Determination of Pesticides in Fruit and Fruit Juices by Chromatographic Methods. An Overview

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ABSTRACT

In order to combat a variety of pests, pesticides are widely used in fruits. Several extraction procedures (liquid extraction, single drop microextraction, microwave-assisted extraction, pressurized liquid extraction, supercritical fluid extraction, solid-phase extraction, solid-phase microextraction, matrix solid-phase dispersion, and stir bar sorptive extraction) have been reported to determine pesticide residues in fruits and fruit juices. The significant change in recent years is the introduction of the Quick, Easy, Cheap, Effective, Rugged, and Safe (QuEChERS) methods in these matrices analysis. A combination of techniques reported the use of new extraction methods and chromatography to provide better quantitative recoveries at low levels. The use of mass spectrometric detectors in combination with liquid and gas chromatography has played a vital role to solve many problems related to food safety. The main attention in this review is on the achievements that have been possible because of the progress in extraction methods and the latest advances and novelties in mass spectrometry, and how these progresses have influenced the best control of food, allowing for an increase in the food safety and quality standards.

Introduction

Pesticides have allowed growers and handlers of food products to expand production into new geographical areas, increase production volume, extend shelf life, and improve the appearance of many commonly grown foods (1). As a consequence, residues of these substances can be found in food, thus constituting a potential risk for human health considering their toxicity and the exposure to these compounds (2,3).

Increasing public concern about health risks from pesticide residues in the diet has led to strict regulation of the maximum residue levels (MRL) and total dietary intake of pesticide residues in foodstuffs. Food Safety legislation is not harmonized throughout the world, though. However, well known international bodies, the most representative of which is the Codex Alimentarius Commission (4), established by the Food and Agriculture Organization (FAO) (5), and the World Health Organization (6) (WHO) established a risk-based food safety standards that are a reference in international trade, and a model for countries to use in their legislation and in the United States Department of Agriculture (USDA) (7). As one of the world's largest food importers, the European Union (EU) (8) exerts a major influence on food safety testing globally, and has strict legislation in this area (9). Since 1976, the EU has introduced several directives, establishing more than 45,000 MRL for 245 pesticides in a wide range of commodities, including cereals (Directive 86/362/EEC), foodstuffs of animal origin (Directive 86/363/EEC), and fruit, vegetables, and other plant products (Directives 76/895/EEC and 90/642/EEC). During these years, Member States were allowed to set MRL at the national level for the tens of thousands of pesticide/commodity combinations for which no official MRL existed. Directive EC 396/2005, introduced on September 1, 2008, harmonizes all MRL for pesticides within the EU Member States.

SANCO describes the method of validation and the analytical quality control (AQC) requirements to support the validity of data used for checking compliance with MRL, enforcement actions, or assessment of consumer exposure to pesticides. The guidance in this document is intended for laboratories control, or in the monitoring of pesticide residues in food involved in official and feed in the EU (10). Monitoring programs are necessary to ensure that pesticides are being applied according to Good Agricultural Practice (GAP) and that MRL are not exceeded.

Residue-monitoring laboratories are geared to perform multi-class, multi-residue methods to detect a wide variety (in the hundreds) of pesticides potentially in the sample (11). Because of the wide range of chemical properties of pesticides (including acidic, basic, and neutral), and the wide variety of matrices (polar, non-polar, fatty, waxy, and so forth), the sample must initially be cleaned up using a compatible sample preparation technique before injection into the chromatographic system. Ideally, a multi-residue method should be fast and easy to perform, require a minimum amount of chemicals (especially solvents), provide a certain degree of selectivity, and still cover this wide array of analyte–matrix pairs. Although many sample preparation protocols involve lengthy multistep procedures, if the number of steps can be minimized by use of a simple sample preparation procedure, reproducibility (precision) and accuracy can be improved, and time can be saved.

Techniques, such as solid-phase extraction (SPE), solid-phase microextraction (SPME), and, more recently, QuEChERS, allowed solving some of the drawbacks of other extraction techniques, making the experimental approach more selective, faster, and environmentally friendly. The full range of extraction techniques encompass nowadays other types of methods: super-critical fluid extraction (SFE), matrix solid-phase dispersion (MSDP), single drop microextraction (SDME), stir bar sorptive extraction (SBSE), pressurized liquid extraction (PLE), and microwave-assisted extraction (MAE) being, however, less prevalent.

In terms of chromatographic analysis, the evolution follows a path that led to the appearance of devices with a mass spec trometry (MS) detector, tandem mass spectrometry (MS–MS) as an operation mode, and a time-of-flight mass spectrometry (TOF-MS) as a mass analyzer.

In liquid chromatography (LC) the major improvement is the ultra performance liquid chromatography (UPLC), coupled with MS–MS, while for gas chromatography (GC), is the GC × GC–TOF-MS.

Extraction and cleanup methods

Preliminary sample preparation is inevitable for efficient separation from complex matrices by chromatographic columns at low detection levels. The choice of solvent, extraction, and cleanup technique to use depends on what kind of crop and what kind of pesticide residue is being studied (12). Different kinds of fruits are a very different matrix; therefore, the extraction and cleanup method selected must take into account the matrix.

The extraction process is the first and major limiting step in the pesticide residue analysis, often involving sample preparation such as chopping and maceration in fruits, followed by solvent extraction. In liquid samples extraction is performed more directly, without sample preparation, a dilution may be including. Typical procedures begin with product blending for at least 3 min for sample homogenization and initial pesticide extraction. The homogeneity, particle sizes, and representatively of the samples are important topics to consider during the sampling and pretreatment process. With regards to the stability of analytes and homogeneity of subsamples following the process, it is an important, unavoidable prerequisite. Where there is evidence that comminution (cutting and homogenization) at ambient temperature has a significant influence on the degradation of certain pesticide residues, it is recommended that samples are homogenized at a low temperature (10).

This initial step is followed by further steps of sample cleanup and concentration, such as liquid–liquid extraction (LLE) or solid phase extraction methods, to eliminate or reduce the presence of matrix components that can interfere with the chromatography.

The disadvantage of the conventional methods, such as LLE, is the large quantities of solvent utilized, the multiple operation steps needed, the pre-concentration of the extract required prior to analysis, and the interfering compounds that are more likely to be co-extracted (13,14).

Because in single fruit only trace amounts of pesticides are usually found, pre-concentration and purification steps are required (15). The presence of natural pigments makes the analysis of fruit and fruit juices difficult. When dealing with matrices having a high load of chlorophylls, terpenes, or anthocyanines, the cleanup procedure is improved by adding graphitized carbon black (GCB) (16). Cleanup should eliminate most interfering peaks and allow good recoveries at low fortification levels (2). Cleanup is necessary almost every time in order to reduce the background and interferences from the matrix. A study at different spiking levels is needed, because often the recovery may be dependent of the spike concentration.

Sample extraction and cleanup techniques may include, in general, gel permeation chromatography, liquid–liquid partitioning using various solvents, adsorption chromatography, and membrane technologies (1). Extracts cleanup is carried out with a number of techniques, which vary greatly in efficiency, simplicity, speed, and analyte recoveries (1).

Concerns about costs and hazard associated with solvents disposal have led to the development of alternative sample extraction methods such as SPE, MSDP, SPME, and SBSE. These techniques are mainly based on the extraction of pesticides in a solid phase, which allows for the concentration of analytes in the sorbent and their subsequent elution or desorption, frequently in a selective way. Two of these techniques (SPE and SPME), have become elective approaches for pesticide analysis in fruits and fruit juices. They are the main examples of these extraction techniques applied for multi-class pesticide analysis in fruits and fruit juices. In these last cases, a simultaneous extraction and cleanup of extracts may occur, which often allows for direct analysis (15).

Other extraction procedures have been developed with liquid extraction (LE) but with specific instruments such as PLE, MAE has attracted the attention, providing quality results with a minimal number of steps (17). The extraction by SFE marks the difference by the use of supercritical fluids and is therefore free of organic solvents, clean, and safe (1,18,19).

In recent years, the major breakthrough in pesticide analysis was the introduction of the QuEChERS approach, which has been readily accepted by many pesticide residue analysts (20).

Extraction method: LE, SFE, PLE, MAE and SDME

LE

LE has to meet the following requirements: the solvent must have a low water solubility oppositely to the extract analytes, which much also have good drop stability when stirring, and a low level of toxicity (21). The efficiency of an extracting solvent depends on the affinity of the compound for the solvent, as measured by the partition coefficient, on the volume ratio of each phase, and on the number of extraction steps.

Many authors have reported the efficiency of extraction methods with different solvents such as ACN (22), hexane (23), dichloromethane (DCM) (24), acetone (25), petroleum ether (26), ethyl acetate (27), cyclohexane (28), toluene (29), and methanol (MeOH) (30) because these solvents play rather different roles and allow good recoveries of a wide range of pesticides. The *n*-hexane extraction will selectively yield the non-polar pesticides, while the DCM extraction will cover a wider polarity range, but obviously also include more matrix interferences.

The main advantages of LLE are its simplicity, and the requirement of simple and inexpensive equipment. The major drawbacks of LLE are the low sample throughout due to manual concentration steps, and the large amounts of organic solvents used creating a waste problem.

Water is, to some extent, soluble in suitable polar solvents like ethyl acetate or methyl tert-butyl ether (MTBE), while in DCM the solubility of water is low. Acetone is commonly used and was preferred in this study because it is completely miscible with water, thus allowing a good penetration in the aqueous part of the sample. The most common solvent used in LE is ethyl acetate; the advantage of extraction with ethyl acetate is that the procedure is claimed to be less laborious, whilst yielding comparable results. Ethyl acetate seems to be sufficiently miscible with water to allow good penetration into the sample and its polarity is sufficient to extract the more polar pesticides. Ethyl acetate is not completely miscible with water, hence after extraction no extra partition step is required, and the water is simply removed by the excess of an hydrous sodium sulfate.

In some works, the pesticides were extracted with solvents, but a cleanup should be added with florisil (23), active charcoal (24), or silica gel (24). In general, the recoveries obtained by the LE methods have good results. However. Granby et al. (31) showed that in the case of benfuracarb, the recoveries are very low (8–37%) in apples and oranges. Both matrices, extracted by the same extraction method (LE), showed low values.

SFE

In SFE, pressurized carbon dioxide replaces the organic solvents typically employed in classical extraction. Supercritical fluids diffuse through solids like gases, but dissolve analytes like liquids, so that the extraction rate is enhanced and less thermal degradation occurs. In addition, many sample pretreatments can be performed with environmentally friendly, non-toxic, supercritical fluids such as carbon dioxide; these act as an alternative to the potentially hazardous and expensive organic solvents used in extraction, and allow SFE to be a green technology. The high rate of penetration of the supercritical fluid in food, even if slightly porous, permits a fast back-diffusion of he analytes and reduces the extraction time. SFE has gained increased attention as a potential replacement for conventional liquid solvent extraction (sonication or Soxhlet), owing to the properties of supercritical fluids: high diffusivity and low viscosity. The use of modifiers increases the range of the materials which can be extracted. Modifiers such as ethanol, methanol (18), or acetone (1) (added to the samples) can often be used and can also help in the collection of the extracted material, but reduces some of the benefits of using a solvent which is gaseous at room temperature.

SFE is advantageous because the extraction and the sample purification are attained in one step, but this technique requires expensive equipment and careful manipulations in order to get good recoveries (18,19) (Table I).

Table I. Summary of SFE Extraction Methods for Pesticides in Fruits

Fruit	Class	Sample treatment and cleanup Step	Recovery (%)	Spiking Level (mg/kg)	Ref
Kiwi	3 multi-class	$mass_{Sample}$ 3 g; CO_2 modified with 30% MeOH; P = 300 Atm; T = 80°C	72–109	0.1–5.0	18
Apple Tomato	11 multi-class	$mass_{Sample}$ 3 g; CO_2 modified with 10% acetone or MeOH; Hydromatrix; P: 19971, 44935 and 69898 Kpa; T = 70°C Cleanup: SPE-aminopropyl	83–94* 82–96*	0.04-0.10	1
Orange	Organophosphorus	$mass_{Sample}$ 1 g; CO_2 Pure or CO_2 modified with 5% of MeOH; P = 299 Bar; T= 50°C Cleanup: GPC with ethyl acetate and cyclohexane	92-10†	–	19

* CO_2 – 10% MeOH-69898 Kpa -70°C
† Pure CO_2

PLE

PLE is similar to Soxhlet extraction, with the exception that during the extraction process the solvents inside the PLE extraction cartridge are near their supercritical region, which has high extraction properties. The principle behind PLE is that pressurizing the solvent ensures that liquid extraction can be carried out at a temperature higher than the boiling point of the solvent, thus enhancing the extraction capacity and efficiency. PLE is performed at temperatures in the range of 40–200°C and pressures in the range of 1000–2500 psi. At a high temperature, the rate of extraction increases because the viscosity and the surface tension of the solvent drop, while the solubility and the rate of diffusion into the sample increase. Pressure keeps the solvent below its boiling point and forces its penetration into the pores of the sample. Moreover, since sample handling is reduced due to the automation of the extraction, more precise results are obtained. Additional advantages of PLE are: reduced levels of waste, less exposure to harmful solvents by laboratory personnel, lower operational costs, and a reduced need for laboratory materials. However, a drawback of PLE is that samples with high moisture contents require desiccation before the extraction step. In fact, fruit samples need the addition of a drying agent in order to remove water (32).

This technique has gained acceptance because it allows for quantitative extraction with a short extraction time (18,33). Cho et al.(18) tested the three extraction techniques (PLE, LLE, and SFE) in kiwi with three different pesticide classes (organophosphus, organochlorines, and dicarboximide) (18). The results were relatively similar (i.e, the PLE recoveries were similar to the LLE, and higher than SFE).

Blasco et al. (33) showed that 50% of the pesticides studied (benzimidazoles, azoles, organophosphorus, carbamates, neonicotinoids, and acaricides) achieved values of recoveries above 76% by PLE. In the case of methidathion, a 60% recovery was featured, this being the lowest value obtained in oranges. However, imizalil has the lowest recovery value (48%) in peaches.

MAE

MAE is an extraction technique, which utilizes microwave energy to heat the solvent and the sample to increase the mass transfer rate of the solutes from the sample matrix into the solvent.

In MAE, the temperature and the nature of the extraction solvent strongly affect partitioning of the analytes from the sample matrix into the solvent. For method development, several variables such as solvent composition, solvent volume, extraction temperature, extraction time, and matrix characteristics, including water content, are usually studied. However, in order to heat a solvent (or a mixture of solvents), part of it must be polar (examples include methanol, water, and ethanol). In the case of non-polar solvents with low dielectric constants, the so-called sensitizers are added. Sensitizers are molecules that preferentially absorb the microwave radiation and pass it on to other molecules. The MAE technique, which has been used in the case of fruits for the determination of some pesticide residues with low solubility in water, was shown to require a preliminary step in order to facilitate the transfer of pesticide analytes from the fruit into the aqueous extracting solution (34). Therfore, the addition of an organic co-solvent is necessary to extract this type of compounds from fruit samples into the aqueous solution. Moreover, it appeared of major importance not to degrade the fruit tissues to prevent eventual matrix effects between the analytes and the endogenous substances (35). MAE offers many advantages over LLE, such as shortened extraction times and lower consumption of the solvents; furthermore, stirring is possible in some microwave ovens, and it makes the extraction conditions more homogeneous (36).

Lack of selectivity is a problem in MAE, resulting in the co-extraction of significant amounts of interfering compounds (such as pigments), and therefore an additional cleanup step is necessary. In the case of pesticides with MAE, carbamates and ureas were studied in tomato with recoveries between 51% to 106% (34) using ACN, DCM–MeOH (9:1), hexane–acetone (1:1), and anhydrous sodium sulphate.

SDME

SDME has been used for the extraction and concentration of pesticides from simple aqueous samples since 1996, and in some works has been performed in the analysis of pesticide residues in fruit juice. The complex matrices of such products may cause interference in the extraction procedure (37).

The extractant phase of SDME is a drop of an organic solvent, and in a hollow fiber liquid phase microextraction (HP-LPME) system, a hollow fiber impregnated with an organic solvent is used to accommodate or protect microvolumes of the acceptor solution. There are two modes of SDME sampling: direct SDME (DI-SDME), and headspace SDME (HS-SDME) (21). The author summarizes DI-SDME in organophosphorus, showing good recoveries in apples (21), pears (21), and oranges (21,37).

Extraction and purification: SPE, MSDP, SPME, SBSE, and QuEChERS

SPE

SPE is a simple, fast, and easily automated process, and one of the most popular techniques in sample preparation. Pesticides extracted from the liquid phase into the solid phase are eluted later with a small amount of an organic solvent. The efficiency of SPE (sample cleanup and analyte recoveries) depends on the selection of the appropriate sorbent (38).

SPE is used mainly to remove interferences for pre-concentration and for sample storage and transport. Bonded phases having C_{18} on silica are the most used sorbents in SPE.

This procedure has a good performance, lower cost, simplicity, and reduction of toxic residues compared to SLE or LLE. Aminopropylsilicas are polar phases that exhibit both polar and non-polar interactions. These materials can act as normal phase or weak anion-exchangers and have also been used in reversed-phase applications. New SPE materials have been developed, such as mixed-mode sorbents as well as restricted access sorbents, immunoaffinity extraction sorbents, molecularly imprinted polymers, and conductive polymers (39).

SPE is being increasingly used in food analysis, mainly for sample cleanup. Many of the published methods for pesticide determination in fresh fruits and fruit juices use a combination of two or more commercially available SPE columns for cleanup in the normal-phase (NP) mode. Weak anion-exchange sorbents such as primary-secondary amine (PSA), aminopropyl (NH_2) (39,40), or diethylaminopropyl (DEA) modified silica are often used for the cleanup of food samples, together with strong anion-exchange sorbents [quaternary amine (SAX), silica-based (40,41), and quaternary methylammonium (QMA)]. Other sorbents have been used for the SPE extraction of pesticides such as hydrophilic-lipophilic balanced (HLB) (15,42–46), silica, octadecylsilica (C18) (2,39,44,47–50), strata-X (44), and graphitized carbon black (47,51,52).

Different solvents are used in SPE with the function of conditioning, washing, and elution. This extraction method has a wide application in liquid samples like fruit juice (diluted or not).

This technique is advantageous and has frequently comparable features, such as a high sensitivity and selectivity, a minimum sample manipulation, and automation. Vacuum manifold equipment allowed by this technique has been widely applied in SPE. Its flexible settlement enables more convenient and easy operation. Vacuum manifolds allows one to process many SPE samples simultaneously.

The developments also allowed the existence of a fully automatic SPE system for unattended sample preparation and chromatographic analysis. It offers multiple automatic options for cartridge conditioning, sample loading, washing, elution, dilution, derivatization, and injection (53).

The application of SPE has been shown for a number of pesticides from fruits and fruit juices as summarized in Table II and III. One of the major disadvantages of SPE is its susceptibility to clogging when samples containing suspended solids are to be analyzed and the co-extraction of interferences as LE leading to a need for more selective sorbents. Selectivity can be enhanced by chemical modification of the resin.

Hernández et al. (46) achieved different recoveries in different samples (lemons, tomato, and raisins) with triflumizole, as well as with different spiking levels (0.01 mg/kg and 0.1 mg/kg).

Azinphos-methyl analysis in oranges has showed the lowest recovery range (29–62%) in samples spiked between 0.02–0.5 mg/kg, when compared with 40 pesticides studied (51).

MSPD

MSPD, based on the dispersion of the sample on an adsorbent, such as silica gel (14,59), florisil (14, 59–63), C18 (14), alumina

(14,59), hydromatrix (1), and diatomaceous earth (64), allows for the extraction and the cleanup of the analytes in one single step. These different solid phases can be used as non-polar or polar phases (60). The dispersion of solid samples is first done in a mortar, and then the mixture is transferred to a column filled with the adsorbent material for the extraction of compounds using small amounts of organic solvents (60). In the case of liquid samples, the dispersion of the matrix in the adsorbent can be done directly in the extraction column (61). MSPD with several samples often requires further cleanup, especially in samples with pigments (14). Albero et al. (62) conclude that MSPD is a rapid method, and the extraction and cleanup was performed in a single step, requiring a low volume of organic solvent. However, others studies are performed with the use of SPE as a cleanup (1).

Radišic et al. (64) showed that the recoveries obtained for several different juices (apple, peach, orange, and raspberry) are satisfactory (70 to 120%).

Table II. Summary of SPE Extraction Methods for Pesticides in Fruits

Fruit	Class	Sample treatment and cleanup step	Recovery (%)	Spiking Level (mg/kg)	Ref
lemon raisin	15 multi-class	MeOH–water (80:20) containing 0.1% HCOOH; mass$_{sample}$: 20 g; SPE: Oasis HLB, 30 µm	41–150 40–159	0.01–0.1	45
lemon	Benzimidazole, phenol	0.5% TFA in ACN; ethyl acetate–petroleum ether (2:1); ammonia solution 30%; water; mass$_{sample}$ 2 g; Cleanup: SPE-Oasis HLB; Conditioned: MeOH; water; SDS solution; 0.1M HCl; Elution: ACN; volume$_{sample}$: 3 mL	81–106	1–5	38
lemon raisin	19 multi-class	MeOH–water (80:20) 0.1% HCOOH; mass$_{sample}$ 20 g; SPE: OASIS HLB; Conditioned: MeOH; MeOH–MTBE (10:90); 0.1% HCOOH; acidified water 0.1% HCOOH; volume$_{sample}$:5 mL	13–146 13–122	0.01–0.1	46
grape	Organochlorines Pyrethroids	Ethyl acetate; sodium sulfate; mass$_{sample}$: 20 g; SPE: SAX/PSA; Conditioned: acetone–hexane (3:7); Elution: acetone–hexane (3:7); Volume$_{Sample}$: 3 mL	54–104 82–102	0.01–0.1	41
grape	3 multi-class	Volume$_{Sample}$: 1 mL; SPE: LiChrolut NH$_2$, LiChrolut RP-18, Laboratory-made 40% loaded-NH$_2$ cartridges, Laboratory-made 10% loaded-NH$_2$ cartridges, Laboratory-made polymethyloctylsiloxane (PMODS) cartridges; Conditioned: DCM; Elution: DCM–MeOH (95:5); Redissolved: MeOH;	8.0–143	0.1–1	39
grape pear tomato	5 neonicotinoid	MeOH; mass$_{sample}$:20 g; SPE: ENVI-Carb, ENVI-Chrom P; Conditioned: MeOH, water; Elution: MeOH; volume$_{sample}$: 10 mL	79–86 77–88 75–85	0.1–1 0.1–1 0.1–1	52
grape peach, apple orange, tomato	Carbamates	MeOH; mass$_{sample}$:20 g; SPE: Carbograph; Elution: MeOH, DCM–MeOH (80:20)	–	20–200	54
grape peach tomato cherry	Organophosphorus	Acetone; mass$_{sample}$ 10 g; SPE: Isolute NH2 and SAX; Conditioned: MeOH, 0.5 N acetic acid, 0.05 N acetic acid; Elution: 1% TFA in MeOH	100–103 90–107 84–104 93–97	0.001–0.1 0.001–0.1 0.001–0.1 0.001–0.1	40
grape orange tomato	3 multi-class	Ethyl acetate; sodium sulfate; mass$_{sample}$ 20 g; SPE: SAX/PSA, Florisil, C18; Conditioned: acetone–hexane (3:7); Elution: acetone–hexane (3:7); volume$_{sample}$: 5 mL	54–104 51–107 83–352	0.01–0.1 0.01–0.1 0.01–0.1	50
peach pear strawberry	4 neonicotinoid	Acetone; mass$_{sample}$: 25 g; SPE: Extrelut-NT20 column; Elution: DCM; Redissolved: MeOH; volume$_{Sample}$: 20 mL	75–102 81–98 68–98	0.1–1.0 0.1–1.0 –	55
peach pear apple cherry orange kiwi melon	5 multi-class	Hexane; volume$_{sample}$: 5 mL; SPE: silica; Conditioned: hexane; Elution: ethyl acetate; Dissolved: ACN, hexane	70–98 83–96 66–97 80–99 69–98 84–96 70–100	– – – – – – –	56
apple orange	19 multi-class	Acetone; SPE: LiChrolut EN, ENVI-Carb, C18, PSA, NH2; Conditioned: ethyl acetate, MeOH, water; Elution: Ethyl acetate with 1% triethylamine, ethyl acetate:acetone (90:10); Cleanup: SPE-weak anion-exchange DEA column	63–114 29–147	0.01–0.50 0.02–0.50	51
tomato	18 multi-class	MeOH–water (80:20) 0.1% HCOOH; mass$_{sample}$ 20 g; SPE: OASIS HLB; Conditioned: MeOH, MeOH:MTBE (10:90) 0.1% HCOOH, acidified water 0.1% HCOOH ; volume$_{sample}$: 5 mL	12–137	0.01–0.1	46

Tables IV and V summarize the recoveries and spiking levels for the determination of different types of pesticides in fruits and fruit juices with MSPD using florisil (the most used), hydromatrix, C_{18}, alumina, silica-gel, or diatomaceous earth as solid phase.

SPME and SBSE

SPME is an extraction technique using a fused silica fiber externally coated with an appropriate stationary phase. SPME is a solvent-free extraction technique that represents a convenient alternative to conventional extraction methods. It allows for simultaneous extraction and the pre-concentration of the analytes from the sample matrix; furthermore, SPME eliminates some disadvantages of conventional extraction techniques such as the plugging of cartridges in SPE and the use of toxic solvents in LLE (65). Notwithstanding in some studies of SPME, when water is a solvent, sometimes a small percentage of organic solvents is added (66).

It is usually combined with GC and LC for determining a wide variety of compounds, including pesticides in food samples (67). Although SPME has been used in a number of studies for the analysis of pesticides residues in juices (67,68), the limited number of available phases will not make it possible to selectively extract every class of analyte. However, the selectivity could be improved, and some SPME methods may be considered as selective. The sensitivity of an SPME method greatly depends on the right selection of the fiber coating and its thickness with respect to the compounds of interest.

Two modes of application of SPME have been extensively reported: direct immersion (DI-SPME) and headspace (HS-SPME) extraction. In case of fruits, the HS mode is more commonly used, but in juices the DI is more common, as shown in Tables VI and VII.

SBSE (69,70) is a technique in which ca. 50 µL polydimethylsiloxane (PDMS) are coated around a glass-coated magnetic stir bar and was developed to use thermic desorption. The SBSE desorption, nowadays, is made or by a suitable injection system from Gerstel, where the bar is placed to desorb, or with an organic solvent (like acetonitrile) and performed liquid desorption.

A larger volume of PDMS increases absorption capacity and lowers the detection limits of the analytes in such extent that a full scan measurement of pesticide residues beneath MRL in fruit and fruit juices becomes feasible. There are automatic devices for both extraction techniques (SPME and SBSE) (71,72).

Similarly, polymer-based microextraction techniques such as SPME (35,65–68,73–78) and SBSE have been reported for the extraction of several pesticides. These microextraction techniques have been shown to have good cleanup performance and analyte enrichment properties (79).

Nowadays, SPME and SBSE are applied successfully for pesticides residues control in fruits and fruits juices using PDMS (most used for SPME and the only one used for SBSE), polydimethylsiloxane-divinylbenzene (PDMS-DVB), activated charcoal PVC fiber, polyacrylate (PA) and carbowax templated resin (CAR-TPR).

S. Cortés-Aguado et al. (68) proposed a SPME methodology fast and miniaturized extraction of the juice samples with 1 mL of ethyl acetate. Zambonin et al. (65) developed a solvent-free

Table III. Summary of SPE Extraction Methods for Pesticides in Fruit Juices

Fruit juice	Class	Sample treatment and cleanup step	Recovery (%)	Spiking Level (mg/kg)	Ref
orange, lemon	5 multi-class	MeOH; SPE: HLB cartridges	74–106	0.005–0.02	43
apple orange, grape pineapple	Organophosphorus	SPE: multi-walled carbon nanotubes (MWCNT); Conditioned: ACN: Water; Elution: DCM; Redissolved: cyclohexane; anhydrous magnesium sulfate; volume$_{\text{sample}}$: 2 mL	73–103	0.015–0.03	57
tomato	Dithiocarbamate	SPE: silica and octadecylsilica (C18) cartridges; Conditioned: dichlormethane, MeOH, water; Elution: dichlormethane, dichlormethane–MeOH (8:2); Redissolved: MeOH; volume$_{\text{sample}}$: 10 mL	92–99	0.1–5	48
peach orange pineapple apple	33 multi-class	SPE: Oasis-HLB, C18 Sep-Pak, Strata-X; Conditioned: DCM, MeOH, water; Elution: DCM, MeOH; Redissolved: MeOH; volume$_{\text{sample}}$: 2 mL	72–110	0.025–0.050	44
apple	4 multi-class	SPE: C18 column; Conditioned: MeOH, water; Elution: dichlormethane; Redissolved: ACN–water (40:60); volume$_{\text{sample}}$: 50 mL	94–100	2–16	2
orange	Azole Dicarboximide	SPE: Oasis-HLB; Conditioned: MeOH, water; Eluition: MeOH; Redissolved: MeOH, water; volume$_{\text{Sample}}$: 30 mL	71–109 74–77	0.01–0.02	15
grape, peach orange, apple pineapple	16 multi-class	SPE: C18 columns; Conditioned: ACN, water; Elution: hexane–ethyl acetate (1:1); volume$_{\text{sample}}$: 10 mL	91–102	0.02–0.1	58
apple grape	Carbamates	SPE: Oasis HLB columns; Conditioned: tert-butyl methyl ether (MTBE), MeOH, water; Elution: MTBE: MeOH (90:10); Redissolved: DCM; Volume$_{\text{Sample}}$: 10 mL Cleanup: SPE-aminopropyl columns; conditioned: DCM; Elution: DCM–MeOH (99:1); Redissolved: ACN; volume$_{\text{sample}}$: 2 mL	50–148	0.0025–0.250	42

procedure, simple (direct SPME without further sample pre-treatment) and highly sensitive. The authors studied the behavior of organophosphorus and obtain 5% of recovery for fenthion in lemon juice and 21% of recovery for malathion in orange juice, but all the others compounds has results between 70 and 110% (65). Tables VI, VII, and VIII provides a summary of SPME and SBSE extraction methods for pesticides their recoveries and spiking levels in fruits and fruit juices.

QuEChERS

The recently introduced QuEChERS method for pesticide residue analysis uses ACN (9,17,80–82) for extraction of the analyte and simultaneous liquid-liquid partitioning resulting on adding anhydrous magnesium sulphate ($MgSO_4$) and sodium chlorine (NaCl). After centrifugation, a portion of the extract (typically 1 mL) is transferred to a tube containing PSA sorbent and anhydrous $MgSO_4$. Removal of residual water and cleanup are performed simultaneously by using a rapid procedure, called dispersive solid-phase extraction (DSPE). After brief mixing and centrifugation steps, the extract is ready for GC or LC analysis.

The buffered QuEChERS method involves the extraction of the sample with ACN containing 1% acetic acid (HAc) and simultaneous liquid-liquid partitioning formed by adding sodium acetate (NaAc) instead of NaCl along with the $MgSO_4$ (44,83–85).

Two different DSPE methods exist, the European Norms (EN) (86) and Association of Analytical Communities (AOAC) (87), which differ in the following ways. Firstly, the buffered extraction system in the EN method uses sodium chloride, sodium citrate and disodium citrate sesquihydrate instead of sodium acetate in the AOAC extraction system. Secondly, in the DSPE step, the EN method uses 25 mg PSA per mL of extract rather than 50 mg PSA per mL of extract as stated in the AOAC method (86,87).

There is already a range of QuEChERS of different compositions produced by different manufacturers and their choice is made according to the matrix, the analyte and chromatographic conditions.

It has already received worldwide acceptance because of its simplicity and high throughput enabling a laboratory to process a high number of samples in a short period of time (80). In all the studies, the authors classify this technique as extremely rapid, inexpensive, rugged, and suitable for a wide range of pesticide residues in many different products, compared to traditional methods. Romero-González et al. (44) compared the results obtained by QuEChERS and different SPE cartridges, and concluded that when compared to conventional SPE (C_{18}), observing that for most of the selected pesticides better results were obtained when buffered QuEChERS was applied. However, SPE provides better or similar results than QuEChERS for some pesticides, if Strata-X or Oasis were used (44).

Table V. Summary of MSPD Extraction Methods for Pesticides in Fruit Juices

Fruit juice	Class	Sample treatment	Recovery (%)	Spiking Level (mg/L)	Ref
apple	7 multi-class	Solid phase: diatomaceous earth; Extraction: DCM, MeOH; volume$_{\text{sample}}$: 10 mL	72–107	0.001–0.5	64
peach			72–118		
orange			72–117		
raspberry			77–119		
tomato	Organochlorines	Solid phase: Florisil; Extraction: Acetone, ethyl acetate, anhydrous sodium sulfate; volume$_{\text{sample}}$: 2 mL	81–101	0.0025–0.1	63

Table IV. Summary of MSPD Extraction Methods for Pesticides in Fruits

Fruit	Class	Sample treatment and cleanupstep	Recovery (%)	Spiking Level (mg/kg)	Ref
tomato	10 multi-class	Solid phase: hydromatrix; Extraction: acetone, anhydrous sodium sulfate; Cleanup: SPE-aminopropyl; Conditioned: ethyl acetate–hexane (50:50); Eluted: acetone–hexane (80:20), ethyl acetate–hexane (20:80)	66–84	0.05–0.10	1
apple			65–86	0.05–0.10	
tomato	3 multi-class	Solid phase: C18, alumina, sílica-gel, florisil; Extraction: DCM, ethyl acetate, hexane, ethyl acetate–hexane (1:1 e 1:3); mass$_{\text{sample}}$: 2 g	77–100	0.05–4	14
grape	Organophosphorus	Solid phase: florisil; Extraction: ethyl acetate, MeOH; volume$_{\text{sample}}$: 1 mL	72–109	0.010–0.100	62
orange			84–103	0.010–0.100	
apple			70–110	0.010–0.100	
pineapple			78–105		
peach			75–99		
grape	4 multi-class	Solid phase: florisil; Extraction: MeOH, ethyl acetate; volume$_{\text{sample}}$: 1 mL	82–107	0.01–0.1	61
grape	6 multi-class	Solid phase: florisil, alumina; Extraction: ethyl acetate, acetone; volume$_{\text{sample}}$: 2 mL	88–107	0.01–1.0	60
orange			86–104		
apple			89–106		
pineapple			75–103		
peach			74–111		
passion fruit	Organophosphorus, pyrethroids	Solid phase: florisil, silica-gel; Extraction: ethyl acetate	90–113	0.3–1	59
Cashew nut			81–125		

Table IX show the matrices tested by QuEChERS, their recoveries and spiking levels of the different class of pesticides. The cleanup selection depends not only on the matrix but also of the chromatographic analysis (LC or GC).

Chromatography analysis

Methods for the analysis of pesticides have made significant progress in the last years mostly because of developments in chromatographic instrumentation.

The need for rapid high-resolution methods of analysis is as pressing today as it ever was. Today's analytical chemistry environment demands the deployment of more sophisticated methods and instrumentation to keep pace with the profound changes in separation techniques being adopted by many laboratories.

A combination of MS with chromatographic equipment is essential for comprehensive analysis and fulfils the EU requirements for identification, quantification and verification of the important pesticides (10).

Gas chromatography

Until now, the majority of pesticides investigated in food samples have been insecticides, acaricides and fungicides, which normally are GC amenable. However, an important amount of well-known and frequently used pesticides is gradually being retracted in the EU as a consequence of the Regulation EC 396/2005 concerning the placing of plant protection products on the market.

The most commonly used GC detectors are element selective detectors such as the ECD (1,12,23,24,29,41,56,59,63,90,91), used for the detection of chlorinated pesticides, the nitrogen phosphorus detector (NPD) (57,62,75,80), used mostly for the detection of nitrogen containing pesticides, and the FPD (21,37,92), used for the detection of organophosphorus pesticides. Even after such extensive sample cleanup, pesticide analysis is confronted with a large variety of matrix related interferences that hamper the detection sensitivity, especially with the NPD and ECD (93).

Others detectors, such as the electrolytic conductivity detector (ELCD), FID (76), thermionic specific detector (TSD) (19,94) and the atomic emission detector (AED) also find some limited use, while GC–MS use is increasing, especially for confirmation and identification (68,95,96). The most widely used and recommended confirmatory technique for pesticide residue analysis has been the MS with electron ionization (EI) (10). The introduction of GC–MS using an ion trap detector (IT) led to the possibility of the simultaneous screening of up to 180 pesticides and their metabolites (11). Through the features of electronic pneumatic control (EPC), retention time locked libraries (RTLs) (70) for GC-amenable pesticides can be constructed, and by linking the locked retention times to the mass spectral data, hardly any pesticide that is in the library can escape detection and elucidation. In selected ion monitoring (SIM) certain ion fragments are entered into the instrument method and only those mass fragments are detected by the mass spectrometer. The advantages of SIM are that the detection limit is lower since the instrument is only looking at a small number of fragments during each scan.

Table VI. Summary of SPME Extraction Method for Pesticides in Fruit Juices

Fruit juice	Class	Extraction method	Recovery (%)	Spiking Level (mg/L)	Ref
orange peach pineapple	14 multi-class	DI-SPME; Fibers: PDMS, 100 µm, PDMS-DVB, 65 µm; Extraction: ethyl acetate, water–acetone (9:1); $\text{volume}_{\text{sample}}$: 1 mL	71–108 77–99 84–96	– 0.05–0.1	68
orange	Urea	DI-SPME; Fibers: PDMS, 100 µm, PDMS-DVB, 60 µm, CW/TPR, 50 µm; Conditioned: ACN–water (45:55); $\text{volume}_{\text{sample}}$: 3 mL in water			73
orange apple cherry strawberry	Carbamates Phenylurea	DI-SPME; Fibers: CW/TPR, 50 µm, PDMS-DVB, 60 µm, PA, 85 µm; Conditioned: MeOH; $\text{volume}_{\text{sample}}$: 0.5 mL in water and sodium chlorine.	–	0.2–0.5	67
lemon grape orange	Organo-phosphorus	DI-SPME; Fibers: silica fiber, PA; Extraction: water	5–79 28–98 21–88	0.050 0.050 0.0125–0.025	65
grape	Organo-phosphorus	DI-SPME; Fibers: activated charcoal PVC fiber; Extraction: hexane–acetone (90:10), sodium chlorine, hydrochloric acid, sodium hydroxide	42–54	0.0005–0.005	76

Table VII. Summary of SPME Extraction Method for Pesticides in Fruits

Fruit	Class	Extraction method	Recovery (%)	Spiking Level (mg/kg)	Ref
apple	8 multi-class	HS-SPME; Extraction: ethyl acetate, anhydrous sodium sulfate Cleanup: gel permeation chromatography system; ethyl acetate–cyclohexane (1:1), toluene	72–110	0.1	74
apple pear peach, grape	Organo-phosphorus	HS-SPME; Fibers: PA, 85 µm, PDMS, 100 µm; Extraction: MeOH, water, sodium chlorine	–	–	75
tomato strawberry	Pyrethroids	DI-SPME; Fibers: PDMS–DVB Extraction: hexane–acetone (1:1), water, sodium chlorine; $\text{mass}_{\text{sample}}$: 0.5 g	–	–	66
strawberry cherry	Organo-phosphorus	HS-SPME; Fiber: PDMS; Extraction: water, sodium sulfate; $\text{mass}_{\text{sample}}$: 5 g	76–94 74–90	0.075–0.3	77
strawberry apple tomato	Chlorobenzenes Organo-chlorines	DI-SPME; Fibers: PDMS–DVB; Extraction: water–acetone (90:10), water	–	0.010	78
strawberry	Pyrethroids	DI-SPME; Fibers: PDMS, PDMS–DVB; Extraction: ACN; $\text{mass}_{\text{sample}}$: 0.5 g; $\text{volume}_{\text{sample}}$: 9 mL	–	0.005–0.20	35

However, GC–MS determination/confirmation of pesticides can be complicated by the interference of matrix components, co-eluting with the analytes of interest (97).

Conventional GC–MS methods may, therefore, fail to determine and confirm these analytes at sufficiently low concentration levels. This problem becomes critical if a low regulation limit is set for the particular commodity, e.g. baby food, MRL = 0.01 mg/kg (27). To achieve low LODs, quadrupole instruments must operate in the SIM mode, while IT instruments normally operate in the MS–MS (98).

The MS–MS mode increases selectivity and sensitivity being more adequate for quantitative purposes. It reduces drastically the negative influence of matrix interferences on quantitative data (68).

The use of an IT has given access to the use of MS–MS in many routine analytical laboratories at reasonable prices due to its applicability to detection of a wide range of modern pesticides using EI and chemical ionization (CI) modes (28).

TOF-MS is a very attractive tool for non-target analysis, in which the use of libraries (theoretical and/or empirical) can facilitate identification and discovery of known and unknowns in different types of samples (27). TOF measure the time an ion takes to travel through a field-free region. The ions generated in the ion source are accelerated as discrete packages into the field-free flight tube by using a pulsed electrical field. The mass analyzer efficiency of a TOF-MS is 20–30%, as against 0.1–1% for other scanning instruments, such as quadrupole, generating high sensitivity full spectral acquisition data and recording all quantitative and confirmatory ions simultaneously (98). GC coupled with TOF-MS should overcome many of the limitations and allow coverage of a much larger number of pesticides, since TOF mass spectrometers provide high performance across the full mass range. High-speed TOF-MS offer very fast spectral acquisition rates, allowing the separation of overlapping peaks using automated mass spectral deconvolution of overlapping signals (98).

Recently introduced technique, the comprehensive two-dimensional (2D) gas chromatography (GC × GC) brings the

Table VIII. Summary of SBSE Extraction Methods for Pesticides in Fruits

Fruit	Class	Sample treatment	Ref
Peach, orange, pineapple, grape, lemon, apple, strawberry, pear	Azole, organophosphorus, fenoxiacids, dicarboximide, *n*-trihalomethylthio, pyrimidine, benzilate, phenol, organochlorine, amine, quinones, unclassified.	Thermodesorption; $\text{mass}_{\text{sample}}$ 15 g; Extraction: MeOH (ultrasonic bath); $\text{PDMS-volume}_{\text{sample}}$: 1 mL in water	69
pear grape	*n*-Trihalomethylthio, organochlorine, benzilate, dicarboximide, pyrethroids.	Thermodesorption; $\text{mass}_{\text{sample}}$ 15 g; Extraction: MeOH (ultrasonic bath); $\text{PDMS-volume}_{\text{sample}}$: 1 mL in water	70

Table IX. Summary of QuEChERS Extraction Method in Fruits and Fruit Juices

Matrix	Class	Sample treatment and cleanupstep	Recovery (%)	Spiking Level (mg/kg)	Ref
apple, tomato, grape, pear	Urea, dicarboximide	$\text{mass}_{\text{sample}}$ 15 g; Solvent:15 mL ACN; QuEChERS:1.5 g sodium chlorine, 4 g magnesium sulfate; Cleanup: 250 mg PSA, 750 mg magnesium sulfate	–	–	81
apple orange	23 multi-class	$\text{mass}_{\text{sample}}$ 15 g; Solvent: 10 mL ACN; QuEChERS: 4 g Anhydrous magnesium sulfate, 1 g sodium chloride; Cleanup: 150 mg anhydrous magnesium sulfate	55–136 74–140	– 0.01–0.1	9
apple	26 multi-class	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL ACN; QuEChERS: 1 g sodium chlorine, 4 g magnesium sulfate; Cleanup: dispersive solid-phase extraction - 25 mg primary–secondary amine, 150 mg magnesium sulfate	–	–	88
	18 multi-class	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL 1% acetic acid in ACN; QuEChERS: 4 g anhydrous magnesium sulfate, 1.6 g sodium acetate trihydrate Cleanup: 300 mg anhydrous magnesium sulfate, 100 mg primary–secondary amine sorbent.	–	0.01	85
banana	Organo-phosphorus	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL ACN; QuEChERS: 4 g anhydrous magnesium sulfate, 1 g sodium chlorine, 1 g sodium citrate dehydrate, 0.5 g di-sodium hydrogen citrate sesquihydrate; Cleanup: dispersive solid-phase extraction: 125 mg primary–secondary amine, 750 mg magnesium sulfate	68–118	0.1–1	80
strawberry orange	20 multi-class	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL 1% of acetic acid in ACN solution; QuEChERS: 4 g anhydrous magnesium sulfate, 1 g ammonium acetate; Cleanup: florisil cartridge	71–1 70–104	0.0115–0.15	83
fruit juice	27 multi-class	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL 1% of acetic acid in ACN solution; QuEChERS: 4 g anhydrous magnesium sulfate, 1 g sodium acetate;	68–102	0.025–0.075	44
strawberry	14 organo-chlorines	$\text{mass}_{\text{sample}}$ 10 g; Solvent: 10 mL ACN; QuEChERS: 6 g of anhydrous magnesium sulfate, 1.5 g of sodium chloride, 1.5 g of trisodium citrate dehydrate, and 0.75 g of disodium hydrogencitrate sesquihydrate; Cleanup: 150 mg PSA, 150 mg of $MgSO_4$,and 50 mg C18.	46–128	0.030–0.180	89

separation potential superior to any conventional gas chromatographic separation (99–101). Detectors used for GC × GC analyses must be adequately fast in order to reliably detect the multiple peaks rapidly emerging from 2D which typically has a base width of 150 ms or smaller. Detection acquisition frequency of 50–200 Hz is required. Examples of detectors that were found suitable for GC × GC include a FID, ECD, AED, a sulfur chemiluminescence detector (SCD), a nitrogen chemiluminescence detector (NCD), and a TOF-MS (102).

TOF-MS is rapidly emerging as an important spectroscopic detector for fast GC, including GC × GC. This detector can present data at 500 Hz (it acquires thousands of spectras). Conversely, quadruple MS detectors are normally operated at lower frequencies and cannot cope with the influx of fast GC peaks (103).

GC × GC increases the separation space and improves the chromatographic resolution, leading to separation of the analyte of interest from the coeluting compounds and/or matrix components (27,102). In GC × GC, two columns of different selectivity are serially coupled via a modulation device, which cuts small portions (typically 2–10 s) of the effluent from the first column, refocuses them and samples onto the second column. A suitable computer programm has to be used to generate a two-dimensional chromatogram. GC × GC offers increased peak capacity and enhanced mass sensitivity (102). The 2D space has capacity available for many thousands of individual components, and so its ability to locate many different volatile/semivolatile components of different chemical nature (100).

The GC × GC–TOF-MS instrument has been introduced and this system uses a robust dual-stage jet cryogenic modulator and the integrated software enables to fully exploit the capabilities of this powerful technique (27,104,105). The limits of detection of the pesticides comprised in the study (27) (determined at S/N = 5) ranged from 0.2 to 30 pg, injected with the exception of the last eluted deltamethrin, for which 100 pg could be detected. When compared to one-dimensional GC–TOF-MS analysis under essentially the same conditions the detectability enhancement was 1.5–50 fold (27). In fact, when compared to GC–TOF-MS, GC × GC obtained better separation in four minutes than the one-dimensional method after one hour of analysis time (102).

Usually a 30 m column is used and the most recent studies, are performed with the MS detector and the others (ECD and NPD) are getting into unused.

The chromatographic column, detector and ionization, LOD regardless the extraction technique used in studies with different classes of pesticides and GC are summarized in Table X.

Liquid chromatography

New active ingredients are being developed in the last decennia, with physico-chemical characteristics that fit better with LC analysis (46). The analytes were chosen from compounds with physicochemical properties incompatible with GC analysis (high polarity, low volatility, and readily thermally degraded) (45). Final determinations are carried out using LC with DAD (2,48), UV-vis (38,39,94,108) and fluorescence detector (FD) (26,42,73) or MS (14,48,54,55,67,109).

Nowadays, the LC–MS technique has been applied to residue analysis of polar pesticides in fruits, due to its inherent benefits in sensitivity and selectivity. Electrospray ionization (ESI) is common technique used in LC–MS to produce ions.

The most common tandem mass spectrometers for LC, triple quadrupole (TQ) (109) and quadrupole ion trap (QIT) (46,109–111), are becoming important tools in food analysis, especially in the area of pesticide residues determination in fruits (112–114). TQ combines two mass analyzers by means of a RF-only (quadrupolar or multipolar) collisions cell. The fragmentation is due to the collisions of DC-accelerated ions to a neutral gas, argon in most cases. In the QIT, ions are generated in an external source. A package of ions is trapped in the ion trap by means of low RF voltage on the ring electrode (109).

Moreover, LC coupled to MS–MS has also been applied in this field as a powerful confirmation tool, improving the sensitivity. Methods published using LC-MS–MS achieve satisfactory results even without making use of cleanup treatments. Although MS–MS detection (IT or TQ) can be considered as very selective technique, this selectivity should not be overestimated. Otherwise, may result in false positive findings, especially when low resolution MS detector, as IT, is used (64).

Soler et al.(109) studied the mass spectra obtained by IT and TQ. The results obtained by LC-TQ-MS correlated well with those obtained by LC-IT-MS. Recoveries were 70–94% by LC-TQ-MS and 72–92% by LC-IT-MS and matrix effects were tested for both techniques by standard addition to blank extracts. Although the matrix effects are not originated in mass analyzer but in the LC-MS interface, they were, generally, more marked by LC-IT-MS than by LC-TQ-MS. The results indicate that the TQ provides higher precision, better linearity, it is more robust, and when the purpose of the analysis is quantitative determination, preferable over the IT (109).

LC–MS–MS, with its enhanced selectivity, promises to be the most useful technique complementary to GC–MS analysis (9).

However, in the analysis of complex matrixes, coeluting interferences could inhibit or enhance the analyte ionization, decreasing or increasing its signal and, therefore, avoiding a correct quantification. A technology, UPLC, it uses higher linear velocities, and therefore faster run times, and increased sensitivity and improved peak resolution are achieved, which are of particular interest in the analysis of complex matrices (45). Relatively recent advances in chromatographic instrumentation have enabled the development of alternative methods, such as UPLC–MS–MS. UPLC uses a new generation of columns with 1.7 µm diameter particles (new bridged ethylsiloxane/silica hybrid particles) which can operate at higher back pressures. UPLC characteristics in conjunction with MS–MS advantages allow significant decreases in run times, as well as in sample treatment (44).

Romero-González et al. (44) developed and validated an analytical method for rapid and simultaneous determination of more than 90 pesticides in fruit juices by UPLC–MS–MS. The proposed analytical and extraction method allows an analysis time (less than 22 min). The determination is shorter compared to traditional methods, so high sample throughput can, therefore, be achieved, which is useful in monitoring food programs, in which a large number of samples is normally analyzed (44).

LC–TOF-MS collects full mass spectra typically with better sensitivity than full-scan quadruple based MS. Some limitations

Table X. Summary of GC Determination of Pesticides in Fruits and Fruit Juices

Class	Detection	Column / Chromatography	LOD (mg/kg or mg/L)	Ref
Strobilurines	ECD	100% PDMS 25 m × 0.32 mm × 0.25 µm	3	24
Organochlorine, pyrethroid	ECD; MS;EI	5% phenyl methyl polysiloxane 30 m × 0.25 mm × 0.25 µm; 30 m × 0.25 mm × 0.25 µm; Splitless mode	0.003–0.015	41
3 multi-class	ECD; MS;EI	5% phenyl methyl polysiloxane 30 m × 0.25 mm × 0.25 µm; 30 m x 0.25 mm x 0.25 µm; Splitless mode	0.0003–0.015	50
10 multi-class	ECD; MS	5% phenyl 95% dimethylpolysiloxane 30 m × 0.25 mm × 0.25 µm; 35 m × 0.25 mm × 0.25 µm; Splitless mode	–	1
Azole	ECD	30 m × 0.53 mm × 1.25 µm	0.05	29
Organochlorine	ECD; MS	Methylpolysiloxane 30 m × 0.25 mm × 0.25 µm; 5% phenyl polysiloxane 30 m × 0.25 mm × 0.25 µm	0.001	63
6 multi-class	ECD; MS	Methylpolysiloxane 30 m × 0.25 mm × 0.25 µm; Diphenyl dimethylpolysiloxane 30 m × 0.25 mm × 0.25 µm	0.001	60
Organophosphorus, pyrethroids	ECD; MS; EI	25 m × 0.25 mm; 50 m × 0.25 mm × 0.33 µm	– 0.004–	59
Organochlorines	ECD	30 m × 0.32 mm × 0.25 µm; 25 m × 0.22 mm × 0.25 µm	0.057	12
Pyrethroids	ECD	–	0.1–0.2	23
Organochlorines	ECD, FPD	30 m × 0.25 mm × 0.25 µm	–	90
5 multi-class	ECD; MS	5% phenyl methylpolysiloxane 30 m × 0.25 mm × 0.25 µm	– 0.000008–	56
Organophosphorus	FID	100% dimethylpolysiloxane 30 m × 0.25 mm × 0.1 µm	0.00004	76
Organophosphorus	FPD	30 m × 0.32 mm × 0.25 µm	0.00021–0.00056	21
Organophosphorus	FPD	30 m × 0.32 mm × 0.25 µm	0.00098–0.00220	37
Organophosphates	FPD	30 m × 0.53mm × 1 µm	0.01	92
8 multi-class	GC–TOF-MS; GC × GC–TOF-MS	30 m × 0.25 mm × 0.25 µm; 1 m × 0.1 mm × 0.1 µm	–	27
7 multi-class	MS	30 m × 0.25 mm × 0.25 µm; Split/splitless mode	– 0.00001–	95
14 multi-class	MS; MS–MS; Alternatively CI/EI	30 m × 0.25 mm × 0.25 µm; Split/splitless mode	0.0083	68
3 multi-class	MS; EI	5% phenyl 95% PDMS 30 m x 0.25 mm x 0.25 µm; Split/splitless mode	0.01–0.02	14
13 multi-class	MS	30 m x 0.25 mm x 0.25 µm		69
17 multi-class	MS; EI	5% phenyl polysiloxane 30 m × 0.25 mm x 0.25 µm; Split/splitless mode	0.0001–0.0047	58
4 multi-class	MS	5% phenyl polysiloxane 30 m × 0.25 mm × 0.25 µm	0.0001–0.0016	61
Organophosphorus, organochlorines	MS; EI	30 m × 0.32 mm	–	47
Pyrethroids	MS; EI	30 m × 0.25 mm × 0.25 µm	0.0009–0.0138	35
18 multi-class	MS	30 m × 0.25 mm × 0.25 µm; Splitless mode	– 0.003–	51
Pyrethroids	MS	30 m × 0.25 µm × 0.25 µm	0.025	66
5 multi-class	MS	30 m × 0.25 µm × 0.25 µm	– 0.0052–	70
Organophosphorus	MS	5% phenyl methylpolysiloxane 30 × 0.25 mm × 0.25 µm	0.0127	77
Organophosphorus	MS; EI	30 m × 0.25 mm × 0.25 µm		40
Chlorobenzenes, organochlorines	MS	30 m × 0.25 mm × 0.25 µm	0.001–0.024	78
Unclassified	MS	30 m × 0.25 mm × 0.25 µm	–	106
8 multi-class	MS-MS	30 m × 0.25 mm × 0.25 µm	– 0.0019–	28
Organophosphorus, unclassified	NPD	30 m × 0.25 mm × 0.25 µm	0.0073	57
Organophosphorus, unclassified	NPD	30 m × 0.25 mm × 0.25 µm	0.019–0.082	80
Organophosphorus	NPD	30 m × 0.32 mm × 0.25 µm	0.00007–0.006	75
Organophosphorus	NPD; MS;EI	Dimethylpolysiloxane 30 m × 0.25 mm × 0.25 µm; 5% phenyl polysiloxane 30 m × 0.25 mm × 0.25 µm	0.0001–0.00006	62
8 multi-class	MS; EI	60 m × 0.25 mm × 0.25 µm	0.001–0.003	74
26 multi-class	MS; EI	5% diphenyl 95% dimethylsiloxane 15 m × 0.15 mm × 0.15 µm; PTV mode	0.0001–0.0065	88
3 multi-class	MS	5% diphenyl 95% dimethylpolysiloxane 30 m × 0.25 mm; Split/splitless mode	0.005–0.025	18
Organophosphorus	MS	30 m × 0.20 mm × 0.25 µm; Splitless mode	0.002–0.090	65
Organophosphorus	MS; EI	30 m × 0.25 mm × 0.25 µm; Large volume injection (LVI)	–	107
Organophosphorus	TSD	30 m × 0.25 mm × 0.25 µm	–	19

Table XI. Summary of LC Determination of Pesticides in Fruits and Fruit Juices

Class	Chromatography Detection	Column /Eluent	LOD (mg/kg or mg/L)	Ref
Dithiocarbamates	DAD/APCI-MS	CN: 250 mm × 4.6 mm × 5 µm; C18 - 250 mm × 4.6 mm × 5 µm water–MeOH (80:20): isocratic	0.01–0.1	48
4 multi-class	DAD	C18: 250 mm × 4.6 mm × 5 µm fitted with guard column 4 mm × 3 mm ACN and water: gradient	0.5–1	2
Carbamates, phenylureas	ESI-MS	C18: 150 mm × 4.6 mm × 5 µm; MeOH and water: gradient	0.001–0.01	67
Neonicotinoids	ESI-MS	125-4: 100 mm × 5 µm; water and 0.01% acetic acid in MeOH: gradient	0.02–0.1	55
Guanidines	ESI-MS–MS	C18: 150 mm × 2.1 mm × 5 µm; 0.3% HCOOH in water and 0.3% HCOOH in ACN: gradient	0.010–0.025	118
Azadirachtoids	ESI-MS–MS	C18: 250 mm × 4.6 mm × 5 µm; ACN, 0.1% HCOOH and 0.01% sodium acetate: gradient	0.0004–0.008	119
9 multi-class	ESI-MS–MS	C18: 150 mm × 2.1 mm × 3.5 µm; 0.1% HCOOH in water and 0.1% HCOOH in ACN: gradient	0.002–0.007	112
6 multi-class	ESI-MS–MS	75 mm × 2.0 mm × 4 µm; 10 mM aqueous ammonium formate, pH 3.9 and ACN: gradient	–	120
8 multi-class	ESI-MS–MS; TQ	C18: 100 mm × 2.1 mm × 5 µm; 0.01% HCOOH in MeOH and 0.01% HCOOH in water: gradient		46
7 multi-class	ESI-MS–MS	C18: 100 mm × 3 mm × 4 µm; ammonium acetate–acetic acid 20 mM in water and ammonium acetate acetic acid 20 mM in MeOH–water (95:5): gradient	0.002–0.013	31
3 multi-class	ESI-MS–MS	C18: 125 mm × 2.1 mm × 5 µm; 2.5mM ammonium acetate in water and 0.01% HCOOH in MeOH: gradient	0.005–0.025	25
12 multi-class	ESI-MS–MS	150 mm × 2.0 mm / 0.1% HCOOH, 0.1% HCOOH in ACN and ACN: gradient	-	22
Triazoles	ESI-MS–MS	C18: 50 mm × 2.1 mm × 5 µm; 0.01% HCOOH in ACN–water (35:65): isocratic	0.0007	30
Carbamates	ESI-MS–MS	C18: 10 mm × 2.1 mm × 5 µm; 0.01% HCOOH in water; 0.01% HCOOH in MeOH: gradient		13
8 multi-class	ESI-TOF–MS	C8: 150 mm × 4.6 mm × 5 µm: gradient	0.0005–8	117
Carbamates	ESI-MS	C18: 25 cm × 4.6 mm × 5 µm; MeOH–ACN–water (85:15): gradient		54
Carbamates	FD	C8: 150 mm × 4.6 mm × 5 µm; MeOH–water (70:30): Isocratic		123
Ureas	FD	C18: 150 mm × 63 mm × 3 µm; ACN–water (45:55): gradient	0.000055-0.00015	73
Carbamates	FD	C18: Guard column: 20 mm × 3.9 mm × 4 µm; MeOH, water and ACN: gradient		42
Phenols, azoles	FD	C18: 30 × 4 mm x 5 µm / 0.01 M ammonium, acetate–ACN (70:30) and 0.01 M ammonium acetate–ACN (45:55): gradient	0.01	26
Neonicotinoids	MS	C18: 75 mm × 4.6 mm × 3 µm; MeOH and water: gradient	0.01–0.02	52
7 multi-class	MS–MS	C18: 75 mm × 4.6 mm × 3.5 µm; water, MeOH and 10% acetic acid: gradient	0.00001–0.00097	64
Carbamates, organophosphorus	MS–MS	C18: 150 mm × 4.6 mm × 5 µm; MeOH, water with 10 mM ammonium formate: gradient		49
Carbamates	MS–MS; TQ	150 mm × 2.1 mm × 5 µm; water–MeOH and ACN with 1.0mM ammonium acetate: gradient	0.0004–0.003	111
Benzoylphenylureas	MS–MS	C18: 50 mm × 2.1 mm × 3.5 µm; ACN–MeOH 5mM aqueous ammonium–acetate (43:43:14): gradient		121
23 multi-class	MS–MS	C18: 150 mm × 2.1 mm × 5 µm; 10 mM aqueous ammonium acetate and MeOH: gradient		9
11 multi-class	MS–MS	C18: 150 mm × 2.0 mm × 5 µm with a C18 Metaguard cartridge 30 mm × 2.0 mm MeOH–buffer (2mM ammonium formate, pH 2.8): gradient		122
5 multi-class	TOF-MS	C8: 150 mm × 4.6 mm × 5 µm; 0.1% HCOOH in water and ACN: gradient	0.000006–0.00009	43
Azole, dicarboximide	TOF-MS	C8: 150 mm × 4.6 mm × 5 µm; 0.1% HCOOH in water and ACN: gradient	0.00025–0.0008	15
Ureas	TOF-MS	C8: 150 mm × 4.6 mm × 5 mm; 0.1% HCOOH in water and ACN: gradient		81
Organophosphates	TQ-MS-MS	C18: 50 mm × 2.1 mm × 5 µm; water and MeOH: gradient	0.010–0.025	110
5 multi-class	TQ-MS; QIT-MS	C18: 150 mm × 4.6 mm × 5 µm; MeOH in water: gradient	0.5–20	109
18 multi-class	ULPC–MS–MS	C18: 100 mm × 2.1 mm × 1.7 µm; 0.005 M ammonium acetate in water and MeOH: gradient		85
34 multi-class	UPLC–MS–MS	C18: 100 mm × 2.1 mm × 1.7 µm; MeOH and 0.01% HCOOH in water: gradient	0.0007–0.0031	44
20 multi-class	UPLC–MS–MS	C18: 100 mm × 2.1 mm × 1.7 µm; 0.01% HCOOH in water and MeOH: gradient	0.0001–0.003	83
15 multi-class	UPLC–MS–MS; ESI	C18: 100 mm × 2.1 mm × 1.7 µm; 0.01% HCOOH in MeOH and 0.01% HCOOH in water and MeOH: gradient	< 0.01	45
Tetrazines	UV	NH_2; 250 mm × 4.6 mm × 5 µm connected to NH_2 guard column 20 cm × 4.6 mm × 5 µm; MeOH–water (70:30): isocratic	0.05	108
Benzimidazoles	UV	C18: 25 cm × 4.6 mm × 5 µm; ACN, water and ammonia solution: isocratic	0.21–0.51	38
3 multi-class	UV–vis	C18: 125 mm × 3 mm × 5 µm, guard column 4 mm × 4 mm; ACN–0.01% aqueous; ammonium hydroxide, pH 8.4 (35:65): isocratic	0.036–0.071	39
3 multi-class	UV–vis	C18: 15 cm × 4 mm × 5 µm; MeOH–phosphate buffer (60:40) and MeOH–ammonium hydroxide (90:10): isocratic	–	94

have been observed in this challenging task, as the deconvolution software has failed when trying to discriminate ions from background when the ions were present in samples at low levels of concentration (115).

Thus, TOF-MS can be operated at very high repetition rates, typically 5–30 kHz, i.e. 5000–30000 individual mass spectra can be generated per second. Fast detector electronics (which were not available or were too expensive until a few years ago) are required to record the arrival times of the ions at the end of the flight tube. Typically, 10–500 individual mass spectra are added or averaged and stored by the computer system (116). LC–TOF-MS should overcome many barriers and allows the detection of a wide variety of pesticides, since TOF mass spectrometers provide high performance across the full mass range. By contrast with quadruple and IT which use an electrical or magnetic field to separate ions with different *m/z* values. Linearity of up to 3 orders of magnitude and LODs at low picogram levels injected are features of LC–TOF-MS for quantitative target pesticide residue in crops, obtaining limits of quantitation in compliance with established MRL (15,27,43,81,117). TOF-MS offers more possibilities for further investigating the identity of the compounds detected due to the valuable information obtained from MS–MS experiments on product ion accurate mass spectra.

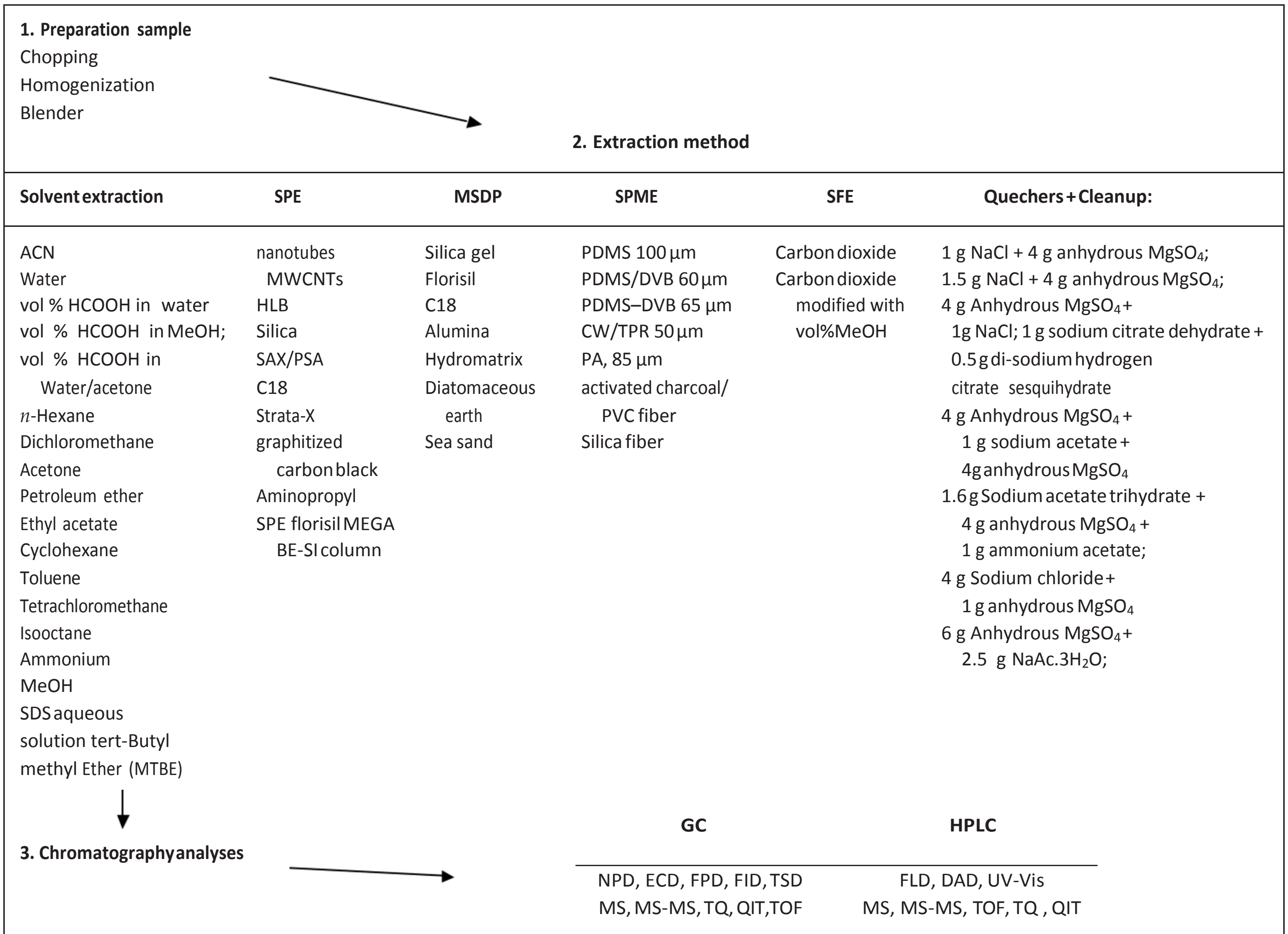
Most of the studies on multi-residue pesticide analysis are based on determinations by GC rather than LC. However, the requirement for LC–MS–MS (9,13,22,25,30,31,46,49,64, 110–112,118–122), UPLC–MS–MS (44,45,83,85) and LC–TOF-MS (15,43,81,117) is becoming more important in monitoring programmes because the majority of modern pesticides tend to be more amenable to LC than GC. The columns most commonly used in liquid chromatography are the C18 columns in gradient and there are few recent studies without being in MS.

The chromatographic column, detector, LOD and ionization used in studies with different classes of pesticides and LC are summarized in TableXI.

Conclusions

Different extraction methods have been studied in order to find the technique with the best recoveries, so several approaches have been proposed to increase the performance of sample extraction.

In the last years, new extraction procedures have been developed to overcome the drawbacks caused by using high amounts of glassware, time and toxic solvents in the classical liquid extraction methods. With this aim, the number of published



1. Preparation sample
Chopping
Homogenization
Blender

2. Extraction method

Solvent extraction	SPE	MSDP	SPME	SFE	Quechers + Cleanup:
ACN Water vol % HCOOH in water vol % HCOOH in MeOH; vol % HCOOH in Water/acetone *n*-Hexane Dichloromethane Acetone Petroleum ether Ethyl acetate Cyclohexane Toluene Tetrachloromethane Isooctane Ammonium MeOH SDS aqueous solution tert-Butyl methyl Ether (MTBE)	nanotubes MWCNTs HLB Silica SAX/PSA C18 Strata-X graphitized carbon black Aminopropyl SPE florisil MEGA BE-SI column	Silica gel Florisil C18 Alumina Hydromatrix Diatomaceous earth Sea sand	PDMS 100 µm PDMS/DVB 60 µm PDMS–DVB 65 µm CW/TPR 50 µm PA, 85 µm activated charcoal/ PVC fiber Silica fiber	Carbon dioxide Carbon dioxide modified with vol%MeOH	1 g NaCl + 4 g anhydrous $MgSO_4$; 1.5 g NaCl + 4 g anhydrous $MgSO_4$; 4 g Anhydrous $MgSO_4$+ 1g NaCl; 1 g sodium citrate dehydrate + 0.5 g di-sodium hydrogen citrate sesquihydrate 4 g Anhydrous $MgSO_4$ + 1 g sodium acetate + 4g anhydrous $MgSO_4$ 1.6 g Sodium acetate trihydrate + 4 g anhydrous $MgSO_4$ + 1 g ammonium acetate; 4 g Sodium chloride + 1 g anhydrous $MgSO_4$ 6 g Anhydrous $MgSO_4$+ 2.5 g NaAc.3H_2O;

3. Chromatography analyses

GC	HPLC
NPD, ECD, FPD, FID, TSD	FLD, DAD, UV-Vis
MS, MS-MS, TQ, QIT,TOF	MS, MS-MS, TOF, TQ , QIT

Figure 1. Schematic summary of the extraction and chromatographic methods for pesticides in fruits and fruit juices

papers in the area of the analysis of pesticides in fruits and fruit juices makes extraction techniques SPE, SPME, and QuEChERS the most frequently used.

However, this paper described here the amount of work done in this area and highlights the developments in analytical techniques (Figure 1).

GC and LC provide the basis of numerous determination methods in combination with very sensitive and selective detection methods in lower concentrations.

Detectors TOF-MS, MS–MS combining with UPLC and GC × GC are the latest applications that enable a very sensitive and selective technique for both multiresidue determination and trace level identification.

In case of the GC × GC, the separations power greatly increased and a perfect analyte identification and quantification.

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