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The role of GC-MS/MS with triple quadrupole in pesticide residue analysis in food and the environment

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Abstract

Gas chromatography coupled to tandem mass spectrometry (GC-MS/MS) using a triple quadrupole (QqQ) analyzer has in the last few years become a powerful technique for the determination of pesticide residues due to its robustness, and excellent sensitivity and selectivity. This review gives an overview of currently published applications of GC-MS/MS with a QqQ analyzer for pesticide residue analysis of different food and environmental sample matrices. This technique allows the reliable quantification and identification of low pesticide concentrations for non-polar (semi) volatile compounds belonging to different chemical families. It has allowed a notable improvement of methods performance in comparison with the traditional GC methods with single stage quadrupole MS.

1. Introduction

Pesticide residue analysis (PRA) of food and environmental materials has become an important specialized field of modern analytical chemistry. The necessity of advanced analytical methods for its application in monitoring programs that ensure food-safety and environmentally responsible agricultural practices has been frequently highlighted. Reliable and sensitive analytical methods able to reach the low limits of quantification (LOQ) required by the legislation are needed. In most cases, LOQs lower than 0.01 mg kg^{-1} in food and lower than 0.1 μg L^{-1} in water are needed for monitoring purposes, where the reliable identification and quantification of hundreds of pesticide residues in many different matrices is normally pursued. In recent years, new developments in sample preparation and instrumentation, especially dealing with chromatographic techniques coupled to mass spectrometry (MS) or tandem MS, have allowed the high quality standards required from a qualitative and quantitative point of view in PRA to be achieved.

In the past decades, gas chromatography coupled to mass spectrometry (GC-MS) methods have been mostly based on selected ion monitoring (SIM) or full scan modes, evolving from single quadrupole (Q) to ion trap (IT) analysers. The first papers dealing with PRA by GC-MS can be traced back to 1970's when the determination of a reduced number of pesticides was carried out using packed column GC systems coupled to mass spectrometers with single quadrupole analyzers. In a recent review,[1] it has been reported that the single quadrupole is still the most used analyzer in combination with GC. Similarly, Botitsi *et al.*[2] showed that during the period of 2006 to 2009, 26 out of the 47 reviewed papers that employed GC-MS for the determination of pesticides in food and water were based on single quadrupole analysis. According to data reported, only 9 papers dealt with the use of triple quadrupole (QqQ), the rest being methods based on IT and time-of-flight (TOF) analyzers. In the review article from Andreu and Picó[1] on PRA in biota, 18 out of 24 papers reviewed dealt with the use of single quadrupole GC-MS.

Despite the wide existing applications, methods based on the use of single quadrupole instruments suffer from low sensitivity when working in the full scan mode. The sensitivity can be improved by working in the SIM mode, but the identification potential and the non-target/retrospective analysis capabilities are sacrificed. After development of the single quadrupole, the next step in the evolution of mass analyzers in pesticide residues analysis (without eliminating the use of the single quadrupole) was the increased use of ion trap mass spectrometers that allowed full spectra based methods to be developed with suitable sensitivity (similar to that obtained by a quadrupole in the SIM mode) in a single run. A number of papers have been published demonstrating the capability of ion trap analyzers for carrying out tandem MS experiments, improving sensitivity and selectivity, but losing the non-target capabilities. The fact that the MS/MS working mode of an ion trap is a product ion scan results in the co-elution of several analytes, or sample matrix components and notably reduces sensitivity and the number of points across the chromatographic peak. In the late 90s, the introduction of GC-TOF MS resulted in an improvement of full scan based methods and a step forward in non-target analysis. TOF MS is able to provide full spectrum acquisition data at high sensitivity. High-speed (HS) TOF MS, with a fast data acquisition rate (up to 500 spectra per second), is an excellent technique for GC × GC MS detection, for which the data acquisition speed is the most limiting factor. On the contrary, mainly coupled to 1D-GC and with lower data acquisition rates (20–25 Hz) and a narrower dynamic range, high-resolution (HR) TOF MS provides sensitive full spectrum data with high mass accuracy, allowing the resolution of peaks from closely related interfering matrix components. In the last years, many papers can be found dealing with the determination of pesticides in food and environmental samples by GC × GC-(HS) TOF MS[3,4] but much less related with GC (HR) TOF MS.[5,6] The most important limitation of TOF MS is related to its low sensitivity which can make it troublesome to reach the required limits of detection (LOD) and, in the case of the HR TOF, also the peak saturation problems that occur in short dynamic ranges.

One of the major developments in the field of PRA has been the commercialization of liquid chromatography (LC) coupled to QqQ MS systems, which has benefited greatly from the high sensitivity and selectivity of tandem MS in the selected reaction monitoring (SRM) mode. Thus, QqQ has been the analyzer most used in LC-based methods in the 2006–2009 period,[2] although this fact was not such evident for GC-based methods, which have suffered a notable delay in the wide acceptance of this analyzer in comparison to LC-MS/MS. In fact, LC-QqQ MS/MS started to be applied in PRA in the early 90's, while GC-QqQ MS/MS was applied around 15 years later. The first publications, between 2003 and 2005, reported the use of GC-QqQ MS/MS in food matrices like tobacco, oil, baby food or cucumber[7–10] and in human fat.[11]

Several papers have been published on the comparison of different analyzers in GC-MS. Mezcua *et al.*[12] compared GC-Q MS and GC-IT MS(/MS) for the determination of insecticides in vegetables indicating that no significant differences were found in terms of sensitivity, although IT under MS/MS conditions was superior to GC-Q MS in the identification capability. Garrido *et al.*[13] made an interesting comparison between two MS/MS systems, QqQ and IT, concluding that intraday-precision was similar for both, but interday-precision was found to be worst in the case of QqQ. In contrast, better linearity ranges were achieved for QqQ together with lower matrix effects especially for dirty samples *e.g.* fat containing samples. Additionally, a larger number of compounds can be included in a single injection in QqQ (SRM mode), although regarding identification capabilities IT in the tandem MS mode gives more information for a better confirmation of positive findings due to the MS^n possibilities.

Several ionization techniques have been used in GC-MS over time,[14,15] electron ionization (EI) being the most popular and widely used. EI offers valuable information on the molecule structure (several fragment ions and, in some cases, molecular ions). It is a robust and universal ionization source that generates highly reproducible spectra that can be searched in available commercial spectral libraries for the identification of non-target compounds. However, EI generates highly extensive fragmentation. In some cases, it leads to mass spectra without abundant/intense characteristic peaks (*e.g.* molecular ion), and the sensitivity obtained can be poor. In those cases, alternative approaches, such as chemical ionization (CI), which can be applied in both the positive or negative mode allow mass spectra to be obtained with a predominant molecular ion peak and low fragmentation. CI has been applied in PRA, especially for the determination of organohalogenated pesticides due to its better sensitivity and selectivity for some of these compounds.[16,17] However, there is a low number of applications compared to EI, and it is not posible to carry out spectral library searching as it is not commercially available for CI.

A promising source is atmospheric pressure chemical ionization (APCI), which opens a new perspective in the development of GC-MS/MS methods. This source has been recently tested in PRA and offers very attractive features for compounds that suffer extensive fragmentation in the EI mode.[18,19]

2. GC-MS/MS applications in food analysis

Nowadays, the control of pesticide residues in food commodities has become a requirement for compliance with the legislation, ensuring safety of the population and international and national trade. The determination of GC-amenable pesticides in food samples by using tandem MS with a QqQ analyzer has emerged in the last decade as a valuable approach, which allows higher selectivity and sensitivity and minimizes or even removes most chromatographic interferences. This section reviews the papers published in the last ten years related to the determination of pesticide residues in food samples by GC-QqQ MS/MS (Table 1). The most relevant aspects related to the studied pesticides, types of matrices, sample preparation procedures and analytical measurements are discussed in the present review.

The different physicochemical properties of the pesticide chemical classes increase the difficulty when developing a simultaneous analytical method for multiresidue analysis of food commodities. Thus, analytical methodologies based on GC-QqQ MS/MS for the determination of pesticides from the same family are quite common, *e.g.* for the determination of organochlorine (OC),[8,20,21] organophosphorus (OP) pesticides,[22–24] or of pyrethroids[19,25] in food commodities. Some particular examples are the GC-QqQ MS/MS method developed by Le Faouder *et al.*[26] just for fipronil, or by Peruga *et al.* for chlorothalonil.[27] Other authors have included two families of pesticides, typically OC and OP.[28–32] However, the majority of applications (around 70%) deal with multiresidue methods for multiclass pesticides in food samples,[7,9,10,16–18,33–58] the most adequate strategy available for monitoring purposes that minimizes time, costs, reagents, labors and hazards in order to obtain rapid analytical results in response to urgent demands. Moreover, most multiclass methods published include more than one hundred pesticides in their target list, among insecticides, herbicides, acaricides, fungicides, *etc.*[10,33,35–38,40,41,43,44,46–52,57] In this respect, remarkable papers are those published by Okihashi *et al.*[35] and by Banerjee *et al.*,[57] who have developed analytical methodology for the determination of up to 260 and 349 pesticides in fruits and vegetables, respectively.

Table 1 Pesticide residue analysis in food commodities by GC-(QqQ) MS/MS[a]

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2003, J. Haib *et al.*[7]	Tobacco	Tobacco	42 multiclass pesticides (NCI mode)	PLE (acetone) and SPE cleanup (Florisil, silica gel, GCB)	(NCI)MS/MS	50	1	None	
			26 multiclass pesticides (EI mode)		(EI)MS/MS				
2005, K. Patel *et al.*[8]	Pork and fish, olive and hydrogenated vegetable oil	10 hydrogenated vegetable oils	19 OC pesticides	GPC	(EI)MS/MS	10	2	Acquisition of 2 SRM transitions	Matrix-matched standards
2005, C. C. Leandro *et al.*[9]	Baby food of fruit and rice; fish and pasta; and potato and pork	Baby food of vegetable lasagne; chicken, leek and sweet corn risotto; spaghetti with tomatoes and mozzarella; vegetable and chicken risotto; apple and vanilla dessert; mango and banana with yogurt; tropical fruit salad; banana and peach dessert; creamy rice breakfast, and apple and blueberry	12 multiclass pesticides and TPs	QuEChERS method with d-SPE cleanup ($MgSO_4$, C_{18}, PSA)	(EI)MS/MS	1	2	Ion ratio within the expected range for standards	PTV injection (8 μL) Matrix-matched standards
2005, A. Garrido Frenich *et al.*[10]	Cucumber	2 cucumbers	130 multiclass pesticides	Solvent extraction (ethyl acetate, Na_2SO_4)	(EI)MS/MS	10	2-3	Relative intensity ratios (tolerance of ± 20% compared with standards)	PTV injection (10 μL) 1st injection: screening (1 SRM) 2nd injection: confirmation and quantification (2–3 SRM)

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (µg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2006 (a), A. Garrido Frenich *et al.*[28]	Chicken, pork and lamb muscle	10 chickens, 10 pigs and 10 lambs	45 OC and OP pesticides	Solvent extraction (ethyl acetate, Na_2SO_4) and GPC cleanup	(EI)MS/MS	50	2- 3	Relative intensity ratios (Decision 2002/657/EC)	PTV injection (10 µL) Matrix-matched standards
2006, J. L. Martínez Vidal *et al.*[33]	Cucumber	(15 samples) green bean, pepper, cucumber and tomato	130 multiclass pesticides	Solvent extraction (ethyl acetate, Na_2SO_4)	(EI)MS/MS	25	2-3	Relative intensity ratios (tolerance ± 20% compared with standards)	PTV injection (10 µL) 1st injection: screening (1 SRM) 2nd injection: confirmation and quantification (2–3 SRM) Matrix-matched standards
2006, S. Walorczyk and B. Gnusowski[34]	Tomato and onion	6 tomatoes	78 multiclass pesticides	Solvent extraction (ethyl acetate, Na_2SO_4) and cleanup (aminopropyl, $MgSO_4$)	(EI)MS (EI)MS/MS	200	1–2	A purity search factor above 600 (GC-MS)	Matrix-matched standard
2006(b), A. Garrido-Frenich *et al.*[29]	—	Chicken muscle	6 OC and OP pesticides	Solvent extraction (ethyl acetate, Na_2SO_4) and GPC cleanup	(EI)MS/MS	—	2-3	None	Based on 2006(a), *Garrido Frenich et al.*
2007, A. Garrido Frenich *et al.*[30]	Chicken liver	8 chicken, 8 pork and 9 lamb livers	34 OC and OP pesticides	Solvent extraction (ethyl acetate, Na_2SO_4) and GPC cleanup	(EI)MS/MS	25	2–3	4 IPs (Decision 2002/657/EC)	PTV injection (10 µL) Matrix-matched standards

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2007, M. Okihashi *et al.*[35]	Carrot, banana and grapefruit	(173 samples) fruits, vegetables and rice	260 multiclass pesticides	Solvent extraction (acetonitrile, $MgSO_4$, NaCl) and SPE cleanup (GCB/PSA)	(EI)MS/MS	20	2	Evaluation of relative intensity ratios	Matrix-matched standards Solvent exchange to acetone
2007, Le Faouder *et al.*[26]	Plant, milk and mineral feed	plants, milk and mineral feeds	Fipronil and 4 metabolites	Solvent extraction (ethyl acetate) and SPE cleanup (Florisil, Atoll)	(EI)MS/MS	0.025 μg L^{-1} (milk) 50 (plants)	2	Evaluation of relative intensities in-between two transitions	—
2007 (a), P. Plaza Bolaños*et al.*[36]	Strawberry	20 strawberries	151 multiclass pesticides	QuEChERS method with d-SPE cleanup (PSA, $MgSO_4$)	(EI)MS/MS (EI)MS(SIM)	11.5	2–3	4 IPs (Decision 2002/657/EC)	PTV injection (10 μL) Matrix-matched standards
2007, T. Pihlström *et al.*[37]	Grape, carrot, lettuce and orange	Orange and lemon	122 multiclass pesticides	Solvent extraction (ethyl acetate, Na_2SO_4, $NaHCO_3$)	(EI)MS/MS	10	2 (for most frequent pesticides) 1(for less frequent pesticides)	None	1st injection: screening (1 SRM) 2nd injection: confirmation and quantification(2 SRM) Matrix-matched standards

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2007, S. Walorczyk[38]	Wheat grain, barley, rye, bean, maize and animal feed based on rapeseed oil	(136 samples) cereal grain, bran, maize and by-products of rapeseed oil manufacture	122 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, C_{18}, PSA)	(EI)MS/MS	50 10 (only wheat and grain)	2	2 SRM transitions (Decision 2002/657/EC)	Matrix-matched standards. Solvent exchange to toluene
2007, P. Plaza Bolaños*et al.*[31]	Egg	20 eggs	38 OC and OP pesticides	MSPD extraction (C_{18}, $MgSO_4$) and SPE cleanup (Florisil)	(EI)MS/MS	15	2–3	3 IPs (Decision 2002/657/EC)	PTV injection (10 µL) Matrix-matched standards
2007, P. Payá*et al.*[39]	Lemon, raisin, wheat flour and cucumber	—	38 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA)	(EI)MS/MS	5 (cucumber and lemon) 10 (raisin and flour)	2–3	Maximum acceptable deviation in the relative intensity ion ratios (SANCO/10232/2006)	PTV injection (3 µL) Matrix-matched standards
2007, A. Garrido Frenich *et al.*[40]	Olive oil	8 olive oils	100 multiclass pesticides	LLE (hexane–acetone) and GPC cleanup	(EI)MS/MS	12	2–3	Relative intensity ratios (Decision 2002/657/EC)	PTV injection (10 µL) Matrix-matched standards.
2008, J. L. Fernández Moreno *et al.*[41]	Cucumber and orange	24 cucumbers, 19 tomatoes, 11 aubergines, pepper, 44 beans, 14 courgettes and 10 oranges	142 multiclass pesticides	Acetate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA)	(EI)MS (EI)MS/MS	11.5	2–3	A minimum of 3 IPs (Decision 2002/657/EC)	PTV injection (10 µL) Matrix-matched standards

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2008, J. M. Lee *et al.*[42]	Tobacco	—	49 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, C_{18}, PSA, GCB)	(EI)MS/MS	500	1	None	Matrix-matched standards
2008, E. Fuentes *et al.*[22]	Olive oil	8 olive and 2 avocado oils	9 OP pesticides	MAE (acetonitrile–dichloromethane) and SPE cleanup (ENVICarb)	(EI)MS/MS	30	2	Acquisition of 2 SRM transitions	PTV injection (2 μL) in split mode Matrix-matched standards
2008 (a), S. Walorczyk[43]	Wheat grain and feed mixture	Cereal grain, bran, whole ears, straw, hay and feed mixtures (145 in total); and 11 malts, 2 dried beans, potato starch and dried parsley root.	140 multiclass pesticides and 4 DPs	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, C_{18}, PSA)	(EI)MS/MS	10	2	A minimum of 3 IPs (Decision 2002/657/EC)	PTV injection (5 μL) Matrix-matched standards Solvent exchange to toluene
2008 (b), S. Walorczyk[44]	Lettuce	14 lettuces, 34 cabbages and 18 leeks	129 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA, GCB)	(EI)MS/MS	5	2	Relative intensity ratios (Decision 2002/657/EC)	PTV injection (5 μL) Matrix-matched standards Solvent exchange to toluene
2009, A. Garrido Frenich *et al.*[45]	Cucumber and orange	2 cucumbers and 2 oranges	12 multiclass pesticides	Solvent extraction (ethyl acetate, Na_2SO_4)	(EI)MS/MS	—	2–3	1st injection: 1 SRM transition (to detect positives). 2nd injection: 2–3 SRM transitions (to confirm)	PTV injection (10 μL) Matrix-matched standards

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2009, E. Fuentes *et al.*[23]	Olive and avocado oil	20 olive and 4 avocado oils	9 OP pesticides	APMAE and SPE cleanup (ENVI-C_{18})	(EI)MS/MS	25	2	Acquisition of 2 SRM transitions	PTV injection (2 μL)
2010, Wong*et al.*[46]	Bell pepper, broccoli, cantaloupe, carrot, onion, orange, peach, potato, spinach and tomato	Bell pepper, carrot, peach, spinach and tomato	167 multiclass pesticides and metabolites.	QuEChERS method with d-SPE cleanup (1st: C_{18}, $MgSO_4$; 2nd: PSA, GCB, $MgSO_4$)	(EI)MS/MS	10	2	Relative intensity ratios (Decision 2002/657/EC)	Matrix-matched standards Solvent exchange to toluene
2010 (b), Wong *et al.*[47]	Dried powdered ginseng	12 dried ginseng products	168 multiclass pesticides and metabolites	Solvent extraction (acetonitrile, acetone–cyclohexane–ethyl acetate) and SPE cleanup (C_8, GCB, PSA, Na_2SO_4)	(EI)MS/MS	25	2	Relative intensity ratios (Decision 2002/657/EC)	Matrix-matched standards Solvent exchange to toluene
2010, M. I. Cervera *et al.*[48]	Orange, nectarine and spinach	2 oranges, 2 nectarines and 2 spinach plants	130 multiclass pesticides	PLE (ethyl acetate) and GPC cleanup	(EI)MS/MS	10	2	Relative intensity ratios (Decision 2002/657/EC)	Study of matrix effect Matrix-matched standards
2010, L.-J. Qu *et al.*[24]	Leek	10 leeks	20 OP pesticides	MAE and acetate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA, GCB)	(EI)MS/MS	10	2	None	Solvent exchange to hexane

Table 1 (Continued)

Reference	**Validated matrix**	**Applied samples**	**Analytes**	**Sample preparation**	**Analysis mode**	**Lowest level validated (µg kg^{-1})**	**Number SRM transitions**	**Confirmation criteria**	**Comments**
2010, V. Nardelli *et al.*[20]	Fish feed	37 fish feeds	16 OC pesticides	LLE (hexane/acetonitrile) and SPE cleanup (silicagel-SCX)	(EI)MS/MS	20	2	A minimum of 3 IPs (Decision 2002/657/EC) and evaluation of the relative intensity ratios (tolerance of ±20% compared with standards)	No difference between calibration curves in solvent and in matrix
2010, Q. Lin*et al.*[59]	Corn, potato and cabbage	Corn, potato and cabbage	15 carbamates and chloroacetanilide pesticides	MSPD extraction (neutral alumina, acetone)	(EI)MS/MS	10	2	None	Matrix-matched standards
2011, F. J. Camino-Sánchez *et al.*[49]	Tomato, pepper, lettuce, cucumber, aubergines, courgettes, melon, watermelon and apple	944 tomatoes, 80 peppers, 10 lettuces, 189 cucumbers, aubergines, 61 courgettes, 60 melons, 78 watermelons and 18 apples	121 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA)	(EI)MS/MS	10	2	Relative intensity ratios (Decision 2002/657/EC)	PTV injection (6 µL) Matrix-matched standards Method accredited (UNE-EN ISO/IEC 17025:2005)
2011, Walorczyk & Drozdzynski [50]	Carrot, tomato and strawberry	78 apples, 73 tomatoes, 64 strawberries, 60 cucumbers, 58 currants, 57 mushrooms, 46 carrots, 37 peppers, 25 pears, 24 onions and 19 gooseberries	140 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA)	(EI)MS/MS	10	2	Relative intensity ratios (Decision 2002/657/EC)	PTV injection (5 µL) Matrix-matched standards Solvent exchange to toluene

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2011, M. L. Feo *et al.*[25]	Milk	—	12 pyrethroid pesticides	Solvent extraction (hexane–dichloromethane) and SPE cleanup (C_{18}, basic alumina)	(NCI)MS/MS	25	2	Acquisition of 2 SRM transitions	PTV injection (3 μL) Standards in solvent
2011, J. Dong*et al.*[17]	Cabbage and apple	2 pumpkins, ginger roots, carrots, burdock plants, shallots, spinach plants, garlic bulbs, peaches, grapes and apricots	82 multiclass pesticides	Acetate buffering QuEChERS method modified with d-SPE cleanup (C_{18}, $MgSO_4$, PSA)	(NCI)MS/MS	10	2	Acquisition of 2 SRM transitions	PTV injection (10 μL) Matrix-matched standards
2011, Y.-G. Zhao *et al.*[32]	Cabbage	3 cabbages, kidney beans, spinach plants, lettuces and aubergines	29 OC and OP pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, TEPA-NCM)	(EI)MS/MS	2	2–3	None	Solvent exchange to acetone Standards in solvent
2011, S. Walorczyk *e t al.*[51]	Red, white and rosé wine	22 red, 5 white and 3 rosé wines	161 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA and C_{18})	(EI)MS/MS	10 (red wine) 50 (white and rosé wine)	2	None	PTV injection (5 μL) Study of matrix effect Matrix-matched standards Solvent exchange to toluene

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (µg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2011, J. Sánchez-Avila*et al.*[21]	Mussel	5 mussels	12 OC pesticides, isomers and DPs	Solvent extraction and SPE cleanup (Florisil)	(EI)MS/MS	200	2	Relative intensity ratios (Decision 2002/657/EC)	—
2011, U. Koesukwiwat *et al.*[52]	Broccoli, cantaloupe, lemon and sweet potato	—	150 multiclass pesticides	Acetate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA, C_{18}, GCB)	(EI)MS/MS	10	2	None	PTV injection (5 µL) Matrix-matched standards
2011, J. Robles-Molina *et al.*[53]	Fruit-based soft drink	18 orange and 8 lemon flavoured soft drinks	32 multiclass pesticides	HS-SPME (polyacrylate fiber)	(EI)MS/MS	100 ng L^{-1}	3	Accomplishment of the ion ratio criterion (SANCO/10684/2009)	Matrix-matched standards
2011, J. Zhao*et al.*[54]	Cranberry	Cranberry	78 multiclass pesticides	QuEChERS method modified (H_2O, NaCl, Na_2SO_4, acetone–hexane) with d-SPE cleanup (PSA, GCB, $MgSO_4$)	(EI)MS/MS	10	2	None	Standards in solvent
2012, S. Walorczyk[55]	Apple, blackcurrant, carrot, huckleberry, strawberry and tomato	Apples, barley malt, blackcurrants, carrots, clementines, grapes, leek, plums, rapeseed, rucola, strawberries and tomatoes	36 multiclass pesticides	Citrate buffering QuEChERS method with d-SPE cleanup ($MgSO_4$, PSA, C_{18}, GCB)	(EI)MS/MS	—	2	None	CSR injection (5–20 µL) Solvent exchange to toluene

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2012, K.-G. Lee and E.-K. Jo[56]	Ginseng	118 fresh, 24 red and 10 dried ginsengs	32 multiclass pesticides	Solvent extraction (acetonitrile, NaCl) and SPE cleanup (Florisil)	(EI)MS/MS	30	2	None	Standards in solvent
2012, N. Belmonte Valles *et al.*[16]	Tomato, apple and orange	20 tomatoes, apples, pears, oranges and green beans	53 multiclass pesticides	Solvent extraction (ethyl acetate, NaCl and MgSO$_4$)	(NCI)MS/MS	1	2	The accomplishment ion ratio criterion (SANCO/10684/2009)	—
2012, Banerjee K *et al.*[57]	Grape, pomegranate, onion, okra, tomato	10 grapes, pomegranates, onions, okra, tomatoes	349 multiclass pesticides	QuEChERs method modified with d-SPE cleanup (MgSO$_4$, PSA, GCB)	(EI)MS/MS	5	2	None	PTV injection (5 μL) Matrix matched standards
2012 (a), T. Portolés *et al.*[18]	—	Apples, oranges, tomatoes and carrots	25 multiclass pesticides	Acetate buffering QuEChERS method modified with d-SPE clean-up (C$_{18}$, MgSO$_4$, PSA)	(APCI)MS/MSE I)MS/MS	—	2	None	Solvent exchange to toluene
2012 (b), T. Portolés *et al.*[19]	—	Apples, oranges, tomatoes and carrots	8 pyrethroid pesticides	Acetate buffering QuEChERS method modified with d-SPE clean-up (C$_{18}$, MgSO$_4$, PSA)	(APCI)MS/MS (EI)MS/MS	—	At least 3	None	Solvent exchange to toluene

Table 1 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2013, A. Peruga *et al.*[27]	Courgette, leek, tomato, strawberry, orange	Courgette	Chlorothalonil	Solvent extraction (acetone) and SPE clean-up (Oasis HLB)	(EI) MS/MS	10	2	The accomplishment of ion ratio criterion (SANCO/10684/2009)	EDTA added before extraction as preservative. Matrix matched standards
2013, Sapozhnikova Y and Lehotay S. J.[58]	Catfish muscle	21 catfish samples	18 multiclass pesticides	QuEChERs method with d-SPE cleanup ($MgSO_4$, Z-Sep Plus)	(EI)MS/MS	1	2	None	PTV injection (5 µL) Study of matrix effect

a **DP, Degradation Product; OC, Organochlorine; OP, Organophosphorous; TP, Transformation Product; EI, Electron Ionization; IP, Identification Point; NCI, Negative Chemical Ionization; SRM, Selected Reaction Monitoring; APMAE, Atmospheric Pressure Microwave-Assisted Extraction; CSR, Concurrent Solvent Recondensation; d-SPE, dispersive Solid Phase Extraction; GPC, Gel Permeation Chromatography; HS-SPME, HeadSpace Solid Phase Microextraction; LLE, Liquid–Liquid Extraction; MAE, Microwave Assisted Extraction; MSPD, Matrix Solid Phase Dispersion; PLE, Pressurized Liquid Extraction; PTV, Programmable Temperature Vaporizing; SPE, Solid Phase Extraction; GCB, Graphitized Carbon Black; PSA, Primary Secondary Amine; TEPA-NCM, TetraEthylPentAmine-Nano-Composite Material.**

In PRA, the term Food includes a wide range of treated products, fruits, vegetables, grains and other commodities. Even after being washed, stored, processed and prepared, some pesticide residues may remain in both fresh products and processed foods. From the overview of the applications shown in Table 1, it can be seen that fruits and vegetables are the most frequent samples analyzed.[10,16–19,24,27,32–37,39,41,44,46,48–50,52,54,55,57,59] Other matrices analyzed are oils and fats,[8,22,23,38,40] cereals,[38,39,43,59] muscles and livers,[28–30,58] tobacco,[7,42] ginseng,[47,56] animal feeds,[20,26] milk,[25,26] eggs,[31] wine,[51] mussels,[21] baby food[9] and fruit-based soft drinks.[53]

GC-MS/MS methods for pesticide residues include the extraction of the analytes from the matrix, appropriate cleanup of the raw extracts and final measurement. The most used approach for extraction of pesticides from food samples is nowadays the QuEChERS procedure (Quick, Easy, Cheap, Effective, Rugged and Safe), which has been widely reported in the literature.[60] Some variations of the original method have led to two modified methods: the acetate buffered method (AOAC official Method 2007.1)[61] and the citrate buffered method (CEN Standard Method EN 15662).[39] The QuEChERS procedure in combination with GC-QqQ MS/MS is one of the preferred approaches at present for residue determination of GC-amenable pesticides. Among the methods reported, it can be mentioned that those of Leandro *et al.*,[9] Plaza Bolaños *et al.*[36] and Wong *et al.*,[46] used the original method without modifications. In contrast, other authors obtained good results using the acetate buffered version,[17–19,41,52] although citrate modification seems to be more used in this field. In fact, the citrate buffered version has become the most applied extraction method in pesticide residue analysis in food by GC-QqQ MS/MS.[32,38,39,42–44,49–51,55] In these methods, a subsequent cleanup step is applied based on dispersive-solid phase extraction (d-SPE) using different sorbents, such as primary secondary amine (PSA), C_{18}, Z-Sep Plus and/or graphitized carbon black (GCB), depending on the complexity of the matrix.

Obviously, other sample preparation procedures have also been applied. Some authors performed a simple extraction with solvents such as ethyl acetate,[10,16,26,28–30,33,34,37,45,48] acetone,[7,27]acetonitrile;[35,47,56] or mixtures hexane–acetone,[40] hexane–acetonitrile[20] or hexane–dichloromethane.[25] Most of the reported procedures require the application of an additional cleanup step to remove interferences and also to improve detection limits. Gel permeation chromatography (GPC)[28–30,40,48] and solid phase extraction (SPE)[7,20–23,25,26,31,35,47,56] have been commonly applied for this purpose. As an exception, Robles-Molina *et al.*[53] proposed a method consisting of a solventless sample treatment procedure based on headspace solid-phase microextraction (HS-SPME) for the determination of target pesticides in fruit-based soft drinks.

After sample preparation, the final extract is commonly injected into the inlet system with a classical split/splitless injector. In some cases, the final extracting solvent is not appropriate for injection into the split/splitless system, due to the high volume-expansion coefficient during vaporization. Solvent exchange prior to chromatographic injection to an adequate solvent such as toluene,[18,19,38,43,44,46,47,50,51,55] acetone[32,35] or hexane[24] could be a good choice to solve this problem. Another option is the use of programmable temperature vaporizing (PTV), which is also employed to improve the limits of detection in PRA as it allows the injection sample volumes higher than the typical ones (1–2 µL) in a split/splitless injector.[9,10,17,25,28,30,31,33,36,39–41,43–45,49–52,57,58,62] Apart from PTV, other large volume injection (LVI) systems are on-column injection or concurrent solvent recondensation (CRS) injection.[55]

Regarding to the GC-QqQ MS/MS measurement (Table 1), EI is the most used ionization mode for the determination of pesticides in food, although the use of negative CI (NCI) has also been reported.[7,16,17,25] For some compounds, with highly electronegative elements, such as halogen, oxygen, *etc.*, the use of the NCI mode usually provides better sensitivity and selectivity. The use of the QqQ allows selected reaction monitoring (SRM) to be applied, one of the most selective and sensitive approaches for simultaneous quantification and confirmation in PRA, when adequate precursor and product ions are selected. In this way, most matrix interferences are minimized, or even eliminated, improving the selectivity and the sensitivity, and reaching low detections limits due to the lower chemical noise in the chromatograms.

In general, the criteria used for confirmation/identification of positive samples are not treated in detail in most of the papers published. Some authors do not mention this issue, and only acquire one SRM transition for each analyte without mentioning any confirmation criteria.[7,37,42] Other authors propose the acquisition of two SRM transitions, but do not mention which criteria are applied to consider positive confirmation.[18,24,29,32,37,51,52,54–59] Some authors[8,17,22,23,25] have used the mere presence of a second SRM transition as confirmation criteria for positives in the samples. However, the European Commission Decision 2002/657/EC[63] implements the concept of identification points (IPs). In the case of MS/MS determination, 1 identification point is earned from a precursor ion, and 1.5 identification points are earned from a resulting product ion. For the unequivocal confirmation of the identity of compounds at least 3 and 4 identification points are required for legal and banned substances, respectively.[43] This has been applied by several authors such as Garrido Frenich *et al.*,[30] Plaza Bolaños *et al.*,[31,36] Walorcyzk[38,43] and Fernández Moreno *et al.*[41] in their work. Nowadays, the most widely accepted approach is based on the presence of chromatographic peaks at the two (or three[53]) transitions acquired, together with agreement of the R_t and the evaluation of the intensity ratio between the quantification (Q) and the confirmation (q) transition, and comparison with those of the reference standard within the maximum tolerances established by the European Commission Decision 2002/657/EC[21,28,40,44,46–50] and the SANCO[64] guidelines.[16,27,39,53]

Modern QqQ instruments allow the simultaneous acquisition of two or more transitions in just a single GC analysis. However, some publications reported[10,33,37] performed a sequential approach with two sample injections: the first for rapid screening, with acquisition of only one transition, and the second for the confirmation and quantification of the compounds previously detected in positive samples, with acquisition of 2 or 3 transitions. As a particular example, Fuentes *et al.*[22,23] determined OP pesticides in olive oil by GC with flame photometric detection (GC-FPD) and the identity of residues in positive samples was confirmed through GC-QqQ MS/MS analysis by acquiring two transitions.

Once the identity of the analyte in the sample has been confirmed, quantification of pesticide residues is normally the next objective. Different approaches have been reported for quantification of pesticide residues in food, commonly considered as a complex matrix. Matrix-matched standards calibration is a good option for quantification of analytes affected by matrix effects, and it has been widely applied in PRA of food commodities.[8,9,17,22,27–31,33–53,57,59] Cervera *et al.*[48] studied the matrix effect of several food matrices (orange, nectarine, spinach, raisin, paprika, cabbage, pear, rice, legume and gherkin) comparing the response of reference standards prepared in solvent with the response of matrix-matched standards. Most of the pesticides showed an evident signal enhancement in the presence of matrix, and matrix-matched calibration using relative responses to an internal standard was required for the correct quantification of compounds. On the contrary, Nardelli *et al.*[20] performed the quantification of OC pesticides in fish feed by using standard solutions in solvent and in the matrix as calibration curves, no differences were observed between the results obtained using the different sets of standards. Other applications have been reported in the literature in which standard solutions in solvent were used for analysis of different matrices such as cabbage,[32] milk,[25] mussel[21] and ginseng.[56] As occurs with other analyzers used in GC-MS, the triple quadrupole analyser, even working in the SRM mode, is affected by coextracted matrix components that may lead to an enhancement of the chromatographic signal or to a reduction of the analyte response in comparison to the signal in pure solvent, as these effects are normally a consequence of problems coming from the GC system. Thus, when coextracted matrix components compete with the target pesticides to access the active sites of the GC system and/or when they are protected from decomposition in the hot injector, a matrix-induced response enhancement is observed. Conversely, accumulation of non-volatile coextracted matrix components in the GC system helps to generate new active sites, and matrix-induced response diminishment occurs.[45]

Sensitivity is an important parameter to measure the potential of a method in PRA. LOD and LOQ are usually calculated for this purpose, although their estimation is a controversial issue, due to the different ways of calculation. This makes it troublesome to perform a realistic comparison of the values reported in the literature. In order to compare the sensitivity of the applications reviewed, the lowest concentration level validated was used as an indicator of the sensitivity of GC-MS/MS methods. Most of the publications (Table 1) used a lowest level validated in the range of 5–10 μg kg^{-1}.[8,10,17,24,27,37–39,43,44,46,48–52,54,57,59] The use of a large injection volume resulted in an increase in the sensitivity, and lowered the method validation concentration down to 1 μg kg^{-1}. Thus, Leandro *et al.*,[9] Belmonte Valles *et al.*[16] and Sapozhnikova and Lehotay[58] validated their procedure at the lowest level of 1 μg kg^{-1} in baby foods, fruits and vegetables, or in catfish muscle, using large volume injections of 8, 2 and 5 μL, respectively.

3 GC-MS/MS applications in the analysis of environmental samples

The extensive use of pesticides in agriculture and their industrial applications in the last decades, together with the persistence of some of these compounds, has led to their wide presence in the different compartments of the environment. Consequently, there is a need to know the concentration of these contaminants in the aquatic environment, although they normally are found at the μg L^{-1} level or below. To this aim, strict regulations and environmental monitoring programs have to be adopted to accurately determine the concentration levels of pesticides. GC-QqQ MS/MS is an attractive technique with strong potential in the determination of low levels of pesticides in environmental samples, as occurs in food analysis.

The number of papers published until now related to environmental applications of GC-QqQ MS/MS in pesticide residue analysis is not as large as for food (Table 2). Only eighteen publications have been found and among them eleven developed analytical methodology for the determination of multiclass pesticides.[65–75] Only two articles deal with around hundred target analytes: Barco-Bonilla *et al.*[67] included 139 analytes in waste water samples analysis and Martínez Vidal *et al.*[69] included 98 pesticides in soil analysis. It is noteworthy that the first publication dealing with the use of GC-QqQ MS/MS for pesticides together with other organic contaminants in environmental samples dated 2007,[65] which illustrates the novelty and the recent use of this technique.

Table 2 Pesticide residue analysis of environmental samples by GC-(QqQ) MS/MS[a]

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2007, E. Pitarch *et al.*[65]	Deionized water	2 ground, 3 surface and 2 waste waters	25 multiclass pesticides	SPE (C_{18})	(EI)MS/MS (NCI)MS	25 ng L^{-1}	2	Relative intensity ratios (Decision 2002/657/EC)	Standards in solvent
2010, A. Penetra *et al.*[66]	Drinking, ground and surface water	Drinking, ground and surface water (55 in total)	9 multiclass pesticides	SPE (OASIS HLB)	(EI)MS/MS	25 ng L^{-1}	2	Relative abundances of the 2 selected SRM (tolerance of ±15%)	Standards in solvent
2010, N. Barco-Bonilla*et al.*[67]	Waste water	5 waste waters	139 multiclass pesticides	SPE (C_{18}) for aqueous phase PLE for suspended particulate matter	(EI)MS/MS	100 ng L^{-1}	2–3	None	Study of matrix effect Matrix-matched standards
2010, E. Pitarch *et al.*[68]	Waste water	41 waste waters	26 multiclass pesticides	SPE (C_{18})	(EI)MS/MS	—	2	Relative intensity ratios (Decision 2002/657/EC)	Based on 2007, Pitarch *et al.*
2010, J. L. Martínez Vidal*et al.*[69]	Soil	26 agricultural soils	98 multiclass pesticides	PLE (ethyl acetate–MeOH)	(EI)MS/MS	5 ng g^{-1}	≥ 2	FIT >700 for SRM spectra	PTV injection (10 μL) Study of matrix effect Matrix-matched standards

Table 2 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2010, A. Rashid *et al.*[76]	Soil	6 soils	19 OC pesticides	Acetate buffering QuEChERS method with LLP cleanup (acetonitrile, H_2O, hexane)	(EI)MS/MS	1 ng g^{-1}	2	Acquisition of 2 SRM transitions	Matrix-matched standards
2011, M. L. Feo *et al.*[25]	Water and sediment	—	12 pyrethroid pesticides	Water: UAE (chloroform) Sediment: solvent extraction with hexane–dichloromethane and SPE cleanup (Florisil)	(NCI)MS/MS	0.25 ng L^{-1}(water) 5 ng g^{-1}(sediment)	2	Acquisition of 2 SRM transitions	PTV injection (3 μL) Standards in solvent
2011, F. J. Camino-Sánchez *et al.*[70]	Marine sediment	9 marine sediments	55 multiclass pesticides	PLE (MeOH) and SBSE	(EI)MS/MS	10–30 ng g^{-1}	2	Relative intensity ratios (tolerance of ±25%)	Matrix-matched standards

Table 2 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2011, J. Sánchez-Avila*et al.*[21]	Water and marine sediment	5 WWTP, 5 sea and 5 river waters, 5 sediments	12 OC pesticides	Water: SPE (Oasis HLB) Sediment: solvent extraction and SPE cleanup (Florisil)	(EI)MS/MS	10 ng L^{-1}(river and sea waters) 250 ng L^{-1}(WWTP effluents) 100 ng g^{-1}(sediment)	2	Relative intensity ratios (Decision 2002/657/EC)	Matrix-matched standards
2011, C. Coscollà *et al.*[71]	Airborne particulate matter	38 airborne particulate matters	40 multiclass pesticides	MAE (ethyl acetate) and GPC cleanup (methylene chloride)	(EI)MS/MS	10 ng mL^{-1}	2	Acquisition of 2 SRM transitions	Study of matrix effect Matrix-matched standards
2011, Cervera*et al.*[80]	Mineral water	2 WWTP, 2 SWTP and 1 surface water	8 OC pesticides	HS-SPME (CAR/PDMS)	(EI)MS/MS (EI)MS	100 ng L^{-1}	2	Relative intensity ratios (Decision 2002/657/EC)	Statistical optimization of extraction variables Calibration extracted with same procedure
2011, A. Garrido Frenich *et al.*[72]	Drinking water	41 drinking waters	77 multiclass pesticides	SPME (PDMS-DVB) and HF-LPME cleanup (octanol–dihexyl ether)	(EI)MS/MS	50 ng L^{-1}	≥ 2	Acquisition of 2 SRM transitions	Study of matrix effect Standards in solvent

Table 2 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated (μg kg^{-1})	Number SRM transitions	Confirmation criteria	Comments
2012, F. J. Camino-Sanchez *et al.*[73]	River water	—	50 multiclass pesticides	SBSE	(EI)MS/MS	0.14–10 ng L^{-1}	2	Relative intensity ratios (tolerance of ±25%)	Matrix-matched standards
2012, Devos *et al.*[78]	Mineral water	2 harbor, 1 tap, 1 mineral and 7 waste waters	Tributyltin	SBSE	(EI)MS/MS	1 ng L^{-1}	4	Relative intensity ratios	Two-dimensional GC approach. Calibration extracted with same procedure
2012, Chary *et al.*[77]	River water and WWTP effluent waters	River water and WWTP	25 OC pesticides	SBSE	(EI)MS/MS	10 ng L^{-1}	2	Acquisition of 2 SRM transitions	Matrix-matched standards
2012, Cavaliere *et al.*[79]	Drinking water	Mineral and tap water	5 carbamate pesticides	SPME (PDMS/DVB)	(EI)MS/MS	80 ng L^{-1}	2	Acquisition of 2 SRM transitions (Decision 2002/657/EC)	Statistical optimization of extraction variables Calibration extracted with same procedure
2013, Camino-Sánchez *et al.*[74]	Drinking water	500 drinking waters	45 multiclass pesticides	SBSE	(EI)MS/MS	0.25–10 ng L^{-1}	2	Relative intensity ratios (tolerance of ±25%)	Calibration extracted with same procedure

Table 2 (Continued)

Reference	Validated matrix	Applied samples	Analytes	Sample preparation	Analysis mode	Lowest level validated ($\mu g\ kg^{-1}$)	Number SRM transitions	Confirmation criteria	Comments
2013, Robles-Molina *et al.*[75]	Waste water	33 waste waters	40 multiclass pesticides	LLE (hexane)	(EI)MS/MS	15 ng L^{-1}	3	Relative intensity ratios (Decision 2002/657/EC)	Matrix-matched standards

a **OC, organochlorine; WWTP, Waste Water Treatment Plant; SWTP, Solid Waste Treatment Plant; EI, Electron Ionization; NCI, Negative Chemical Ionization; SRM, Selected Reaction Monitoring; GPC, Gel Permeation Chromatography; HF-LPME, Hollow Fiber Liquid Phase Microextraction; LLP, Liquid–Liquid Partition; MAE, Microwave Assisted Extraction; PLE, Pressurized Liquid Extraction; PTV, Programmable Temperature Vaporizing; SBSE, Stir-Bar Sorption Extraction; SPE, Solid Phase Extraction; SPME, Solid Phase Microextraction; UAE, Ultrasound Assisted Extraction; LLE, Liquid–Liquid extraction; PDMS-DVB, Polydimethylsiloxane-Divinylbenzene.**

Depending on the complexity of the matrix, different techniques have been used to extract the analytes. For example, soil generally requires the use of stronger techniques capable of extracting potentially bound residues. Only two applications dealt with soil analysis: Martínez Vidal *et al.*[69] who used a pressurized liquid extraction (PLE) technique with a mixture of ethyl acetate and methanol for investigation of multiclass pesticides, and Rashid *et al.*[76] who developed a methodology based on acetate buffering QuEChERS with a posterior liquid–liquid partition (LLP) cleanup for the determination of OC pesticides. In the case of sediments, analytical methodologies are based on extraction with different solvents followed by an additional cleanup or concentration step using SPE[21,25] or stir-bar sorption extraction (SBSE).[70] Airborne particulate matter has been another environmental matrix analyzed by GC-QqQ MS/MS,[71] using microwave-assisted extraction (MAE) followed by GPC as a cleanup step. As shown in Table 2, water has been the most common matrix studied in the environmental field. SPE using different sorbents has been the technique of choice by most authors.[21,65–68] Some exceptions applied to pyrethroids pesticides that were extracted using ultrasound-assisted emulsification extraction (UAEE) with chloroform,[25] and SBSE which was used for the analysis of pesticides in river water[73,77] or in drinking water.[74,78] Garrido Frenich *et al.*[72] compared both SPME and hollow fiber liquid phase microextraction (HF-LPME) for the extraction of pesticides in drinking water, concluding that SPME and GC-MS/MS offered the best compromise in terms of quality, speed and reliability.

After extraction (and occasionally cleanup), GC-amenable pesticides described in Table 2 were determined by GC-QqQ MS/MS in the SRM mode. In all the publications, at least two transitions were acquired and most used the EI mode. Feo *et al.*[25] concluded that the best selectivity and sensitivity for the determination of pyrethroids in water and sediment was obtained by using GC-MS/MS in the NCI mode. Pitarch *et al.*[65] developed the first GC-MS/MS methodology for priority organic pollutants in water, including several pesticides. Although the EI mode was used for the general method, a supplementary methodology based on GC-(NCI) MS using the selected ion recording (SIR) mode was proposed for quantification and confirmation of OC pesticides as it allowed notable sensitivity improvement for these compounds. As regards confirmation identity, it is based on the presence of at least two SRM transitions[25,71,72,76,77,79] and R_t agreement, although several authors also took into account the experimental relative intensity ratio of the sample and the theoretical ratio of the reference standard, using the maximum deviations established in the European Commission Decision 2002/657/EC,[21,65,68,75,79,80] or based on other defined tolerances.[66,70,73,74,78]

Quantification for water samples has been mostly based on calibration in solvent.[25,65,66,68,72] For more complex matrices, matrix-matched calibration provided better results, as in the case of soil samples,[69,76] marine sediments[21,70] or even airborne particulate matter.[71]

The GC-MS/MS methods applied in the analysis of environmental samples presented excellent sensitivity. In the case of soils and sediments, the lowest level validated was as low as 1 ng g^{-1}[76] or 5 ng g^{-1}.[25,69] The purity of the air was evaluated by analyzing the airborne particulate matter performing the validation at the lowest level of 10 ng mL^{-1}.[71] As regards water samples, the lowest level validated is reported to be 0.14 ng L^{-1} for a variety of priority organic pollutants.[73] As expected, the lowest level validated in waste water was much higher, as a consequence of the higher matrix complexity.[67,75,77]

4 Trends and perspectives

After its first use for PRA around 10 years ago, GC-QqQ MS/MS has been consolidated in most laboratories. This technique has the degree of robustness required to be widely applied at present, and the improvements offered as regards method sensitivity and selectivity are widely recognized. The determination of pesticide residues by GC-MS is commonly based on the use of relatively long capillary columns (25–30 m) with internal diameters of 0.25–0.32 mm by using typically low polarity stationary phases (from 100% methyl silicone to 5% phenyl methyl silicone in most cases) leading to chromatograms of tenths of minutes. Fast GC coupled to MS has been shown to be an interesting alternative that, through different instrumental approaches, allows increased sample throughput by reducing the analysis time.[81,82] In this way, low-pressure GC-QqQ MS/MS has been applied to pesticide residue analysis, with an important increase in sensitivity, shorter run time, higher sample loading and increased ruggedness.[81,83] Another approach is based on the use of narrower columns with internal diameters of 0.1 mm i.d. combined with fast column temperature programming, resulting in an increase in sensitivity, a reduction in the analysis time and peak width and thus an increase in resolution, thereby making it feasible to determine even more than one hundred pesticides in analysis times lower than 10 minutes.[82,84]

The use of APCI as an ionization source for GC-MS methods, is a major advance that will greatly improve pesticide residue determination (and other GC amenable compounds) due to its soft ionization behaviour in comparison with that obtained by EI. Portolés *et al.*[18,19] have demonstrated the capabilities of this soft ionization source for producing spectra with much lower fragmentation than that obtained by EI, where the molecular ion is commonly absent (or with low abundance). In these cases, when using EI it is necessary to select a fragment ion as a precursor ion in the MS/MS method and, consequently, not only the sensitivity but also the specificity of the method can be affected. With APCI, M^+ or $[M + H]^+$ is the base peak of the spectra in most cases. Under these conditions, precursor-ion selection would no longer require a compromise between selectivity and sensitivity, allowing more specific MS/MS experiments. This approach has not yet been exploited in pesticide residues analysis but it will surely be a major advance in this field in the near future.

A combination of GC-MS/MS and LC-MS/MS, both with a triple quadrupole analyser, is one of the most current powerful approaches in PRA. They are complementary techniques that allow the determination of pesticides and metabolites within the whole range of physico-chemical properties, such as volatility, polarity and thermal stability. The combined use of both techniques allows the monitoring of hundreds of compounds that are GC or LC amenable. The present trend in multiresidue analysis is the application of generic sample preparation leading to sample extracts that are analysed by both LC-MS/MS and GC-MS/MS, this being nowadays one of the most “universal” approach in PRA.

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