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Review

Determination of pesticide residues in food matrices using the QuEChERS methodology

Angelika Wilkowska *, Marek Biziuk

Department of Analytical Chemistry, Chemical Faculty, Gdansk University of Technology, G. Narutowicza Street 11/12, 80-233 Gdansk, Poland

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ABSTRACT

The determination of pesticide residues in food matrices is a formidable challenge mainly because of the small quantities of analytes and large amounts of interfering substances which can be co-extracted with analytes and, in most cases, adversely affect the results of an analysis. However, safety concerns require that pesticides of the wide range of chemical properties (including acidic, basic and neutral) should be monitored. Because of the wide variety of food matrices, the sample must initially be cleaned up before final analysis. That is why the analytical chemist is faced with the need to devise new methodologies for determining such residues to be determined in a single analytical run. To accomplish the goal, QuEChERS methodology has been developed. It is a streamlined and effective extraction and cleanup approach for the analysis of diverse analyte residues in food matrices. So far, there have been achieved promising results by liquid or gas chromatography analysis, including pesticides, but also acrylamide, pharmaceuticals and veterinary drugs.

Contents

1. Introduction

The determination of pesticide residues in food matrices has become a necessity in view of the toxicity and stability of these xenobiotics (Bro-Rasmussen, 1996). Unfortunately, the analytical methods usually applied in laboratories for determining pesticides are far from ideal. Some laboratories determining pesticide residues are still using procedures developed 30 years ago, when analytical and legal requirements were less rigorous and technology was not as advanced as it is today. Traditional procedures are time-consuming, labour-intensive, complicated and expensive; moreover, they produce considerable quantities of wastes, and frequently, a sufficiently low limit of detection is unobtainable

Abbreviations: ASE, accelerated solvent extraction; d-SPE, dispersive solid-phase extraction; FDA, Food and Drug Administration; GC, gas chromatography; GCB, graphitised carbon black; LC, liquid chromatography; MAE, microwave-assisted extraction; MRMs, multiresidue methods; MS, mass spectrometry; MSPD, matrix solid-phase dispersion; QuEChERS, acronym for Quick Easy Cheap Rugged Effective and Safe, the name of a widely used methodology for the analysis of pesticide residues in food; PSA, primary secondary amine; SFE, supercritical fluid extraction; SPE, solid-phase extraction; SPME, solid-phase microextraction.

* Corresponding author. Tel.: +48 58 347 17 83; fax: +48 347 26 94.
E-mail address: angelika.wilkowska@gmail.com (A. Wilkowska).

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(Beyer & Biziuk, 2008). It is also quite a common occurrence that many physically and chemically different compounds have to be determined rather than one analyte or a single class of compounds. So we need to take a fresh look at the methodology of determining pesticide residues in food matrices.

2. Methodologies for determining pesticide residues in environmental samples

Multiclass, multiresidue methods – MRMs – are undoubtedly one way of addressing the problem of pesticide determination, worth looking at given the great diversity of this group of compounds. However, the complex sample matrix may contain abundant quantities of chlorophyll, lipids, sterols and other components that can interfere with good sample analysis. Unfortunately, the subject literature is not very enlightening where this approach to the determination of pesticide residues in food is concerned: hence this attempt to bring to the reader's attention some of the most important methodologies for analysing such residues.

The fundamental assumption underlying any methodology for determining residues is that it should guarantee true and precise results at appropriately low limits of detection for a wide spectrum of analytes. In addition, such a methodology should:

- ensure rapidity of analysis, with only a minimal time lag between collecting the sample and obtaining information on the quantities (concentrations) of analytes in it;
- be easy to carry out;
- be applicable with inexpensive reagents and apparatus;
- enable selective determination of analytes;
- ensure a high level of automation, thus minimising the effect of the human factor on results;
- be applicable with small amounts of solvents and reagents, so as to limit the quantities of wastes produced by the analytical process.

Fulfilling these requirements has never been easy. In Table 1 the methodologies used to determine pesticides in food matrices are chronologically listed. It begins with the first published method for determining non-polar pesticide residues, developed by P.A. Mills of the US FDA in the 1960s, and continues with methods, developed in the 1970s, for determining a wide spectrum of organochlorine, organophosphorus and organonitrogen pesticide residues of different polarities. It then moves onto methodologies worked out in the 1980s, when attention began to be drawn to environmental pollution and its effect on human health, and concludes with methodologies drawn up in accordance with the principles of sustainable development and green chemistry. Also the automated instrument based extraction procedures SFE and ASE, which were introduced in the mid 1990s to speed up extraction, did not succeed to replace traditional multiresidue approaches.

Despite the numerous advantages of the procedures and techniques developed during the last 20–30 years, none of them has succeeded in overcoming the practical limitations that have prevented their universal application. Table 2 compares the extraction techniques most frequently used in analysing food samples for their pesticide content. Although these approaches are useful and have a number of applications, they are not straightforward and efficient enough to be considered first-choice extraction techniques for determining pesticide residues in matrices with a complex composition.

Even though a whole range of methodologies for determining pesticide residues have been described over the past 40–50 years, none of them can be treated as a quick and easy analytical procedure ensuring selectivity and reproducibility in combination with high recoveries of a wide spectrum of analytes.

A quick and inexpensive procedure will now be described for determining pesticide residues in food providing reliable results whilst reducing the number of essential analytical steps, as well as quantities of reagents and laboratory glassware. This methodology simplifies the extraction of analytes and extract cleanup without adversely affecting the magnitude of analyte recoveries.

3. The QuEChERS analytical methodology

Anastassiades, Lehotay, Stajnbaher, and Schenck (2003) developed an original analytical methodology combining the extraction/isolation of pesticides from food matrices and extract cleanup. They coined the acronym QuEChERS for it, i.e. Quick, Easy, Cheap, Effective, Rugged and Safe. This technique involves microscale extraction using acetonitrile and purifying the extract using dispersive solid-phase extraction (d-SPE). Since the development and publication of the method, QuEChERS has been gaining significant popularity. It is the method of choice for food analysis because it combines several steps and extends the range of pesticides recovered over older, more tedious extraction techniques. The method has undergone various modifications and enhancements over the years since its first introduction. These have been designed to improve recovery for specific types of pesticides or types of food.

The traditional methods of determining pesticides in food are usually multi-stage procedures, requiring large samples and one or more extract cleanup steps. Therefore they are time-consuming, labour-intensive, complicated, expensive and produce considerable amounts of wastes. Moreover, the traditional methods often give poor quantitation and involve a single analyte or analytes from a single class of compounds. On the other hand, QuEChERS methodology reduces sample size and quantities of laboratory glassware. Clearly, QuEChERS requires fewer steps (no blending, filtration, large volume quantitative transfers, evaporation/condensation steps, or solvent exchanges required): this is very significant, as every additional analytical step complicates the procedure and is also a potential source of systematic and random errors.

The development of a new methodology requires a number of problems to be addressed, for example – choice of extraction solvent.

For determining pesticide residues in food matrices, the usual solvents have been acetone (Anastassiades, Lehotay, et al., 2003; Becker, 1971; Luke, Froberg, & Masumoto, 1975), ethyl acetate (Andersson & Palsheden, 1991; Banerjee et al., 2007, 2008; Fernandez-Alba, Valverde, Aguera, & Contreras, 1994; Holstege, Scharberg, Tor, Hart, & Galey, 1994; Mol et al., 2007), and acetonitrile (Anastassiades, Lehotay, et al., 2003; Mastovska & Lehotay, 2004; Fillion, Sauve, & Selwyn, 2000; Fillion et al., 2000; Lee, Papathakis, Hsiao-Ming, & Carr, 1991; Lehotay, 2000; Lehotay, Lightfield, Harman-Fetcho, & Donoghue, 2001; Mills, Onley, & Guither, 1963; Schenck, Callery, Gannett, Daft, & Lehotay, 2002; Storherr, Ott, & Watts, 1971), as all of them ensure large analyte recoveries. Although acetone is readily miscible with water but the separation of water from this solvent is impossible without the use of non-polar solvents. On the other hand, ethyl acetate is only partially miscible with water, which renders superfluous the addition of non-polar solvents to separate it from water but the most highly polar pesticides do not separate in it. Acetonitrile extracts of food (fruit and vegetables) contain fewer interfering substances than the corresponding ethyl acetate and acetone extracts, and acetonitrile can be separated fairly easily from water (salting out), therefore it is the extraction solvent of preference in the QuEChERS methodology.

Table 1
Main trends for analysing pesticide residues in food matrices.

	The assumption of the method	Sampling, extraction and cleanup	Additional information	Ref.
1960s	Mills' method for extracting organochlorine insecticides and other non-polar pesticides from low-fat food using acetonitrile	Acetonitrile combined with various amounts of water has been used in Mills' method. High-moisture products (fruits and vegetables) are extracted with pure acetonitrile whilst samples of dry products (hays, grains, feedstuff) are blended with a mixture of acetonitrile and water Extraction is followed by solvent partitioning into a non-polar solvent, e.g. petroleum ether with the addition of sodium chloride, dichloromethane or a mixture of dichloromethane and hexane. A Florisil column is used to cleanup the extract	Non-polar analytes can be determined. But relatively polar pesticides, such as organophosphorus insecticides, are partially lost at the stage of the analysis with non-polar solvent	Funch (1981), Mills et al. (1963), Osadchuk, Romach, and McCully (1971), and Wessel (1967)
	Storherr method – slight modifications of Mills' method to extend the analytical possibilities of Mills' procedure to make it applicable to compounds of different polarity	Extraction with acetonitrile, but the separation, cleanup and final determination steps are different. The non-polar petroleum ether is replaced by the higher polarity dichloromethane and Florisil is replaced by acid-treated charcoal	This method can be used for determination a wide range of organophosphorus in fruits and vegetables	Storherr et al. (1971)
1970s	A new method for determining a broad spectrum of pesticide residues of different polarity (organochlorine, -phosphorus and -nitrogen)	Acetone replaces acetonitrile in the initial extraction. The next step of the procedure is liquid–liquid extraction using non-polar solvents, like dichloromethane or a mixture of dichloromethane and petroleum ether, in order to remove water. A charcoal is used for a cleanup of the extract	This is the first method in which a solution of sodium chloride was added to the first extract; even so, saturation of the aqueous phase with salt was only partial	Becker (1971, 1979)
	Luke method and its modifications – methods for determining residues of various pesticides	The approach uses an acetone extractant, minimal cleanup and various GC systems with element-selective and element-specific detectors. Florisil cleanup is usually used for a combined cleanup of organochlorine and organophosphorous pesticides, but others methods are possible. In this method sodium chloride is added to saturate the aqueous phase, which increased the amount of acetone in the organic phase thereby raising its polarity, and in consequence leading to greater recoveries of polar analytes	This method, in one variation or another, is still used in pesticide residue analyses. The evolution of this method's applicability and general acceptance has been in direct relationship to advances in GC technology since 1975	Luke and Doose (1983), Luke et al. (1975), Specht and Tilkes (1980), and Vogelgesang and Thier (1986)
1980s		Procedures in which operations and processes are introduced that do not require the use of large amounts of chlorinated solvents; these are replaced by others, e.g. a 1:1 mixture of cyclohexane and ethyl acetate instead of dichloromethane, or a 1:1 mixture of dichloromethane and petroleum ether, in order to initiate separation	Acetone continues to be the most common solvent for the initial extraction step	Anastassiades and Scherbaum (1997) and Specht, Pelz, and Gilsbach (1995)
		Procedures in which solid-phase extraction (SPE) began to be used to isolate pesticides from dilute acetone extracts; this obviated liquid–liquid extraction		Casanova (1996)
		Methods using fructose or salts, e.g. $MgSO_4$ and/or NaCl, instead of non-polar solvents to separate water from acetone.		Schenck et al. (2002)
		Modifications of Mills' method: extraction with acetonitrile followed by the addition of a salt, e.g. NaCl, instead of a non-polar co-solvent. The resulting aqueous acetonitrile extract is filtered and cleaned up *via* reverse phase solid-phase extraction apparatus	When acetonitrile is used as an extraction solvent, the addition of a salt ensures the sufficient separation of water	Lee et al. (1991)
		Further methods for the determination of pesticide residues in food samples based on the salting out of acetonitrile extracts. Many possible cleanup techniques		Fillion et al. (2000), Lehotay (2000), and Lehotay et al. (2001)
		MRMs using ethyl acetate, which is only partially miscible with water, rendering	In order to increase recoveries of polar compounds, larger quantities of Na_2SO_4	Andersson and Palsheden (1991) and

(*continued on next page*)

Table 1 (*continued*)

The assumption of the method	Sampling, extraction and cleanup	Additional information	Ref.
	superfluous the addition of non-polar co-solvents to separate water from the extract. But some of the most polar pesticides do not separate in ethyl acetate. Many possible cleanup techniques	are added (to bind water)	Fernandez-Alba et al. (1994)
	Further methods for determining pesticide residues using ethyl acetate. Many possible cleanup techniques	To increase the polarity of the organic phase, polar co-solvents like methanol or ethanol are used	Holstege et al. (1994)
1990s	The development of green analytical chemistry in line with the concept of sustainable development led to a whole range of novel, alternative extraction techniques: SFE, MAE, MSPD, SPME and ASE		(References are in the text and in Table 2)

Abbreviations: SPE – solid-phase extraction; SFE – supercritical fluid extraction; MAE – microwave-assisted extraction; MSPD – matrix solid-phase dispersion; SPME – solid-phase microextraction; ASE – accelerated solvent extraction.

Table 2
Comparison of the modern extraction techniques most often used in the analysis of food matrices for their pesticide content.

Technique	Advantages	Disadvantages	Ref.
Microwave-assisted extraction (MAE)	– easily carried out, – simultaneous extraction of several samples, – only small quantities of solvents required, – short extraction time	– insufficient selectivity of extraction, – extract must be separated from post-extraction residue, – cleanup step needed, – cannot be used for thermolabile compounds, – waiting time for the vessels to cool down	Camel (2000); Papadakis, Vryzas, and Papadopoulou-Mourkidou (2006) and Singh, Foster, and Khan (2004)
Accelerated solvent extraction (ASE)	– extraction can be automated – all steps of the process can be carried out identically, – short extraction time, – moderate consumption of solvents, – simplicity of sample preparation prior to analysis	– high costs of purchasing and maintaining apparatus, – low extraction selectivity, – time-consuming cleanup of extracts and equipment after each use required	Carabias-Martinez, Rodriguez-Gonzalo, Revilla-Ruiz, and Hernandez-Mendez (2005), Giergielewicz-Możajska, Dąbrowski, and Namieśnik (2001), and Ramos, Kristenson, and Brinkman (2002)
Matrix solid-phase dispersion (MSPD)	– relatively low cost per analysis, – simple equipment, – simultaneous performance of several analyses, – can be used under *in situ* conditions, – only small quantities of solvents required	– a sufficiently wide analytical range in a single procedure not possible, – not very suitable for dry samples or samples with high lipids content, – adsorbent consumption is then relatively high and MSPD requires an additional cleanup step, – sometimes low recoveries of analytes	Barker, (2000a, 2000b), and Valsamaki, Boti, Sakkas, and Albanis (2006)
Solid-phase microextraction (SPME)	– use of solvents can be wholly eliminated, – lack of sensitivity to suspended matter, – limited adsorbent capacity, therefore, column cannot be overloaded in case when large amounts of analytes are present in a sample, – possibility to repeatedly re-run the analysis of a given sample, – possibility to use one fibre many times without loss of adsorbate, – chromatographs with ordinary injectors can be used – major changes in design are not necessary	– no way of ensuring a sufficiently broad analytical range in a single procedure, – problems with reproducibility, – frequent problems with method optimisation, – relatively low recoveries of analytes	Correia, Delerue-Matos, and Alves (2001), Pawliszyn (1997), and Wardencki, Michulec, and Curyło (2004)
Supercritical fluid extraction (SFE)	– solvent consumption substantially reduced, – possibility to extract thermolabile compounds, – does not result in degradation of the analysed compounds, – possibility to conduct fractionated extraction, – short extraction time, – relatively low labour intensity – a special device permits extraction in semi-automatic mode	– high costs of purchasing and maintaining the apparatus, – low extraction selectivity, – time-consuming cleanup of equipment after each use, – relatively complicated compared to others extraction techniques	Abbas, Mohamed, Abdulamir, and Abas (2008), Lehotay (2002), Camel (1998), and Ling and Teng (1997)
Membrane extraction techniques	– direct introduction of untreated samples, – decreased or no use of solvent, – possibility to analyse samples with very complex matrix, – high selectivity, – elimination of interferences, – high degree of analyte enrichment,– – easily automated	– high time consumption, – low efficiency, – sensitive to solid contaminants that easily clog membrane pores which leads to extended time of analysis	Hyotylainen, Tuutijarvi, Kuosmanen, and Riekkola (2002), Jakubowska, Polkowska, Namieśnik, and Przyjazny (2005), and Lambropoulou and Albanis (2007)

To avoid the use of co-solvents, which are often toxic and expensive, a series of experiments were carried out during the development of the QuEChERS methodology with the addition of various salts that were intended to induce a phase separation. These salts enabled pesticides of differing polarity to be analysed. Amongst the various salts tested, magnesium sulphate by effectively reducing the volume of the aqueous phase facilitates the partitioning of polar analytes into the organic phase and yields the largest recoveries of pesticides, particularly very polar ones like methamidophos, acephate or omethoate. Based on recoveries alone, $MgSO_4$ appears to be the best choice as the salt used in the method, but selectivity of the extraction process must also be considered. By varying the amount of NaCl added to the sample during partitioning with $MgSO_4$, it is possible to control the polarity range of the method and thus the amount of interferents in the extract. Experiments showed that a mixture of 4 g $MgSO_4$ and 1 g NaCl avoided co-extraction of some interferents (like fructose) and thus was used in later experiments.

The authors of the QuEChERS method expressed the opinion that shaking should always be used in preference to blending if results for incurred samples are demonstrated to be the same by both techniques. In support of their view they presented the following advantages of shaking over blending:

- during shaking the sample does not come into contact with the active metal surfaces of the blender and shaking does not generate heat due to friction (especially when solids are added);
- cleaning of the blender jar/probe between consecutive sample extractions is obviated, so no extra solvent from rinsing is added to the sample;
- shaking takes place in a closed vessel, which is safer, because no solvent vapours are emitted;
- the cost of purchasing and maintaining a vortex mixers/shakers is less than that of a blender.

Conventional column-based solid-phase extraction (SPE) uses plastic or glass columns containing a 250–2000 mg of a sorbent material. Also required is equipment for cleaning up and enriching extracts into the solid phase (vacuum manifold, cover, connectors and valves, pressure gauge, vacuum pump, solvent and sample receivers), not to mention column preconditioning, solvent waste fractions, collection fractions, manual operation and solvent evaporation steps. Although SPE with extraction columns has many advantages, it is not the ideal technique. That is why QuEChERS uses dispersive SPE (d-SPE), which saves time, effort, money and solvents in comparison with traditional SPE.

The tubes used in d-SPE can be prepared in the laboratory but they are also available commercially and may contain:

- magnesium sulphate – to separate water from the organic solvent,
- primary secondary amine (PSA) – to remove various polar organic acids, polar pigments, some sugars and fatty acids,
- graphitised carbon black (GCB) – to remove sterols and pigments such as chlorophyll,
- C_{18} – to remove non-polar interfering substances like lipids.

Table 3 (Anastassiades, Lehotay, et al., 2003; Lehotay, Mastovska, & Lightfield, 2005; Lehotay, Mastovska, & Yun, 2005) compares traditional column-based SPE with dispersive SPE; it was on this basis that d-SPE with a PSA was selected.

4. Determination of pesticide residues in fruit and vegetables

The procedure worked out by Anastassiades, Lehotay, et al. (2003) and Anastassiades, Mastovska, et al. (2003) (Fig. 1) is based on extraction by centrifugation of a food matrix with acetonitrile. Water is separated from acetonitrile by the addition of anhydrous magnesium sulphate and sodium chloride. The extract is then cleaned up using d-SPE with a PSA, which efficiently removes many polar interfering substances present in the matrix. The extract prepared in this way is then ready for final determination.

The researches of Anastassiades et al. were continued by Lehotay, de Kok, Hiemstra, and Van Bodegraven (2005), who validated the procedure for more than 200 pesticides in several matrices of different composition. GC–MS and LC–MS/MS were used for the final determinations. The results were very good for most of the pesticide residues investigated in fruit and vegetables; the exceptions were certain pesticides that exhibited pH-dependent stability problems. In nonacidic matrices, such as lettuce, pesticides sensitive to a basic pH, like captan, folpet, dichlofluanid and chlorothalonil, were degraded. This problem was overcome during the extraction process by the addition of a 0.1% solution of acetic or formic acid (Lehotay, de Kok, et al., 2005; Lehotay, Mastovska, et al., 2005).

Adding analyte protectants is another optional step found to be most useful for analytes that might tail or breakdown on the capillary GC column interior surfaces, on sorbed nonvolatile compounds from previous injection, on the inlet liner or on the precolumn (guard column). These compounds are chosen so that they do not interfere with the separation of the pesticides yet will cut down on interactions of these pesticides with active groups in the GC flowsteam. Thorough studies were devoted to selecting the appropriate analyte protectants, and a combination of sorbitol, gulonolactone and ethylglycerol were found to cover the entire range of pesticides (Anastassiades, Mastovska, et al., 2003;

Table 3
Comparison of traditional column-based SPE with dispersive SPE.

	Traditional column-based SPE	Dispersive SPE (d-SPE)
Advantages	– ensures better sample cleanup	– ensures larger and more reproducible recoveries of analytes with acidic or basic properties (e.g. acephate, carbendazim, imazalil, methamidophos, pymetrozine and thiabendazol),– does not require SPE apparatus, cartridges, vacuum, pretreatment of sorbent, channelling, drying out, collection tube, flow control, elution solvent, dilution of extract or solvent evaporation steps, d-SPE is therefore quicker and cheaper, – uses less sorbent, smaller amounts of sample and less equipment; d-SPE is thus a cheaper and easier technique – provides better interaction with the extract for cleanup
Disadvantages	– requires plastic cartridges containing 250–2000 mg of a sorbent material and vacuum manifolds, – requires a larger sample, – requires column preconditioning, solvent evaporation steps, manual operation and multiple solvents, – generates solvent waste fractions	– can only be used when the SPE sorbent removes matrix components and not the analytes

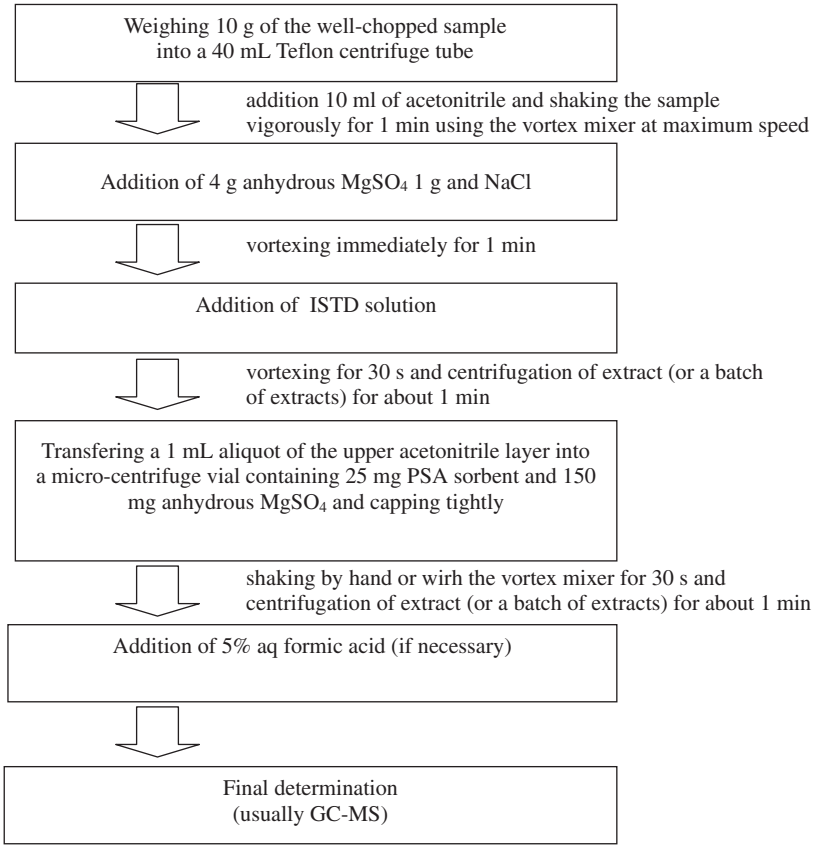

Fig. 1. The main steps in the QuEChERS analytical procedure for determining pesticides in food matrices (fruit and vegetables).

Mastovska, Lehotay, & Anastassiades, 2005). Of course, with LC and LC–MS, the protectants are not required.

Recoveries from different fruit and vegetables containing both polar and basic pesticides were generally in excess of 90 %, usually with a reproducibility of <5%.

5. Determination of pesticide residues in high-fat food matrices

The excellent results for fruit and vegetables obtained with the QuEChERS methodology generated interest in this procedure, and attempts were made to apply it to the determination of pesticide residues in high-fat food matrices (Lehotay, de Kok, et al., 2005).

The objective of Lehotay, Mastovska, et al. (2005) was to determine pesticide residues in foods containing up to 20% fat (milk and eggs) using the QuEChERS methodology. They recognised that foods containing from 2% to 20% fat could also contain residues of both lipophilic and hydrophilic pesticides; hence it would be reasonable to devise and develop analytical methods capable of simultaneously determining analytes with a wide polarity range. Such foods include milk, eggs, nuts, corn, soybeans, wheat and other grains, fish, shellfish and other seafood, kidneys, liver, poultry, pork, beef, and avocados. In contrast, in foods with a >20% fat content, e.g. vegetable oils, animal fats and butter, analytes are mainly non-polar, so there is no need to develop analytical methodologies for determining poplar pesticides in such matrices.

Although fats are not very soluble in acetonitrile, a certain quantity of them will be co-extracted, so they have to be removed prior to the final determination step. Modifications to the QuEChERS method to adapt it to fatty foods began with a fresh look at the extract cleanup step. In the case of samples practically devoid of fat (fruit and vegetables) cleanup using d-SPE (with PSA and anhydrous $MgSO_4$) ensured the removal of interfering substances without the recovery of analytes being affected in any way (Anastassiades, Lehotay, et al., 2003). In the case of fatty matrices, cleanup of extracts with graphitised carbon black very efficiently removed interfering substances, but it also removed certain pesticides like terbufos, thiabendazol, hexachlorobenzene and other planar-ring pesticides. So the cleanup efficiencies of extracts of such fatty matrices as eggs, milk, avocados and animal tissues with the QuEChERS method using sorbents like PSA, GCB and C_{18} together with traditional column-based SPE and d-SPE were compared. In addition, the 'original' QuEChERS method using NaCl and $MgSO_4$ to initiate separation of acetonitrile from water was compared with a modified buffered procedure in which a 1% solution of glacial acetic acid, and sodium acetate instead of sodium chloride, were added to acetonitrile in order to achieve a constant pH for the procedure regardless of the initial pH of the sample.

The modified buffered version of QuEChERS yielded larger recoveries of analytes and ensured the stability of pH-sensitive pesticides, so this method was used in subsequent experiments (Lehotay, Mastovska, et al., 2005). It was also found that GCB may be employed for the cleanup of samples only if they were to be analysed for pesticides other than planar-ring pesticides. For the analysis of these latter pesticides, samples were cleaned up using PSA and C_{18} with d-SPE. Finally, the traditional column-based SPE removed somewhat more interfering substances from egg extracts than d-SPE (Lehotay, Mastovska, et al., 2005).

The QuEChERS method was also applied to the analysis of other high-fat food matrices (olives and olive oil) for pesticides belonging to various classes (organochlorine, organophosphorus and triazines) (Cunha, Lehotay, Mastovska, Fernandes, & Oliveira, 2007; Garcia-Reyes, Ferrer, Gomez-Ramos, Molina-Diaz, & Fernandez-Alba, 2007). The results of extract cleanup with a mixture

Table 4
Applications of the QuEChERS methodologies in food sample preparation.

Food	Analytes	Sample preparation and extraction	Cleanup technique	Quantification method	Ref.
Cabbage and radish	107 Pesticides (fungicides, pyrethroids, OCPs[a], OPPs[b])	(1) A 10 g of homogenised sample of cabbage and radish with mixture of internal standards extract with 10 mL of acetonitrile (acetic acid 0.5 %) for 1 min; (2) keep the sample in a refrigerator for 30 min (until sample mixture reaches 4 °C); (3) add 4 g $MgSO_4$ and 1 g NaCl and vortex for 1 min; (4) centrifuge the extract for 5 min;	(5) sample 2 mL of prepared aliquot from the upper layer into a 5 mL micro-centrifuge vial containing 50 mg PSA and 300 mg $MgSO_4$ and vortex for 1 min, then centrifuge for 5 min; (6) transfer from the upper layer of the prepared sample an aliquot of 1.2 mL into a 1.8 mL vial and put into a vacuum concentrator to dryness;	(7) add 0.4 mL of acetonitrile to dissolve the residue and inject 1 μL of this solution onto the GC–MS system	Nguyen, Yu, Lee, and Lee (2008)
Rice paddies	203 Pesticides	(1) A 5 g of rice paddy samples with 5 mL HPLC-grade water, a mixture of internal standards and 10 mL of acetonitrile (acetic acid 0.5%) vortex two times for 1 min with a vortex mixer with 15 min intervals; (2) put the sample into a refrigerator for 30 min (until sample mixture reaches 4 °C); (3) add 4 g $MgSO_4$ and 1 g NaCl to the well-mixed rice paddy/acetonitrile/water mixture; (4) vortex the mixture immediately for 1 min and centrifuge the sample for 5 min using a refrigerated centrifuge;	(5) transfer 2 mL of the acetonitrile extract to a 5 mL micro-centrifuge tube containing 50 mg PSA, 300 mg $MgSO_4$ and 20 mg GCB; (6) vortex for 1 min and centrifuge the 5 mL micro-centrifuge tube for 5 min; (7) transfer 1.2 mL of the extract to a 1.8 mL vial and reduce to nearly dryness using a vacuum concentrator; (8) add 0.4 mL of acetonitrile to the vial and centrifuge for 5 min;	(9) transfer the extract to the GC auto-sampler vial for GC–MS analysis	Nguyen et al. (2008) and Nguyen, Yu, et al. (2008)
Grape, lemon, onion, tomato	140 Pesticides	(1) A 10 g of chopped fresh sample with 10 mL of acetonitrile shake for 1 min; (2) add 4 g anhydrous $MgSO_4$, 1 g NaCl, 1 g $C_6H_5Na_3O_7{\cdot}2H_2O$ and 0.5 g $C_6H_6Na_2O_7{\cdot}1.5H_2O$ and vortex for 1 min; (3) for acidic sample add a 6 N NaOH solution to reach a pH value between 5–5.5 and centrifuge the extracts for 3 min;	(4) transfer a 6 ml aliquot of the upper layer into a centrifuge tube containing 150 mg PSA and 950 mg $MgSO_4$; (5) centrifuge the extracts for 3 min and filter through 0.45 μm filter;	(6) transfer 1.5 mL of the extract into an auto-sampler vial containing 15 μL of a 5% formic acid solution (for the stabilisation of the extracts) for GC/MS and HPLC/MS analysis	Lesueur et al. (2008)
Barley	Herbicides	(1) A 2.5 g of spiked sample with 7.5 g water (to add the necessary moisture) and with 10 mL of acetonitrile hand-shake for 1 min; (2) add 4 g of anhydrous $MgSO_4$ and 1 g of NaCl; (3) hand-shake the mixture for another minute to provide a well-defined phase separation;	(4) separate two aliquots, with/without PSA clean-up, for different analysis; (5) cleanup the first aliquot with 25 mg of PSA and dry with 150 mg of $MgSO_4$ by mixing; (6) centrifuge 1 mL extract and filter through a 0.45 μm PTFE filter;	(7) analyse the first aliquot using GC–TOF/MS analysis; (8) filter the second aliquot and directly analyse by LC–MS/MS without PSA cleanup because it has been reported to retain acidic herbicides	Diez et al. (2006)
Olive and olive oil	OCPs[a], OPPs[b] and triazines	(1) A 3 g of olive oil (with 7 mL water) or 10 g olives with 10 mL of acetonitrile shake for 1 min and centrifuge;	(2) take aliquot (5 mL) and mix with $MgSO_4$ and [PSA–GCB–C_{18}]; (3) shake for 1 min and centrifuge;	(4) analyse with GC–MS or LC–MS	Garcia-Reyes et al. (2007)
Potato chips, sweet potato chips, various crackers and snacks, peanut butter, chocolate, and chocolate flavoured syrup	Acrylamide	(1) A 1 g of spiked homogenised sample with 5 mL of hexane, 10 mL of deionised water, 10 mL of acetonitrile, 4 g of anhydrous $MgSO_4$ and 0.5 g of NaCl shake for 1 min by hand to prevent formation of crystalline agglomerates and to ensure sufficient solvent interaction with the entire sample; (2) centrifuge the tube with the sample for 5 min; (3) discard the hexane layer;	(4) transfer 1 mL of the acetonitrile extract to a 2 mL minicentrifuge tube containing 50 mg of PSA and 150 mg of anhydrous $MgSO_4$; (5) vortex the extract with the sorbent/desiccant for 30 s; (6) centrifuge the tube for 1 min;	(7) place the supernatant into an auto-sampler vial for LC–MS/MS or GC–MS analysis	Mastovska and Lehotay (2006)
Chicken breasts	Veterinary drug	(1) A 5 g of spiked and homogenised chicken muscle with 15 mL of 1% acetic acid (v/v) in acetonitrile and 5 g anhydrous Na_2SO_4 mix using vortex for 30 s; (2) centrifuge the homogenate for	(3) delay at least 15 min and decant the supernatant into a tube containing 500 mg Bondesil NH_2 sorbent; (4) mix the extract/sorbent mixture intermittently over a period of 15 min and	(7) reconstitute the resulting residues in 1 mL of acetonitrile–water (90:10, v/v); (8) analyse with LC–MS/MS	Stubbings and Bigwood (2009)

(*continued on next page*)

Table 4 (*continued*)

Food	Analytes	Sample preparation and extraction	Cleanup technique	Quantification method	Ref.
		10 min;	centrifuge for 5 min; (5) transfer 3 mL aliquot of supernatant sample extract to a test tube; (6) evaporate each extract to dryness under N_2 at a temperature not exceeding 55 °C;		

[a] OCPs – ogranochlorine pesticides.
[b] OPPs – organophosphorus pesticides.

of three sorbents (C_{18}, PSA and GCB) were promising. Recoveries for most analytes were very good, only in the case of less polar analytes (organochlorine pesticides) were they below 70%.

6. Future to QuEChERS

The QuEChERS approach appears to have a bright future in the analysis of different class of pesticides in foods. In addition to the references cited previously, the methodology has proven successful for the extraction of pesticides from a variety of fruits and vegetables, like peaches, peppers, snow peas, green beans and cabbage (Schenck & Hobbs, 2004), strawberries (Looser, Kostelac, Scherbaum, Anastassiades, & Zipper, 2006), grape, lemon, onion, tomato (Lesueur, Knittl, Gartner, Mentler, & Fuerhacker, 2008), spinach (Li, Li, Qin, Jiang, & Liu, 2009), barley (Diez, Traag, Zommer, Marinero, & Atienza, 2006), rice (Koesukwiwat, Sanguankaew, & Leepipatpiboon, 2008), fatty food matrixes like eggs, milk and avocado (Lehotay, Mastovska, et al., 2005), olive and olive oil (Garcia-Reyes et al., 2007), and others. The articles describing the comparison of different versions of QuEChERS sample preparation approach for the determination of pesticide residues in food can be easily found (Lehotay et al., 2010).

There is no reason to believe that QuEChERS could not be used for extractions of other analytes besides pesticides and other samples besides foods. The QuEChERS methodology has already been applied to the determination of polycyclic aromatic hydrocarbons in fish (Ramalhosa, Paíga, Morais, Delerue-Matos, & Oliveira, 2009), acrylamide in food (Mastovska & Lehotay, 2006), veterinary drugs in animal tissue (Stubbings & Bigwood, 2009) and in milk (Keegan et al., 2009), drugs in blood (Plossl, Giera, & Bracher, 2006), beta-lactam antibiotics in bovine kidney tissue (Fagerquist, Lightfield, & Lehotay, 2005) and hormone esters in muscle tissues (Costain, Fesser, McKenzie, Mizuno, & Macneil, 2008). A simplified version of the QuEChERS method for the extraction of chlorinated pollutant compounds from soil samples (Pinto et al., 2010) and tobacco (Lee, Park, Jang, & Hwang, 2008) has been even proposed.

Some of recently reported studies concerning the QuEChERS sample preparation method (or the variations of the QuEChERS methodology) for the determination of xenobiotics in food matrices are presented in Table 4.

7. Summary

Sample preparation is always the major bottleneck in any analytical procedure for the determination of chemical residues in food products. The QuEChERS multiresidue procedure simplifies, and reduces the time taken to complete, the extraction and clean-up processes. The original procedure was developed several years ago, and since then, there have been adaptions and modifications. In the original procedure the water content of the sample was adjusted before extraction with acetonitrile. A well-defined separation of the acetonitrile phase was obtained by adding a combination of anhydrous magnesium sulphate and sodium chloride. The acetonitrile extract was subjected to dispersive solid-phase extraction using a primary secondary amine sorbent and was then ready for GC–MS analysis. It is without any doubt a useful extraction technique where the analysis of foods for pesticides with a wide range of polarity is concerned.

The QuEChERS method clearly has potential outside of pesticide analysis as it has been shown. This work highlights some of the multiresidue/class procedures applicable to the determination of acidic, basic and neutral drugs in various matrices. Several extraction/cleanup combinations showed promise initially, providing good recoveries of xenobiotics from different groups and classes, but they still need research.

To sum up, the QuEChERS method is adaptable and can be easily tailored to cope with new matrices through the selection of alternative sorbents. In fact the initial extract can be divided across tubes containing different sorbents to cater for problem analytes. Work in progress indicates that the developed extraction conditions will recover the majority of food contaminants including pesticides and veterinary drugs.

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