathion, chlorpyrifos, and profenofos were determined in red apples and purple grapes through SLE/SPE with methyltrimethoxysilane-chloropropyltriethoxysilane (MTMOS-CPTES), an extraction method developed by Veloo et al. [79]. Good recovery values were obtained (88.3–120.7%) with low standard deviations (1.6–3.3%) compared to the commercial octadecyl silica sorbent (70.3–100.2% ± 6.3–8.8%). SFE using supercritical carbon dioxide ($SC\text{-}CO_2$) as a solvent is a very efficient alternative due to the beneficial characteristics of the solvent, thus, favouring its low consumption [80]. Nakamura et al. [80] used this method to extract four insecticides under a heating temperature of 80 °C and a high elution volume (4 mL in total).

The solvent selection is crucial to obtain a green extraction method. For this reason, green solvents such as deep eutectic solvents (DESs) are being used to replace conventional solvents, which are often more toxic [81]. Until now, DESs have rarely been used as solvents in the UAE for the extraction of analytes in food samples because expensive tandem MS instruments are often required [82,83]. However, there are some notable exceptions. Zhao et al. [84] used a UAE/DES-MSPE method for the extraction of seven pesticides in apple, pear, carrot, and cucumber samples, followed by HPLC-UV analysis, and obtained good LOD values (0.02–0.05 μg mL^{-1}). It is important to highlight that UAE has a lower solvent and time consumption than other conventional extraction approaches, increasing the recovery rates of the target analytes. This is possible because the US enhances the interaction between the solvent and the matrix and lower solvent volumes provide satisfactory results [84]. Similarly, Chen et al. [85] also achieved good LOD values (0.05–0.2 μg mL^{-1}) for the extraction of two fungicides and one insecticide in apple, grape, and tomato samples, using a UAE/DES-LLE approach followed by HPLC-DAD analysis. The QuEChERS coupled with dSPE is a salting-out extraction procedure originally proposed by Anastassiades et al. [86] for the multi-residue detection of pesticides in food products. It was rapidly adopted as a standard extraction procedure due to the simplicity of its use (reviewed in [78]). Chiarello et al. [87] used this methodology for the extraction of 82 pesticides in organic carrots. LODs between 0.3–0.5 μg kg^{-1} were obtained through HPLC-HRMS analysis. The results showed that bendiocarb was detected at high concentrations (199.11 μg kg^{-1}) above its MRL. Chlorpyriphos (43.20 μg kg^{-1}) and amitraz (11.22 μg kg^{-1}) were also detected. Yao et al. [88] compared QuEChERS/dSPE and QuEChERS/dSLE. The authors observed that the dSPE clean-up version retrieved a higher sensitivity. Consequently, it was able to extract a broader range of pesticides and achieved recovery levels of 60–120% (RSD values of 2–28%) and LODs of 0.5–1 μg kg^{-1}. The use of QuEChERS/dSPE as an extraction approach for multi-residue analysis has become very popular and many more examples can be found in the literature [89–93]. Woldetsadik et al. [94] used QuEChERS/HS-SPME coupled with GC-MS for the determination of DDT congeners and four HCH isomers in khat samples. The results showed that all samples had HCH above the MRL set by the EC and, in general, HCH was found at higher concentrations than DDT.

Regarding antibiotics, three works were found employing UAE with commercially available SPE cartridges. Tadic et al. [95] extracted ten antibiotics from different vegetables (lettuce, tomato, cauliflower, broad beans) using the Strata-X SPE cartridge, while Merlo et al. [96] and Hu et al. [9] employed the Oasis PRiME HLB cartridges to extract and quantified seven antibiotics from vegetables and 81 antibiotics from banana and cabbage samples, respectively. The most ideal LODs, in the range 0.001–0.26 ng g^{-1}, were achieved by Hu et al. [9], which were certainly boosted by the higher sensitivity of the analytical instruments used (UHPLC-MS/MS). Parabens are food preservatives still widely used despite the controversies around their toxic effects on human health [97]. Maher et al. [98] employed SLE as a rapid extraction method to survey the presence of five parabens in fruits and vegetables from the local market in Riyadh (Saudi Arabia). The authors used methanol (MeOH) as the extraction solvent and achieved LODs of 0.005–5 μg g^{-1}. De Souza et al. [99] also used SLE for the analysis of gallic acid, rutin, and quercetin in tomato samples. The reported method, however, involved 1 h of stirring during the SLE step. Hejji et al. [100] extracted 24 endocrine disruption compounds (EDCs) in different fruits and vegetables using UAS/SPE. The method proposed involved 10 mL of water reconstitution after UAS extraction and 400 μL of acetonitrile (ACN) elution before GC-MS analysis. Gupta et al. [101] employed QuEChERS/dSPE for the determination of preservatives in juice samples and reported LODs ranging from 8.14 to 25.45 ng L^{-1}.

Table 1. Recent examples of chromatographic methodologies reported for the determination of contaminants in fruits and vegetables involving conventional extraction approaches.

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
Pesticides				
SLE/SALLE-dSPE	5 g spiked sample; 10 mL phosphate buffer (pH 6.7); ACN/H_2O (83:17; *v*/*v*); NaCl/Na_2SO_4 (40.50; *w*/*w*); upper layer collection; dry. Clean-up step: redissolved (10 mL H_2O); Florisil cartridge; elution (20 mL DCM); dry; resuspension (1 mL MP)/HPLC-DAD	Thiacloprid/0.03 μg mL^{-1}	Citrus, guava, tomato, cauliflower, and okra	[74]
SLE/LTP	4 g sample; 4 mL ACN; agitation (10 min); centrifugation (3 min); freezer (8.5 h)/GC-ECD	Azoxystrobin, difenoconazole, chlorothalonil/ 0.12–1.73 mg kg^{-1}	Bell peppers	[77]

Table 1. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
SLE/SPE	15 g of sample; 15 mL of 0.1% ac ACN; 2 min vortex; addition of $MgSO_4$, NaCl, CH_3NaO_2; 2 min vortex; 5 min centrifugation; 400 mg activated charcoal; 600 mg PSA; evaporation; reconstitution (1 mL n-hexane)/GC-MS	30 pesticides/ 0.019–0.5 mg kg^{-1}	Peach	[75]
SLE/LLE-SPE	A 150 g sample; 300 mL ACN and 25 g celite; 120 mL PE; shaking; 12 mL NaCl saturated solution and H_2O; upper layer extraction. Preconcentration: Florisil cartridge; 200 mL PE and DEE (50:50; *v*/*v*) elution/UPLC-MS/MS	Carbaryl/0.0003 μg mL^{-1}	Lettuce, cucumber, and spinach	[76]
SLE/SPE-MTMOS-CPTES	A 0.5 g sample; 2 mL MeOH + acetone (1:1, *v*/*v*); 1 mL NaCl (10%; *w*/*v*); H_2O; 1 mL of sample through the cartridge; elution (1 mL EtAc); dry; reconstitution (100 μL ACN)/GC-MS	Malathion, chlorpyrifos, profenofos/ 0.01–0.07 μg mL^{-1}	Red apple and purple grape	[79]
SLE/SPE	A 50 g sample; centrifugation 10 min; mix the precipitate with 5 mL ACN; vortex 5 min; centrifugate; supernatant collection and dilution (H_2O); 150 mL through SPE cartridge; elution (0.9 mL ACN)/HPLC-DAD	Metoxuron, monuron, chlortoluron, monolinuron, buturon/0.06–0.15 ng g^{-1}	Tomato	[102]
SLE/ILPR-SPE	A 20 g sample; centrifugation 15 min; acetate solution; supernatant freeze-dried overnight; redissolved (20 mL MeOH); dry; redissolved (20 mL H_2O); 1 mL sample through ILPR cartridge; elution (9:1 *v*/*v*, 1.5 mL); dry; redissolved (0.5 mL MP)/HPLC-UV	Thidiazuron, forchlorfenuron/ 0.00169–0.00195 μg g^{-1}	Cucumber	[103]
SLE/LTP	A 4 g sample; 4 mL ACN; agitation (10 min); centrifugation (3 min); freezer (6 h); organic liquid phase collection; spike/GC-ECD	Azoxystrobin, difenoconazole, chlorothalonil/ 1.1–3.5 μg kg^{-1}	Bell peppers	[104]
SFE	A 0.3 g sample; 1.5 g Na_2SO_4; 25% (*v*/*v*) MeOH/SC-CO_2 at 80 °C; 25 MPa for 5 min for dynamic extraction; ODS column; elution (5 mL acetone); dry; resuspension (1 mL MeOH, and 3 mL ACN/toluene (3:1; *v*/*v*))/LC-MS	Acetamiprid, dinotefuran, imidacloprid, and thiamethoxam/---	Green onion	[80]
UAE-DES/MSPE	A 0.2 g sample; 2 mL DES (proline and propylene glycol at 1:3 M ratio); 50 min US; 5 min centrifugation; 10 mL dilution (H_2O); pH 8.0; 25 mg of MWCNTs addition; dried; ACN resuspension/HPLC-UV	Fipronil, metalaxyl, paclobutrazol, myclobutanil, napropamide, thiacloprid, penconazole/ 0.02–0.05 μg mL^{-1}	Apple, pear, carrot, and cucumber	[84]
UAE-DES/LLE	A 0.5 g sample; DES (glycerol-proline 5 at 9:4 ratio); 1 min vortex; 20 min US; 5 min centrifugation; supernatant collection; 1 mL PE; 20 s vortex; 3 min centrifugation; PE elimination; re-extraction (DCM); DCM layer collection; dry; resuspended in MeOH/HPLC-DAD	Carbendazim, thiophanate-methyl, imidacloprid/ 0.05–0.2 μg mL^{-1}	Apple, grape, and tomato	[85]

Table 1. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
QuEChERS/dSPE	A 10 g sample; 10 mL of ACN with 0.1% AcAc; shaken for 1 min manually; 4.0 g of $MgSO_4$ and 1.7 g of NaOAC; shaken for 1 min with vortexing; centrifugation (4000 rpm, 8 min); 2 mL of supernatant; 150 mg of $MgSO_4$ and 50 mg of PSA; centrifugation (4000 rpm, 5 min)/HPLC-HRMS (1 mL)	82 pesticides/ 0.3–5 µg kg^{-1}	Organic carrots (pesticide-free)	[87]
QuEChERS/dSPE-IL-DLLME	IL-DLLME: 1 mL sample from dSPE clean-up, 10% NaCl (*w*/*v*) in 9 mL distilled H_2O, 130 µL of IL (5 min; 7000 rpm stirring)/LC-MS/MS (100 µL)	Multi-pesticide residues/0.02–0.32 µg kg^{-1}	Bananas, oranges, cabbage, tomato, and onions	[105]
QuEChERS/dSPE (a) QuEChERS/d-SLE (b)	A (a) 2 g sample; 5 mL H_2O (0.1% FAc); 10 mL ACN; agitation (5 min); 2.5 g NH^4HCO^2; agitation (2 min); centrifugation (5 min); dSPE: 1 mL supernatant + 150 mg $MgSO_4$ + 50 mg PSA + 50 mg C_{18} + 7.5 mg MWCNTs; vortex (1 min); centrifugate (3 min); LC-MS/MS; (b) 4 mL ACN (remaining steps are the same); d-SLE: 0.1 mL supernatant + 100 mg C_{18} + 0.9 mL H_2O; agitation (1 min); centrifugation (2 min); supernatant + 50 mg $MgSO_4$ + 1 mL ACN agitation (1 min); centrifugate (2 min)/LC-MS/MS	34 pesticides/ (a) 0.5–1 µg kg^{-1}; (b) 0.5–2.5 µg kg^{-1}	Black peppers	[88]
QuEChERS/DLLME-SFO	n-hexadecane added to the PSA mixture; US extraction and centrifugation (40 °C); solidification of the organic phase in ice bath; high-speed centrifugation of supernatant/GC-MS (1 µL)	Malathion, chlorpyrifos, parathion, bifenthrin, cyhalothrin, permethrin, fenvalerate, deltamethrin/ 0.3–1.5 µg kg^{-1}	Lettuce, long bean, broccoli, tomato, carrot, pumpkin, siew pak choy, sweet choy sum, sweet pak choy, celery, amaranth, spinach, cabbage, mushroom, and cucumber	[106]
QuEChERS/HS-SPME	PDMS (DDT) and PDMS/DVB (HCH) fibre extraction (headspace 5 min (DDT) and 30 min (HCH), 80 °C, 1000 rpm stirring)/GC-MS	DDT congeners/ 0.1 µg kg^{-1} Four HCH isomers/0.15–0.45 µg kg^{-1}	Khat	[94]
QuEChERS/SPE	A 2 g sample; 10 mL ACN, 4 g $MgSO_4$, 1 g NaCl; 2 min vortex; 5 min centrifugation; re-extraction; dry; 2 mL PBS (pH 8.0); MIP-SPE cartridge; elution with 3 mL MeOH followed by 2 mL MeOH/AcAc (90:10, *v*/*v*); dry and reconstituted (ACN)/LC-MS/MS	29 pesticides/ 0.005–0.07 µg L^{-1}	Corn, soybean oil, cucumber, and pear	[107]

Table 1. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
QuEChERS (a) SLE/dSPE (b)	A (a) 10 g sample; (10 mL H_2O in oranges); 10 mL ACN; 4 g $MgSO_4$ + 1 g NaCl; agitation (1 min); centrifugation (10 min); UHPLC-Q-Orbitrap-MS^2; (b) 10 g sample; (10 mL H_2O in orange samples); 10 mL ACN (or 10 mL ACN containing 1% (*v*/*v*) FAc; agitation (1 min); centrifugation (10 min); (dSPE clean-up in oranges)/UHPLC-Q-Orbitrap-MS^2	21 triazoles and 5 pesticides metabolites/ 0.05–2 mg kg^{-1}	Orange, grape, courgette, and strawberry	[108]
QuEChERS/dSPE	A 10 g sample; 10 mL ACN; agitation (10 min); agitation (1 min); 4 g $MgSO_4$ + 1 g NaCl + 1 g $C_6H_9Na_3O_9$ + 0.5 g $C_6H_8Na_2O_8$; agitation (1 min); centrifugation (5 min); 2 mL supernatant + 25 mg PSA + 5 mg GCB + 150 mg $MgSO_4$; vortex (30 s); centrifugation (2 min); dry; redissolve (acetone)/GC-MS/MS	164 pesticides/---	Basil, broccoli, Chinese cabbage, chives, dill, kale, leek, lettuce, parsley, and spinach	[89]
QuEChERS/dSPE	A 10 g sample; 0.1% FAc in ACN; agitation; 1.5 g NaOAC + 6 g $MgSO_4$; agitation (1 min); centrifugation (5 min); 1 mL supernatant + 25 mg PSA + 150 mg $MgSO_4$; vortex (1 min); centrifugation (5 min)/LC-MS/MS	287 pesticides/---	Mandarin orange and grapefruit	[90]
QuEChERS/dSPE	A 10 g sample; 10 mL ACN; agitation (10 min); 4 g $MgSO_4$ + 1 g NaCl + 0.5 g $C_6H_5Na_3O_7$ + 1 g $C_6H_8O_7$; vortex (1 min); centrifugation (2 min); 2 mL supernatant + 25 mg PSA + 5 mg GCB + 150 mg $MgSO_4$; vortex (30 s); centrifugation (2 min)/LC-MS/MS	45 pesticides/ 0.02–1.90 μg kg^{-1}	Banana, grape, strawberry, peach, kiwifruit, plum, pepper, cabbage, eggplant, cucumber, tomato, leek, cowpea, and lettuce	[91]
QuEChERS/dSPE	A 5 g sample; 20 mL ACN (+10 mL H_2O for longan and Chinese cabbage); agitation (2 min); 4 g $MgSO_4$ + 1 g NaCl + 0.25 g $C_6H_6Na_2O_7$ + 0.5 g $C_6H_5Na_3O_7$; agitation (1 min); centrifugation (5 min); 2 mL supernatant + 150 mg C_{18} + 150 mg $MgSO_4$; agitation (1 min); centrifugation (5 min)/HPLC-MS/MS	Indaziflam, spirotetramat, cyantraniliprole, and their metabolites/ 0.3—1.5 μg kg^{-1}	Papaya, litchi, grape, longan, cucumber, and Chinese cabbage	[92]
QuEChERS/dSPE	A 5 g sample; 10 mL ACN; vortex (5 min); 4 g NaCl; agitation (1 min); centrifugation (5 min); 1 mL supernatant + 20 mg GCB; vortex (1 min); stand (1 min)/LC-MS/MS	Methoxyfenozid, chlorantraniliprole, indoxacarb, lufenuron, and chlorfenapyr/ 3.0 mg kg^{-1}	Spinach	[93]
Antibiotics				
UAE/SPE	A 1 g sample + 10 mL MeOH + 15 min US; centrifugation 15 min; supernatant collection; evaporation to 1 mL; + 10 mL H_2O; Strata-X cartridge; elution with 2 mL MeOH; dry; reconstitution (H_2O); spiked/UPLC-TQ	A total of 10 antibiotics (fluoroquinolones, sulfonamides, lincosamides, and metoxybenzylpyrimidines) and 6 of their metabolites/0.1–5.8 ng g^{-1}	Lettuce, tomato, cauliflower, and broad beans	[95]

Table 1. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
UAE/SPE	A 1 g sample; spiked; 10 mL MeOH/H_2O (4:1, *v*/*v*) acidified with 0.2% FA; 10 min US; centrifugation 10 min (* repeated two more times but in the second step, DisQue salt was added); evaporated to 6 mL; Oasis PRiME HLB cartridge; eluate was dried and reconstituted with 0.5 mL MeOH/UHPLC-MS/MS	81 antibiotics/ 0.001–0.26 ng g^{-1}	Banana and cabbage	[9]
UAE/SPE	A 0.25–0.5 g sample; lyophilized; 3 mL 20% *w*/*v* $Mg(NO_3)_2$ + 2% *v*/*v* NH_3; 10 min (×2) US; spiked; diluted to 25 mL (H_2O); pH 3; HLB cartridges; elution (2 × 2.5 mL 0.1% FAc-MeOH (80:20, *v*/*v*))/HPLC-MS/MS	Marbofloxacin, levofloxacin, norfloxacin, ciprofloxacin, danofloxacin, enrofloxacin, and orbifloxacin/1–3 ng g^{-1}	Spinach, lettuce, and cucumber	[96]
Preservatives				
SLE	A2 g sample; 2 × 5 mL of MeOH solvent; sonication (30 min); centrifugation; supernatant elimination; addition of 5 mL of MeOH to the extracts; filtration/HPLC-PDA	Parabens (P)—MeP, EtP, PrP, BuP, and isoBuP/0.005–0.05 µg g^{-1}	Fruits and vegetables from the local market in Riyadh, Saudi Arabia	[98]
SLE	Sample-25% EtOH (solvent); stirring (1 h) at 45 °C; centrifugation (15 min); supernatant collection; dry; resuspension (H_2O)/HPLC-DAD	Gallic acid, rutin, and quercetin/---	Tomato	[99]
UAS/SPE	A 2 g sample; 6 mL ACN; homogenization; 10 min US; centrifugation (10 min); supernatant collection; dry to 200 µL; reconstitution (10 mL H_2O); pH 4; SPE cartridge; elution (400 µL ACN); evaporation to 25 µL; 70 µL + 1% TMCS mixture for derivatization/GC-MS	A total of 24 EDCs including alkylphenols, BPA, phenylphenols, parabens, organophosphorus pesticides and triclosan/---	Banana, apple, pear, kiwi, orange, mandarin orange, lemon, potato, onion, garlic, tomato, carrot, zucchini, eggplant, lettuce, pepper, white turnip, and cucumber	[100]
QuEChERS/dSPE	Juices vortexed (5 min) and centrifugated (5 min); 5 mL supernatant; pH 6; 1.5 g $MgSO_4$ + 250 mg NaCl; vortex (1 min); 4 mL ACN; vortex (5 min); centrifugation (10 min); collection (1 mL); 200 mg PSA; vortex (1 min); centrifugation (5 min)/GC-MS/MS	PG, TBHQ, NDGA, 3-BHA, 2-BHA, 2,6-BHP, 3,5-BHT, 4-HRC, FA, LG, and OG/8.14–25.45 ng L^{-1}	Fruit juice samples (apple, pineapple, mango, litchi, orange, and mixed fruit)	[101]

Legend: 2-BHA: 2-butylated hydroxyanisole; 2,6-BHP: 2,6-di-*tert*-butyl-4-hydroxymethylphenol; 3-BHA: 3-butylated hydroxyanisole; 3,5-BHT: 3,5-di-*tert*-butyl-4- hydroxytoluene; 4-HRC: 4-hydroxy resorcinol; AcAc: acetic acid; ACN: acetonitrile; BuP: butyl paraben; CH_3NaO_2: sodium hydroxymethanolate; $C_6H_8O_7$: citric acid; $C_6H_6Na_2O_7$: disodium citrate; $C_6H_8Na_2O_8$: disodium citrate sesquihydrate; $C_6H_5Na_3O_7$: trisodium citrate; $C_6H_9Na_3O_9$: trisodium citrate dihydrate; DAD: diode array detector; DCM: dichloromethane; DDT: dichlorodiphenyl-trichloroethane; DEE: diethyl ether; DES: deep eutectic solvents; dSLE: dispersive solid–liquid extraction; dSPE: dispersive solid-phase extraction; ECD: electron capture detection; EDCs: endocrine disrupting chemicals; EtAc: ethyl acetate; EtOH: ethanol; EtP: ethyl paraben; FAc: formic acid; FA: ferulic acid; GC: gas chromatography; GCB: graphitized carbon black; H_2O: water; HCH: hexachlorocyclohexane; HPLC: high performance liquid chromatography; HRMS: high resolution mass spectrometry; IL: ionic liquid; IL-DLLME: ionic liquid-based dispersive liquid–liquid microextraction; ILPR: imidazolium ionic-liquid-modified phenolic resin; isoBuP: isobutyl paraben; LC: liquid chromatography; LG: lauryl gallate; LLE: liquid–liquid extraction; LTP: low temperature partition; MeOH: methanol; MeP: methyl paraben; $Mg(NO_3)_2$: magnesium nitrate; $MgSO_4$: magnesium sulfate; MIP: molecularly imprinted polymer; MP: mobile phase; MS: mass spectrometry; MS/MS: tandem mass spectrometry; MSPE: magnetic solid-phase extraction; MTMOS-CPTES: methyltrimethoxysilane-chloropropyltriethoxysilanes; MWCNTs: multi-walled carbon nanotubes; NaCl: sodium chloride; NaOAC: sodium acetate; Na_2SO_4: sodium sulfate; NDGA: nordihydroguaiaretic acid; NH_3: ammonium; NH_4HCO_2: ammonium formate; OG: octyl gallate;

PBS: phosphate buffered saline; PDA: photodiode array detector; PE: petroleum ether; PG: propyl gallate; PrP: propyl paraben; PSA: primary secondary amine; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; SALLE: salting-out liquid extraction; SC-CO_2: supercritical carbon dioxide; SFE: supercritical-fluid extraction; SFOME: solidification of floating organic drop microextraction; SLE: solid–liquid extraction; SPE: solid-phase extraction; TBHQ: *tert*-butyl hydroxyquinone; TMCS: trimethylchlorosilane; TQ: tandem quadrupole; UAE: ultrasound-assisted extraction; UHPSFE: ultra-high pressure supercritical-fluid extraction; UPLC: ultra-high performance liquid chromatography; US: ultrasonic bath; UV: ultraviolet detector; "---" means the respective information is not available.

2.2. Microextraction Approaches

2.2.1. Sorbent-Based Microextraction Techniques

Sorbent-based microextraction techniques are based on the SPE principles and mainly include microextraction packed sorbent (MEPS), SPME, and different formats and variations of these approaches [109]. The development of better sorbent coating technology, along with the use of packed sorbents and innovative designs and devices, has enhanced the efficiency and recovery of the target analytes [109,110]. These techniques use a solid or semi-solid organic polymer as the sorbent immobilized on a substrate to separate and pre-concentrate the analytes, providing simplicity and the possibility of automating the entire process [12,109].

Sampling and sample preparation can be carried out by headspace extraction or direct immersion extraction. Polymeric sorbents are highly viscous and are prone to irreversibly adsorb matrix interferents. Hence, a sample pre-treatment before the analyte's extraction, such as filtration or centrifugation, is required. After extraction, the desorption can be carried out by applying thermal shock or by exposing it to an organic solvent, followed by chromatographic separation and analysis [109]. Even though sorbent-based extraction techniques cannot handle large sample volumes, they are still valid alternatives to conventional approaches and benefit from the wide range of commercially available fibre phases, as well as stability and reproducibility [12].

SPME, invented by Arthur and Pawliszyn in 1987 [111], is a solvent-free extraction technique that integrates sampling, extraction, and analyte preconcentration into a single step. It is also characterized by its automation, reliability, and sensitivity [12,109]. This technique consists of the partitioning of the analytes from the sample solution into the sorbent coating of the SPME fibre, due to intermolecular interaction for the sorbent material [12]. SPME comprises several configurations that improve the high surface-area-to-volume ratio, resulting in smaller extraction periods and higher recoveries [12]. Given that the SPME fibre is retractable inside a syringe needle, it can be directly introduced into a GC inlet or HPLC system via a special interface [109]. Furthermore, this microextraction benefits from the constant development of new sorption coatings.

The detection of semi-volatile and non-volatile compounds can be performed in the headspace mode, direct mode, or by membrane extraction (reviewed by Câmara et al. [12]). Despite the advantages of SPME over conventional methods, it presents a few limitations mostly related to the sorbent coating technology used in the manufacturing of the SPME fibres. These shortcomings include (i) low operating temperatures; (ii) instability and swelling of the coating if exposed to organic solvents; (iii) SPME fibre short lifetime; and (iv) long extraction equilibrium time due to the slow diffusion of the analyte(s) into viscous sorbents [12].

MEPS is a sample pre-treatment technique based on the miniaturization of SPE, in which the sorbent is integrated into handheld automatic syringes that can control the solvent flow, resulting in low void volumes [12]. In turn, this allows pressure-driven extractions, which are considerably more efficient than conventional SPEs [110,112]. This technique requires low solvent volumes and shorter sample preparation times and can be applied to smaller samples (volume 10–250 µL) [12,109].

MEPS comprises sorbent conditioning, sample loading, washing, and analyte elution, with a two-direction flow potential. Hence, this microextraction technique presents enhanced sample–sorbent interaction, sample loading, and improved analyte elution compared to SPE [12]. MEPS can also be performed online, consisting of a fully automated process in which it is possible to use the same syringe for sample extraction and extract injection in the analytical instrumentations [12,109]. However, when using higher sample volumes, this device often shows limitations.

The technique of dispersive solid-phase extraction (dSPE) and its related formats involve combining the sample matrix with the sorbent to effectively capture the desired analytes in the sorbent particles. This can be accomplished by either column packing or using SPE tubes with vacuum or centrifugation. The analytes are then extracted using an appropriate elution solvent. Additionally, magnetic nanoparticles can be utilized to enhance the extraction process, allowing for easy isolation of the sorbent particles and analyte retention through decantation using a simple magnet [109]. The dSPE is also widely used as a clean-up procedure in the two steps QuEChERS/dSPE methodology previously referred to.

2.2.2. Liquid-Based Microextraction Techniques

Conventional LLE techniques present a few limitations, including emulsion formation, long preparation time, and the use of high volumes of toxic organic solvents. Moreover, the evaporation of the solvent is inevitable, as well as sample reconstitution. To overcome these issues, miniaturized liquid-phase extraction (µLPE) techniques that use microliters of organic solvent to accomplish the selective isolation, preconcentration of the analytes, and clean-up of the sample were developed [12]. These innovations related to the extraction and pre-concentration of analytes have resulted in the development of emergent approaches such as liquid–liquid microextraction (LLME) and dispersive liquid–liquid microextraction (DLLME) [109,110].

DLLME and its modifications offer several advantages; namely, a high pre-concentration factor for the target analytes, small sample volumes, low consumption of solvents, a high extraction efficiency, a low cost, simplicity, and a high enrichment factor [12,109]. These techniques can also be combined with almost every analytical measurement technique [109]. In ionic liquid-based DLLME (IL-DLLME), ILs are used as an alternative to hazardous solvents due to their thermal stability, reusability, high reaction efficiency, and ability to dissolve both organic and inorganic compounds [109]. Due to the cation's fine structure and the anion's identity, it is possible to modify the ILs' properties according to the analytical purpose. Nevertheless, their high cost and toxicity remain the main disadvantages [109]. In ultrasound-assisted DLLME (UA-DLLME), ultrasound is applied to disperse the extraction solvent in the sample, which avoids the reduction of the analyte's partition coefficient between water and the extracting solvent [12]. Single-drop microextraction (SDME), in which the extraction solvent is limited to a single drop, is related to DLLME and allows a great preconcentration factor. The drop is controlled by a microsyringe that loads and withdraws the drop from the solution [109].

2.2.3. The Potential of Microextraction Approaches

In the last decades, the use of microextraction as an alternative to conventional extraction approaches became very popular. The main reasons for this evolution have been generically discussed in the previous sections and mainly include simpler and less cumbersome experimental protocols that are easier and faster to perform and more prone to automation. These features limit the user's intervention and allow a better analytical performance of the following analytical steps.

Among the microextraction approaches SPME is certainly one of the most used, and dozens of applications involving the extraction of pesticides and other food preservatives have been reported in the literature (Table 2). SPME allows a relatively fast and easy sample extraction procedure and can be used in different modes, such as headspace (HS) [73] or direct immersion (DI) [2,113,114]. Furthermore, many variations of the sorbent material and format are commercially available [115–117] and both volatile compounds analysed by GC, and non-volatile, such as diazinon and chlorpyrifos, analysed by LC [115], have been reported.

The use of dSPE has been widely reported in the literature for multi-residue pesticide analysis. This is essentially a clean-up procedure that can follow different extraction procedures, although its sole use has been already reported [118,119]. Eventually, dSPE's most popular use is associated with QuEChERS, a procedure that we included both in Table 1, devoted to conventional extraction procedures [88–93,107,108], as well as in Table 2, that presents microextraction approaches. The reason for this is that the miniaturization of QuEChERS (µQuEChERS) is being pursued by different researchers and the examples presented in Table 2 are variations of the original protocol downscaled to a microextraction format.

Tolcha et al. [120] used ultra-high pressure supercritical fluid extraction (UHPSFE) for the extraction of one herbicide and three insecticides at a heating temperature of around 50 °C and with an elution volume of the order of µL.

Table 2. Recent examples of chromatographic methodologies reported for the determination of contaminants in fruits and vegetables involving microextraction approaches.

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
Pesticides				
DI-SPME	$TpPaNO_2$-coated fibre extraction (45 min RT immersion, 1000 rpm stirring)/GC-ECD	A total of 11 pesticides/ 0.04–0.25 µg kg^{-1}	Apple, pear, melon, peach, plum, cucumber, oilseed rape, lettuce, summer squash, and celery cabbage	[113]
DI-SPME	Triazine-based conjugated microporous polymer-coated fibre extraction (immersion; 40 min, 55 °C, 1000 rpm stirring)/GC-ECD	A total of 12 halogens-containing environmental hormones/0.02–0.04 ng g^{-1}	Apple, nectarine, pear, Chinese cabbage, pakchoi, baby cabbage, rape, and lettuce	[2]
DI-SPME	A total of 20% acetone (*v*/*v*), 10% NaCl (*w*/*w*), 0.02% NaN_3, DI extraction (60 min, 55 °C)/GC-MS	PAHs, PCBs, and pesticide residues/1–30 µg kg^{-1}	Edible seaweeds	[114]
HF-SPME	A 10 mL sample (extraction device); MIL-101@GO-HF withdrawn from the vial; analytes placed in another desorption vial with MeOH; desorption (sonication); elution (solvent)/HPLC-UV (25 µL)	Diazinon, chlorpyrifos/ 0.21, 0.27 mg L^{-1}	Tomato and cucumber	[115]
MD-SPME	pesticide standard solutions (10 mL each, 15 ng mL^{-1}); 15 mg rGOQDs@ Fe (sorbent); 5 min ultrasonication; extraction; sorbent separated from the solution under external magnetic field; 0.4 mL of acetone under sonication for 3.5 min (elution)/GC-MS (10 µL)	Sevin, fenitrothion, malathion, parathion, diazinon/ 0.04–0.07 mg L^{-1}	Fruit juices	[116]
Online SPE	Monolith column for on-line solid-phase extraction coupled with LC-MS/MS	A total of 15 amide herbicides	Rice	[117]
dSPE	dSPE using PSA and MWCNTs as a mixed sorbent material/GC-MS	Multiple pesticide residues analysis	Strawberry, raspberry, blueberry, and blackberry	[118]
dSPE	ACN extraction, octadecylsilane-dispersive SPE (clean-up); UPLC HSS T3 column connected to a MS/MS via an electrospray ionisation source	Thiamethoxam, clothianidin, fipronil, fipronil sulfone, fipronil sulfide, fipronil desulfinyl, and pyraclostrobin/10 µg kg^{-1}	Rice, corn, cucumber, tomato, apple, and banana	[119]
MEPS	Metal-organic framework MIL-101(Cr)	Triazine herbicides (desmetryn, prometon, ametryn, prometryn, atraton, and dipropetryn)/ 0.01–0.12 ng g^{-1}	Corn	[121]

Table 2. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
DLLME	Glyphosate converted to dithiocarbamic acid with carbon disulphide, followed by copper in the presence of ammonia; complex formation; collection in dichloromethane drop/UV-Vis	Glyphosate (herbicide)/ 0.21 mg L^{-1}	Legumes	[122]
DLLME	A total of 0.6 mL of CTAB (0.01 mol L^{-1}), ziram, 0.6 mL ascorbic acid (0.01 mol L^{-1}); 4.5 mL H$_2$O (dilution);400 µL carbon tetrachloride, 2.75 mL ethanol, 0.75 mL of HAuCl$_4$ (1.52 × 10^{-4} mol L^{-1}); cloudy mixture centrifugation (80 s, 6000 rpm)/ UV-Vis analysis (530 nm) of red sediment phase	Ziram/0.06 ng mL^{-1}	Potato, carrot, and wheat	[123]
GA-DLLME	A gas bubbled into a test tube to disperse the DES (extraction solvent); cloudy solution formation; centrifugation; collection of the sedimented phase/GC-FID (1 µL)	Diazinon, penconazole, haloxyfop-R-methyl, hexaconazole, diniconazole, clodinafop-propargyl, tebuconazole, bromopropylate, and fenazaquin/0.24–1.4 µg L^{-1}	Grape juice, apple, fresh cucumber, tomato, and onion	[124]
MCNOs-DLLME	Magnetic carbon nano-onions absorbed the analytes; clean-up and preconcentration by DLLME/GC-MS	Several pesticides/ 0.001–0.005 ng mL^{-1}	Fruit juices and vegetables	[125]
VA-DLLME	VA extraction; DDLME of the supernatant by chloroform/LC-MS/MS (10 µL)	Fipronil/0.07 µg kg^{-1} fipronil sulfone/0.04 µg kg^{-1}	Tomato	[126]
dSPE–DLLME	Analytes adsorbed into the poly (ε–caprolactone) grafted graphene quantum dots sorbent; centrifugation and elution by MeOH; eluent mixed with 1,1,2-TCE; centrifugation/GC-FID (1 µL)	Penconazole, chlorpyrifos, haloxyfop–R–methyl, oxadiazon, clodinafop–propargyl, diniconazole, fenazaquin, fenpropathri, and fenoxaprop–P–ethyl/ 0.32–0.76 ng mL^{-1}	Pomegranate, watermelon, apricot, grape, sour cherry, apple, and orange packed fruit juices	[127]
CNPs-dSPE-DLLME	Analytes adsorbed into the amorphous CNPs sorbent; centrifugation and elution of supernatant with *iso*-propanol under sonication; eluent mixed with 1,2-DBE; cloudy solution formation; centrifugation/GC-FID (1 µL)	Fenpropathrin and chlorpyrifos (insecticide), clodinafop–propargyl and oxadiazon (herbicide), and tebuconazole, penconazole, and diniconazole (fungicide)/ 0.83–1.16 ng mL^{-1}	Apricot, grape, peach, pear, pomegranate, sour cherry, and orange juices	[128]
IL-DLLME	A 5.0 mL sample diluted with ACN (0.3–280 µg L^{-1}); spiked with 450 µL of Cu(II) (5 mg L^{-1}) at pH 5.5; TBZ-Cu complex formation; 15 mg [C$_4$mim][PF$_6$] (extraction solvent); 300 µL ACN (disperser solvent); extraction of the complex to IL phase; 15 mL H$_2$O; clouding by ultrasonication (40 °C, 10 min); analyte extraction into droplets of [C$_4$mim][PF$_6$]; centrifugation (3500 rpm 2 min); IL phase dilution with 400 µL MeOH/UV-Vis (340 nm)	TBZ/0.8–50 µg L^{-1}	Mushroom, cherry tomato, green pepper, corn, carrot, grape, apple, banana, orange, lemon, and apricot	[129]
dSPE-SFOME	ACN extraction; clean-up and concentration by SFOME/GC-ECD	Organochlorine pesticides/0.45–1.33 µg kg^{-1}	Cabbage, spinach, and lettuce	[130]
QuEChERS-MSPE-DLLME	MSPE: 5 mL of sample absorbed in 50 mg of Fe$_3$O4@SiO$_2$ magnetic nanoparticles; ACN desorption; DLLME: 40 µL 1,1,2-TCE (extraction solvent)/GC-FID (1 µL)	Diazinon, penconazole, oxadiazon, diniconazole, fenazaquin/ 5–200 µg L^{-1}	Peach, grape, apricot, grape, sour cherry, peach, and tomato	[131]
Preservatives				
LDS-DLLME-MSPE	LDS-DLLME: 5 mL sample, 50 µL 1-heptanol (30 s; 2000 rpm); MSPE: 160 µL DA@Fe$_3$O$_4$ nanoparticles (30 s; 2000 rpm); 200 µL acidified ACN desorbed 1-heptanol by vortex (20 s)/HPLC (20 µL)	Synthetic phenolic antioxidants/1.2–5.8 ng mL^{-1}	Olive oil	[132]

Table 2. *Cont.*

Extraction Method	Description/Analytical Technique	Contaminants/LODs	Matrix	Ref.
DLLME	A 4 mL sample, 0.50 NaCl, 0.50 mL acetone (dispenser), 50 µL trichloromethane (extraction solvent); cloudy solution formation; centrifugation (6 min at 1789 g)/GC-MS (1 µL)	A total of 7 preservatives and 4 parabens/0.15–0.50 mg kg^{-1}	Fruit juices	[133]
DLLME	A 5 mL sample, 0.85 g NaCl, 625 µL acetone (dispenser), 350 µL chloroform (extraction solvent); cloudy solution formation; centrifugation (10 min, 4500 rpm)/HPLC-DAD (20 µL)	Benzoic acid, sorbic acid, butylated hydroxyanisole, butylated hydroxytoluene/0.03 µg mL^{-1}	Fruit juices	[134]
QuEChERS-MSPE	QuEChERS extraction; MSPE by magnetic graphene nanoparticles/GC-MS	A total of 16 preservatives/ 0.21–11.50 µg kg^{-1}	Cabbage	[135]
QuEChERS-SPE	A 1.5 g sample, 10 mL distilled H_2O, 150 µL AcAc, 10 mL ACN; sonication (1.5 min); 4.0 g $MgSO_4$, 1.0 g NaCl; centrifugation (5 min, 5500 rpm); SPE with chitosan/HPLC-UV	Sodium benzoate, potassium sorbate, propylparaben, methylparaben/1.1–2.4 mg kg^{-1}	Fruit juices	[136]
HS-SPME	PA fibre extraction (headspace, 30 min, 50 °C, 600 rpm)/GC-FID	Benzoic acid, sorbic acid, propionic acid/1.1–1.7 mg L^{-1}	Pickled vegetables and soy sauce	[73]
UALLME	A 0.10 g sample, 3 mL n-hexane, 600 µL NADES; US (30 min); centrifugation (10 min, 3000 rpm); two clear phases formation; NADES-rich phase withdrawn/HPLC-UV (10 µL)	TBHQ/0.02 mg kg^{-1}	A total of 12 kinds of edible oils	[137]
CPE	Tergitol (19% *v*/*v*), NaCl (0.83 g), ultrasonic stirring (15 min; 36 °C)/HPLC-ECD	TBZ/5.4 µg L^{-1}	Tomato	[138]
SERS	Paper-based SERS 12 µL sample; spectra taken during the transition process from wet state to dry state in a dispersive spectrometer-CCD and a laser diode (785 nm, 250 mW, 30 s exposure time, 4 laser accumulations, between 3200 and 200 cm^{-1}, 2 cm^{-1} spectral resolution, 100% nominal power)/HPLC-DAD (296 nm)	TBZ/>2 ppm	Mango peels	[139]
UHPSFE	A 0.1 g sample; 1.0 g glass beads; 5 min heating at 53 °C; dried; reconstituted in *n*-heptane (100 µL)/GC-MS	Atrazine, 2,4′-DDD, 4,4′-DDT, and endrin/0.2–2.0 ng g^{-1}	Onion	[120]

Legend: 1,1,2-TCE: 1,1,2-trichloroethylene; 1,2-DBE: 1,2–dibromoethane; 2,4′-DDD: 2,4′-dichlorodiphenyldichloroethane; 4,4′-DDT: 4,4′-dichlorodiphenyltrichloroethane; ACN: acetonitrile; CCD: charge coupled device; CNPs: carbon nanoparticles; CTAB: cetyltrimethylammonium bromide; CPE: cloud-point extraction; COF: covalent organic framework; DAD: diode-array detection; DDT: dichloro-diphenyl-trichloroethane; DES: deep eutectic solvents; DI-SPME: direct immersion solid-phase microextraction; DLLME: dispersive liquid–liquid microextraction; DLLME-SFO: dispersive liquid–liquid microextraction based on solidification of floating organic droplet; dSPE: dispersion solid-phase microextraction; ECD: electron capture detection; FID: flame ionization detection; GA-DPLME: gas-assisted dispersive liquid-phase microextraction; GC: gas chromatography; $HAuCl_4$: chloroauric acid; HCH: hexachlorocyclohexane; HF-LPME: hollow fibre-based liquid-phase extraction; HS-SPME: headspace solid-phase microextraction; HPLC: high-performance liquid chromatography; IL: ionic liquid; IT: ion trap; LC: liquid chromatography; LDS: low-density solvent; MCNOs: magnetic carbon nano-onions; MD-SPME: magnetic dispersive solid-phase microextraction; $MgSO_4$: magnesium sulfate; MIL-101@GO-HF: MIL-101 (Cr) @ graphene oxide-reinforced hollow fibre; MMF: multiple monolithic fibre; MS: mass spectrometry; MS/MS tandem mass spectrometry; MSPE: magnetic solid-phase extraction; MWCNTs: multi-walled carbon nanotubes; NaCl: sodium chloride; NADES: natural deep eutectic solvents; NaN_3: sodium azide; PA: polyacrilate; PAHs: polycyclic aromatic hydrocarbons; PCBs: polychlorinated biphenyls; PSA: primary-secondary amine; QuEChERS: quick, easy, cheap, effective, rugged, and safe method; RT: room temperature ; SERS: surface enhanced Raman spectroscopy; SFOME: solidification of floating organic drop microextraction; SPE: solid-phase extraction; SPME: solid-phase microextraction; SPR: surface plasmon resonance; TBHQ: *tert*-butylhydroquinone; TBZ: Thiabendazole; UALLME: ultrasonic-assisted liquid–liquid microextraction, UPLC: ultra-high performance liquid chromatography; US: ultrasonic bath; UV: ultraviolet detector; UV-Vis: ultraviolet–visible spectroscopy; VA: vortex-assisted.

3. Concluding Remarks

The increasing demand for food and the use of different substances to increase the productivity and shelf life of fresh fruits and vegetables create enormous pressure on the food chain, causing concerns among consumers and public authorities. Conventional extraction techniques such as SLE, UAE, and QuEChERS are often used in combination with HPLC or GC coupled with MS in the analysis of fruits and vegetable safety. However, the use of microextraction techniques has shown promising results to survey the presence of pesticides, antibiotics, hormones, and preservatives. Most of these microextraction approaches are green extraction techniques, which are more environmentally friendly due to simpler and faster protocols, reduce amounts of solvents and samples, and consequently, reduce waste produced during analysis while conserving a high potential for automation. This will drive a progressive substitution of the conventional extraction approaches by microextraction processes in the analytical layout used in the assessment of food safety.

Author Contributions: J.A.M.P. and J.S.C. planned and managed the manuscript; C.V.B. and L.G.-C. collaborated in Section 1.1; C.V.B. was responsible for Section 1.2; L.G.-C., M.L.M. and M.Á.G. collaborated in Section 2.1; C.V.B., J.S.C. and J.A.M.P. collaborated in Section 2.2; J.A.M.P. was responsible for Section 3; J.A.M.P., J.S.C., M.L.M. and M.Á.G. collaborated in the edition of the manuscript and J.A.M.P. managed the manuscript submission. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Fundação para a Ciência e a Tecnologia (FCT) through the CQM Base Fund, UIDB/00674/2020, the Programmatic Fund, UIDP/00674/2020, Madeira 14–20 Program, project PROEQUIPRAM, Reforço do Investimento em Equipamentos e Infraestruturas Científicas RAM (M1420-01-0145-FEDER-000008), Agência Regional para o Desenvolvimento da Investigação Tecnologia e Inovação (ARDITI) through the project M1420-01-0145-FEDER-000005-Centro de Química da Madeira-CQM + (Madeira 14–20 Program) and Project M1420-09-5369-FSE-000001 for the post-doctoral fellowship granted to J.A.M.P. Funding from the Community of Madrid and European FSE and FEDER programs (project S2018/BAA-4393, AVANSECAL-II-CM) is also acknowledged. L.G.-C. thanks the University of Alcalá for her predoctoral contract and the mobility grant to stay at Madeira University.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

AChE: acetylcholinesterase enzyme; ACN: acetonitrile; ADI: Admissible Daily Intake; APVMA: Australian Pesticides and Veterinary Medicines Authority; BHA: terbutylhydroxyanisol; BHT: butylhydroxytoluene; CIB&RC: Central Insecticides Board and Registration Committee; Codex: Codex Alimentarius Commission; DAD: diode array detection; DDT: dichloro-diphenyl-trichloroethane; DES: deep eutectic solvents; DI: direct immersion; DLLME: dispersive liquid–liquid microextraction; DNA: deoxyribonucleic acid; dSLE: dispersive solid–liquid extraction; dSPE: dispersive solid-phase extraction; EC: European Commission; EDCs: endocrine disruption compounds; EFSA: European Food Safety Authority; EPA: Environmental Protection Agency; EU: European Union; FAO: Food and Agriculture Organization; FDA: Food and Drug Administration; FSANZ: Food Standards Australia New Zealand; FSSAI: Food Safety and Standard Authority of India; GC: gas chromatography; GreETs: green extraction techniques; H_2O: water; HCH: hexachlorocyclohexane; HPLC: high-performance liquid chromatography; HS: headspace; IL: ionic liquid; ILPR: imidazolium ionic liquid-modified phenolic resin; ITAB: France's Organic Food and Farming Institute; JECFA: Joint Food and Agriculture Organization; LC: liquid chromatography; LLE: liquid–liquid extraction; LLME: liquid–liquid microextraction; LOD: limit of detection; LPE: liquid-phase extraction; LTP: low temperature partition; MeOH: methanol; MEPS: microextraction packed sorbent; MRLs: maximum residue limits; MS: mass spectrometry; MS/MS: tandem mass spectrometry; MSPE: magnetic solid-phase extraction; MTMOS-CPTES: methyltrimethoxysilane-chloropropyltriethoxysilanes; NADES: natural deep eutectic solvents; OSHA: Occupational Safety and Health Administration; PG: propyl gallate; PMRA: Pest Management Regulatory Agency; PUHs: phenylurea herbicides; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; ROS: reactive oxygen species; REACH: Registration, Evaluation; Authorisation, and Restriction of Chemicals; SALLE: salting-out assisted liquid–liquid extraction;

SC-CO_2: supercritical carbon dioxide; SDME: single-drop microextraction; SFE: supercritical-fluid extraction; SLE: solid–liquid extraction; SFO: solidification of floating organic droplet; SPME: solid-phase microextraction; TBHQ: tert-butylhydroquinone; WHO: World Health Organization; UAE: ultrasound-assisted extraction; UHPSFE: ultra-high pressure supercritical fluid; UPLC: ultra-high performance liquid chromatography; USA: United States of America; UV: ultraviolet.

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