Determination of pesticides residues in food of vegetal origin: sample preparation, chromatographic techniques and applications

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Abstract The determination of pesticide residues in trace levels contained in complex matrices, such as food, often requires extensive sample preparation including extraction and/or clean-up followed by instrumental analysis. The development of reliable, accurate, selective and sensitive analytical methods for the simultaneous determination of more than one residue in a simple analysis is crucial and essential. This review presents the techniques that have been developed and are applied all over the world for the qualitative and quantitative determination of pesticides in fruit and vegetable samples. Advantages and difficulties occurring at each stage of the analytical procedure are also outlined.

Keywords: Pesticides, food, sample preparation, residue analysis, chromatography

1. Introduction

Pesticides are mainly used in agriculture for the prevention, destruction or control of harmful organisms (pests) or diseases, or for the protection and preservation of plant products during production, storage and transport. Their application in agriculture has progressively increased after World War II and became a widespread practice that led to an increase in world food production. However, the extensive use of organic synthetic pesticides has resulted in the occurrence of residues of these chemicals and their metabolites in different environmental compartments such as water, soil and also in food commodities in quite small concentrations [Ahmed, 2001].

Global scientific concerns have been raised regarding the potential toxicity of pesticides that have promoted their strict regulation in order to protect consumers, environment and also the users of pesticides. MRLs values defined as the highest levels of a pesticide residues that are legally tolerated in or on food or feed when pesticides are applied correctly (adoption of Good Agricultural Practices, GAPs) were established. Legislations were enacted in the USA, the European Commission (EC) and other countries to regulate pesticides in food products. More specific in EC, the European Food Safety Authority (EFSA) in order to assess the safety for consumers based on the toxicity of the pesticide, the maximum levels expected on food and the different diets of Europeans established EC legislation on MRLs that harmonizes and simplifies pesticide MRLs, and sets a common EC assessment scheme for all agricultural products for food or animal feed. Regulation EC 396/2005 and amendments cover pesticides currently or formerly used in agriculture in or outside the EC (around 1100 compounds) [European Commission, 2017]. Therefore, the development of reliable, accurate and sensitive analytical methods is essential so as to protect human health and to support the compliance and enforcement of laws and regulations pertaining to food safety. As a consequence, several techniques have been developed and optimized for the qualitative and quantitative determination of pesticides residues in complex matrices, such as food. Taking into account the multiplicity of food along with the fact that measurement of trace levels for target organic contaminants must be achieved numerous multi-residue methods (MRMs) capable of simultaneously determining more than one residue in a simple analysis have been proposed and applied [Lacorte *et al*., 2006, Ridgway *et al*., 2007, Beyer *et al*., 2008]. Due to the fact that several compounds of different physicochemical properties such as polarity, solubility, volatility and pK_a value have to be simultaneously extracted and analyzed makes the development of MRMs a difficult task [Biziuk and Stocka, 2015].

According to relevant literature fruit and vegetables are capable of retaining large quantities of pesticides. Moreover, several pesticides have the ability to accumulate in fruit skins. It has been reported that the crops most exposed to the presence of pesticides are grapes, citrus fruits and potatoes [Biziuk and Stocka, 2015].

The aim of present paper is to review the application of sample preparation and chromatographic techniques in the analysis of pesticide residues in food of vegetal origin and to compare the use of each method with other well-established sample preparation and analysis techniques. Thus, traditional and alternative new techniques recently

developed in the area of food analysis are summarized and the applicability of each technique is discussed. Principles, potentials and advantages as well as limitations of each MRM used in the literature to screen, quantify, and identify polar, non-polar, and thermolabile pesticides and their degradation products in fruits and vegetables will be also highlighted. Finally, the most recent applications of these techniques in food analysis are provided.

2. Analytical procedures

2.1. Matrix modification

The main object of matrix modification is the transfer of the sample into a phase that is suitable for further analytical preparation techniques. Depending on the heterogeneity of the food matrix containing pesticide residues, a number of different matrix pretreatment methods are available in order to acquire representative and correct portions of sample mass. More specific, in the case of disintegration of solid samples (fruits, vegetables) homogenization (via blender, shaker, stirrer etc.) or sonication (with solvent or sorbent) has been applied, whereas in the case of liquid samples (oils) blending has been employed [Ahmed, 2001].

2.2. Extraction and clean-up techniques

Extraction and clean-up techniques involve the isolation and/or enrichment procedures which aim to the removal of analytes from the primary matrix to a secondary one (that is suitable for injection into the chromatographic analysis system) with the concomitant elimination of interferences and the increase of analytes concentrations to levels above the limit of determination (LOD) of the analytical technique used [Biziuk and Stocka, 2015; Farajzadeh et al., 2017].

There are numerous sample preparation methods for pesticides extraction such as liquid-liquid extraction (LLE), pressurized liquid extraction (PLE), Soxhlet extraction (SOX), superheated water extraction (SHWE), supercritical fluid extraction (SFE), matrix solid-phase dispersion extraction (MSPDE), magnetic solid phase extraction (MSPE), stir bar sorptive extraction (SBSE), accelerated solvent extraction (ASE), microwave-assisted extraction (MAE), ultrasonic extraction (USE), cloud-point extraction (CPE), liquid-phase micro-extraction (LPME), solid-phase micro-extraction (SPME), single-drop micro-extraction (SDME), hollow-fiber liquid-phase micro-extraction (HP-LPME), dispersive solid-phase extraction (DSPE) and dispersive liquid-liquid micro-extraction (DLLME).
LLE is a conventional method of extraction that has been applied for many years and involves a water-immiscible solvent that directly extracts the target compounds. However, in practice LLE has a number of drawbacks including the limited selectivity, difficulty of automation, emulsions formation and large requirements in non-environmental friendly organic solvents. SPE is a sample preparation process that is based on the affinity of dissolved pesticides on a solid sorbent acting as a stationary phase. SPE is a wide-used extraction and clean-up technique that has several advantages over LLE among which low solvent consumption, enormous saving of time, increased extraction efficiency, decreased evaporation volumes, higher selectivity, cleaner extracts, greater reproducibility, avoidance of emulsion formation, and easier automation are included. Therefore, a wide variety of SPE columns containing various weak or strong anion-exchange sorbents, such as primary secondary amine (PSA), aminopropyl (NH_2), diethylaminopropyl (DEA), modified silicas and porous polymers (polystyrene-divinylbenzene resins and carbon-based materials, C18, SAX, QMA) and graphitized carbon black (GCB) are commercially available, whereas a growing interest on sorbents based on nanostructured materials is observed. The most recent tendency on the research focusses on electrospun nanofibers and carbon nanotubes [Augusto et al., 2013].

Micro-extraction methods usually require both smaller sample size and organic solvent volumes when compared with the conventional methods. The main advantages of these procedures are the high degree of enrichment for the analytes in complex matrices, which enable DLs down to the levels required by the regulatory bodies to the analysis of pesticide residues in food. Moreover, micro-extraction techniques are easily associated with gas or liquid chromatography due to the compatibility of the solvents used, and the low volumes involved. Based on bibliographic data the majority of micro-extraction applications have been employed for the isolation of nonpolar or moderately polar high molecular weight target substances contained in liquid samples and only few attempts have made for the extraction of analytes in solid matrices.

Anastassiades et al. (2003) developed a highly effective sample preparation technique for the pesticide multiresidue analysis in various sample matrices that is quick, easy, cheap, effective, rugged and safe which is known by the name QuEChERS ("catchers") method. This method is based on a salting-out extraction with a solvent (mainly acetonitrile) followed by a DSPE [Biziuk and Stocka, 2015]. This proceedure offers a user-friendly alternative to traditional LLE and SPE and involves an extraction method for pesticides in fruits and vegetables, coupled with a clean-up method that removes sugars, lipids, organic acids, sterols, proteins, pigments, and excess water.

Table 1. Selected examples of applications for the determination of pesticides residues in food of vegetal origin. Reports in chronological order.

Analyte(s)	Food matrix	Extraction/Clean up	Separation		Determination		Reference
			Column	Carrier gas (for GC) or mobile phase (for LC/HPLC)	Detection	Sensitivity	
Selected pesticides: bitertanol, carbendazim, fenthion, flusilazole, hexythiazox, imidacloprid, methidathion, methiocarb, pyriproxyfen and trichlorfon	Oranges	Comparison: SBSE MSPDE and LLE (EtAc)	Luna C_{18} (150 × 4.6 mm i.d., 5 µm) (Phenomenex, Spain)	MeOH –H_2O (40:60, v/v) at 0.8 ml min^{-1}	LC–MS	LOQs: 0.001–0.05 µg g^{-1} LOQs: 0.008–0.3 µg g^{-1} LOQs: 0.002–0.2 µg g^{-1}	Blasco *et al.*, 2002
Selected pesticides: dimethoate, simazine, atrazine, diuron, terbuthylazine, methyl-parathion, methyl-pirimiphos, endosulfan I, endosulfan II, endosulfan sulphate, cypermethrin and deltamethrin	Olives and olive oil	MSPDE (ACN) / silica and florisil column	**GC:** ZB-5MS (30 m×0.25 mm i.d., 0.25 µm) (Phenomenex, USA) **LC:** Zorbax Eclipse C_8 (150 mm×4.6 mm, 5µm)	**GC:** He at constant flow rate of 1 mL min^{-1} **LC:** H_2O with 0.1% v/v HCOOH (A) and H_2O with 0.1% v/v ACN (B) at a flow rate of 0.6 mL min^{-1}	GC-MS and LC–MS-MS	LODs: 8–80 ng g^{-1} (olives) 3–60 ng g^{-1} (olive oil) LODs: 0.4–4 ng g^{-1} (olives) 0.2–3 ng g^{-1} (olive oil)	Ferrer *et al.*, 2005
Fungicides (imazalil, prochloraz and their degradation products)	Citrus	LLE (ACN) / primary secondary amine (PSA)	Zorbax Eclipse XDB-C_8 (150 mm×4.6 mm, 5µm)	H_2O (A) and ACN (B) both containing HCOOH (0.1% v/v) at a flow rate of 0.6 mL min^{-1}	LC/TOF-MS	Not available	Thurman *et al.*, 2005
20 representative compounds of organochlorine pesticides	Horticultural samples (lettuce, tomato, spinach, potato, turnip leaf and green bean)	Comparison: PLE and MAE / SPE	Not referring	He at constant flow rate of 1.0 mL min^{-1}	GC-ECD	PLE: LODs: 1.2–4.2 ng g^{-1} and LOQs: 4.9–15.2 ng g^{-1} MAE: LODs: 0.2–2.0 ng g^{-1} and LOQs: 1.9–5.8 ng g^{-}	Barriada-Pereira *et al.*, 2007
349 pesticides (multiclass-various)	Fruit and vegetable samples (grape, pomegranate, okra, tomato and onion)	LLE (EtAc) / DSPE with primary secondary amine (PSA) and/or graphitized carbon black / bonded silica	HP-5MS (15 m × 0.25 mm i.d., 0.25 µm) (Agilent, USA)	He at constant flow rate of 1.2 mL min^{-1}	GC–EI-MS/MS	LOQs: <5 ng g^{-1} for most of the compounds and 5-10 ng g^{-1} for few compounds. Order of LOQ of individual compounds: grape< okra≈tomato<onion<pomegranate.	Banerjee *et al.*, 2012
38 representative compounds (multiclass-various)	Fruit and vegetable samples (rice, orange, apple and spinach)	QuEChERS	**LC:** Prodigy ODS-3 (150 mm×3 mm, 5µm) (Phenomenex, USA) **GC:** Rxi-5ms (15 m × 0.53 mm i.d., 1 µm) (Restek, USA)	**LC:** H_2O with 0.1% v/v HCOOH (A) and MeCN with 0.1% v/v HCOOH (B) **GC:** He at constant pressure of 1 psi	LC–MS/MS and GC-MS	Not available	Kwon *et al.*, 2012
Fungicides (vinclozolin, dichlofluanid, penconazole, captan, quinoxyfen, fluquinconazol, boscalid and pyraclostrobin)	Grapes	Comparison: MAE, MSPDE, SLE and QuEChERS	HP-5MS (30 m × 0.25 mm i.d., 0.25 µm) (Agilent, USA)	He at constant flow rate of 1.5 mL min^{-1}	GC–MS (SIM)	LODs: MAE:0.7-1.7ng g^{-1}; MSPDE: 1.0-2.6 ng g^{-1}; SLE: 1.5-4.1 ng g^{-1} and QuEChERS: 1.2-4.3ng g^{-1}	Lagunas-Allue *et al.*, 2012
199 pesticides(multiclass-various)	Fruit and vegetable commodities (apple, broccoli, celery, leek, melon, nectarine, onion, pear, pepper, tomato and grapes)	QuEChERS (citrate buffered method)	ACQUITY BEH C18column (100 × 2.1 mm i.d., 1.7 µm) (Waters, Milford, MA, USA)	H_2O (A) and MeOH (B) both containing NH_4OAc (10 mM) at a flow rate of 0.45 mL min^{-1}.	UPLC–QTOF–MS	Screening Detection Limits SDLs: 10 and 50 ng g^{-1} for 57% and 79% of the compounds tested	Lopez *et al.*, 2014
Carbamates (carbofuran & carbaryl), triazines (atrazine & ametryn), and organophosphates (methyl parathion)	Papaya and avocado	QuEChERS (AOAC; acetate buffering and CEN, citrate-buffering versions)	Zebron ZB-5MS Crossbond (30 m×0.25 mm i.d., 0.25 µm) (Phenomenex, USA)	He at constant flow rate of 1.1 mL min^{-1}	GC-MS	LODs: 0.03–0.35 ng g^{-1} (papaya) 0.14–0.28 ng g^{-1} (avocado) LOQs: 0.06–0.75 ng g^{-1} (papaya) 0.22–0.40 ng g^{-1} (avocado)	Pano-Farias *et al.*, 2016
Multi-class pesticides (including carbamates, organophosphates, sulfonylureas, pyrethroids and neonicotinoids)	Fruit and vegetable samples (cabbages, cucumbers, tomatoes and strawberries)	DSPE using polyaniline-modified zeolite NaY	RP18 (4.6×150 mm, 5 µm) (Waters, Massachusetts, USA)	ACN (A) and H_2O (B) at a flow rate of 1.0 mL min^{-1}	HPLC-PDA	LODs: 0.001–1.00 µg mL^{-1} LOQs: 0.005−2.50 µg mL^{-1}	Arnnok *et al.*, 2017
76 representative compounds (multiclass-various)	Green tea	PLE / SPE column (GCB/PSA)	HSS T3 column (100 mm×2.1 mm i.d., 1.8 µm, (Waters, USA)	H_2O with 0.1% v/v HCOOH (A) and MeOH with 0.1% v/v HCOOH (B) at a flow rate of 0.25 mL min^{-1}	UPLC-MS/MS	LOQs: 6–691 ng L^{-1} infusion and 0.4–36.4 ng g^{-1} in samples	Chen *et al.*, 2017
Aryloxy pesticides (metalaxyl, haloxyfop–r–methyl, clodinafop–propargyl, diclofop–methyl, and bromopropylate)	Vegetables (potato, tomato, onion, garlic, celery, radish, beet and carrot)	Combination: DSPE and DLLME	CP–Sil 8 CB (50 m × 0.25mm i.d., 0.12 µm) (Chrompack, the Netherlands)	He at a constant linear velocity of 30 cm s^{-1}.	GC–FID	LOQs: 0.08–0.83 ng mL^{-1} in solution and 0.04–2.9 ng g^{-1} in samples	Farajzadeh *et al.*, 2017

According to the published data extract clean-up techniques that are most commonly used are SPE, SPME, SBSE and gel permeation chromatography (GPC), especially used for the removal of lipids (mainly triglycerides) from fatty food matrices (typically vegetable oils, e.g. corn oil, sunflower oil, olive oil, palm kernel oil, cacao butter, etc). A summary of selected applications for the determination of pesticides residues in food of vegetal origin is presented in Table 1.

2.3. Qualitative and quantitative determination

The final stage in the analysis of pesticide residues in food matrices is the identification of individual compounds (qualitative) and their quantitative determination. Instrumental analysis has traditionally been performed by gas chromatography (GC), high pressure liquid chromatography (HPLC), liquid chromatography (LC) and ultra-performance liquid chromatography (UPLC).

The use of GC in food analysis is a technique applied for the determination of volatile and thermally stable pesticides. Because of the high number of theoretical plates of the GC columns employed and the variety, selectivity and sensitivity capabilities of the detectors that can be coupled such as flame photometric (FPD), pulsed flame photometric (PFPD), nitrogen–phosphorus (NPD), electron-capture detectors (ECD) or mass spectrometry detector (GC-MSD) several MRMs using GC have been developed.

Among the detectors used, MS is the preferred tool for determination of multi class pesticide residues because it permits: i) the simultaneous quantification and identification of detected analytes; ii) the detection of a wide range of analytes independently of its elemental composition; iii) mass-spectrometric resolution of co-eluting peaks; and iv) potentially faster analysis time [Cunha et al., 2009]. Besides all the above, confirmation of the analysis results without ambiguity is achieved. MS can operate in Single Ion Monitoring (SIM) mode, which provides for greater sensitivity than the SCAN mode. The detection by MS employing quadrupole, ion trap and/or time-of-flight (TOF) analysers offers simultaneously the confirmation and the quantification of numerous pesticides. However, in some cases GC analysis is avoided; for instance in the analysis of polar or/and thermally unstable (thermolabile) compounds, and especially when laborious and costly derivatisation steps are necessary.

Therefore, HPLC, LC and UPLC analysis are applied coupled to conventional detectors such as photo diode array and fluorescence detectors. Similarly with GC, mass spectrometry (MS) is preferred because it provides confirmatory evidence of the identity of the determined compounds. The analytical techniques of LC coupled with mass spectrometry (LC–MS) or with tandem mass spectrometry (LC–MS–MS) or with time-of-flight (LC-TOF-MS) or ultra-performance liquid chromatography–quadrupole-time of flight–mass spectrometry (UPLC–QTOF–MS) have lately become powerful tools for the identification and quantification of residues in fruits and vegetables. Ferrer et al. (2005) described a MRM for determination of pesticides in olives and olive oil samples by LC-TOF-MS. Recently, David et al. (2017) developed a

MRM for the analysis of pesticide residues in fatty matrices, such as vegetable oils by using gel permeation clean-up followed by GC-MS/MS and LC-MS/MS determination. These emerging techniques require high quality equipment and offer rapid and efficient separation of individual target chemical, high selectivity and accurate mass measurement [Biziuk and Stocka, 2015].

2.4. Conclusions

The development of analytical methods for the determination of pesticide residues in fruit and vegetable samples is crucial not only for the implementation of laws, but for the protection of human health as well. Based on the presented data the qualitative and quantitative analysis of different classes of pesticides in food matrices can be achieved by numerous reliable, accurate and sensitive MRMs that contain the steps of analyte extraction, extract purification and modern techniques of instrumental analysis. Currently, hundreds of pesticides are screened using state-of-the-art gas and liquid chromatography combined with very sensitive and specific detectors such as triple quadrupole MS instruments (GC-MS/MS, LC-MS/MS).

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