Chapter 3

Determination of Pesticide Residues in Environmental and Food Samples Using Gas Chromatography–Triple Quadrupole Mass Spectrometry

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Chapter Outline

1 INTRODUCTION

To ensure the compliance with the regulations and guidelines of maximum residue limits (MRLs) of pesticides in the environment and foods established by government agencies (e.g., *U.S.* 40 *CFR Part* 180; *Ontario Regulation* 169/03; 2005/396/*EC*; 2008/299/*EC*) [1–4], various analytical technologies have been evaluated and analytical methods developed so that pesticide residues could be identified and quantitated with high confidence for timely enforcement of tolerances. Over the past 30 years, the applications of mass spectrometry (MS) have been promoted by the advances in ionization sources and commercial availability of MS instruments. MS has become an

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indispensable tool in the routine analysis of chemical contaminants in the environment and foods [5–9].

Among various MS instruments, triple quadrupole mass spectrometry (QqQ-MS), first reported by Yost and Enke [10,11], has its unique designs and applications and the first commercial QqQ-MS was introduced by Finnigan and Sciex in the early 1980s [12,13]. The QqQ-MS is different from single quadrupole (Q) MS systems, which can be operated only in two data acquisition modes, that is, single ion monitoring (SIM) or full scan. A typical QqQ-MS consists of two quadrupole MS analyzers (Q1 and Q3) and a collision cell (q) sandwiched between the two MS analyzers. Depending on the purposes of applications (structure elucidation or quantitation), the instrument can be operated in several modes such as full scan, precursor ion scan, neutral loss scan, product ion scan, or selected reaction monitoring (SRM) mode (also referred as multiple reaction monitoring, MRM). When operating in SRM mode, QqQ-MS can be used as a quantitative tool for target analysis of small molecules in environmental and food samples.

When operated in the SRM mode, the first and second mass analyzers (Q1 and Q3) focus on a set of predefined ions, precursor ions at Q1 and the corresponding product ion at Q3. A collision gas (typically N_2 or Ar) is introduced into the collision cell (q) at a pressure to ensure that ions entering the collision cell will undergo collision-induced dissociation (CID) with collision gas molecules. Only ions with the same m/z as those predefined precursor ions will be selected by Q1 and sent into the collision cell (q). These ions will be subjected to CID in the collision cell (q), generating fragments. Those fragments with the same m/z as the predefined product ions will be selected by Q3 and measured by the detection system. The use of a molecular-specific precursor/product ion pair in the SRM mode for each molecule analyzed also implies a MS-based separation of molecules and, as it will be discussed in this review, an ideal approach in multiresidue pesticide analysis.

The intensity of detected product ions is usually less than that of their precursor ions because of fragmentation and imperfect ion transmission efficiency. The loss of signal is offset by noise eliminated in the product ion m/z. Signal-to-noise ratio (SNR) is enhanced by the absence of any signal arising from the precursor and product ion monitored, except when the specified pesticide is present. Additionally, U shaped collision cells are often used to minimize interference of neutral species. Therefore, the overall SNR is increased, resulting in better sensitivity of GC–QqQ-MS as compared to GC–MS full scan or GC–MS-SIM. Meanwhile, higher selectivity is achieved by choosing specific precursor and product ions informed by molecular structures associated with mass spectra ions. Theoretically, it is possible to perform higher order MS^n experiments by combining N ($N > 2$) mass analyzers together. This approach, however, will increase the complexity and cost of the system and makes it a less practical instrument for routine analysis.

Pesticide residue analysis using GC–QqQ-MS takes advantage of both chromatographic separation and mass spectrometric determination and has been

applied in many multiresidue pesticide methods [14]. A large number of pesticides can be included in one GC–QqQ-MS method, improving the screening efficiency of pesticide laboratories. Unlike SIM methods where four ions are generally needed for confirmation of each pesticide, QqQ methods only require two transitions and unlike full scan methods, QqQ does not sacrifice sensitivity in a comprehensive method. In a GC–QqQ-MS analysis, target pesticides are first separated from matrix components on a GC column and sequentially introduced into a QqQ-MS analyzer. Using pesticide-specific SRM mode, pesticides undergo ionization in the ion source; precursor ions are selected and separated in the Q1, and fragmented in the collision cell; and those selected product ions are detected in the Q3. The SNR of a detected pesticide can be further improved by setting a specific detection time window on Q1 and Q3 based on each pesticide's GC retention time (RT; time-segment-based SRM data acquisition). This approach reduces the number of MRM transitions monitored by the QqQ at a specific time, allows Q1 and Q3 to be operated in a more efficient manner, and distributes more QqQ measurement time (dwell time) for each pesticide to improve the SNR of the target pesticides [15,16].

2 METHOD DEVELOPMENT

To develop a GC–QqQ-MS method, one needs to first generate MRM transitions for each pesticide. According to EU identification criteria [17], it is enough to achieve identification of a pesticide using two MRM transitions and their relative ion abundance ratio, provided the RT matches. The transition with higher abundance could be used for quantitation and the other transition can be served as a confirmatory ion, but the selection should be dependent on the conditions of the analysis.

An optimized MRM transition should include a precursor ion, a product ion, and an optimized collision energy; optimal choices can be generated based on the structure and full scan mass spectra. This is done by first selecting a precursor ion with the highest *m/z* (molecular ion) and abundance because background interferences decrease with an increasing *m/z* [18] and enhances the SNR further. The 70 eV energy used by electron ionization (EI) source of GC–QqQ-MS often cannot generate molecular ions with enough abundance. Under this circumstance, a compromise has to be made between selectivity and sensitivity by choosing EI-induced fragments with enough abundance in full scan spectra as precursor ions [19]. Then each selected precursor ion will undergo CID to generate products ions at different collision energies. The optimal SRM transitions carry specific structural information of the target pesticides for identification (selectivity and separation) and have enough abundance to be detectable (sensitivity and SNR). To ensure selectivity of GC–QqQ-MS analysis, unspecific MRM transitions such as $[M]^+ \rightarrow [M]^+$ (such a transition does not provide additional specificity than would be obtained through SIM) as well as $[M]^+ \rightarrow [M-1]^+$ or $[M]^+ \rightarrow [M-2]^+$ (due to deprotonation in the course of ionization) ought not be used to avoid interferences.

Once all transitions are ready, one needs to arrange those transitions in different time segments based on each pesticide's GC RT. When performing multiresidue pesticide analysis, a QqQ-MS has to monitor many coeluting MRM transitions in one GC chromatographic run. A QqQ-MS needs a minimum of a few milliseconds to monitor a transition. In a given cycle time, too many concurrent transitions will overwhelm the QqQ-MS. However, if the cycle time is increased to accommodate those transitions, insufficient data points might be collected to actually define a peak. There are no official documents that define the minimum data points required for peak definition, but six to eight points per peak would be sufficient [20]. When building MRM data collection segments, one needs to factor in the cycle time, number of transitions in a segment, dwell time of each transition, minimum data points per peak required, and RT shifts due to matrix effects or column performance. It is challenging to have a large number of overlapping segments based on RTs because of the large number of targeted analytes included in the method. In recent years, scheduled multiple reaction monitoring (sMRM) or similar software algorithms have been introduced. The main advantage of these algorithms is to automatically optimize dwell time, data points, and response for each MRM transition within a user-defined time window. Compared to the conventional time segment approach, sMRM decreases the number of concurrent MRM transitions monitored at any time, thus increasing SNR and reproducibility, and simplifying the method development [15,16].

3 APPLICATIONS OF GC–QqQ-MS

The determination of pesticides in environmental and food samples involves sample preparation (including extraction, cleanup, solvent exchange, concentration, etc.) and instrumental analysis. The purpose of sample preparation is to selectively extract the targeted pesticides based on their physicochemical properties and further separate from the matrix components to make the sample more suitable for instrumental analysis. If the instruments do not have sufficient sensitivity, selectivity, and ruggedness, the emphasis will rely on sample preparation, which could be time consuming and laborious. With the availability of sensitive and selective instruments, the sample preparation task could be significantly simplified, enabling sample dilution to minimize matrix interferences and eliminating or reducing additional concentration and cleanup efforts.

3.1 Determination of Pesticides in Environmental Samples

One of the main areas of interest to environmental chemists is the identification and quantification of pesticides in water, air, soil, and sediments. Pesticides are an important class of hazardous organic chemicals in the environment due to their potential persistence and bioaccumulation. The applications of QqQ-MS in environmental analysis can be traced back to the early 1980s [21], but the high cost and technological limitations such as data acquisition speed and

operating software of QqQ-MS slowed down the use of this technology until 2000s.

A recent environmental application of GC–QqQ-MS involves the potential adsorption of pesticides onto aerosol particles (<2.5 μ), which can pose a threat to human health, so it is important to monitor pesticides in particulate matters. Coscollà *et al*. [22] developed a GC–QqQ-MS method that can monitor 40 pesticides in airborne particulate matter (PM 10). PM 10 samples were collected using quartz filters (150 mm, diameter). Pesticides were extracted using microwave-assisted extraction, cleaned up using gel permeation chromatography (GPC), and determined using two MRM transitions for each pesticide. To ensure the selectivity of the QqQ-MS system, Coscollà *et al*. also proposed to use accurate masses, using a 10 mDa mass accuracy for each transition. Unlike time-of-flight (TOF) or magnetic-based sector MS systems, QqQ-MS is designed to carry out unit MS resolution experiments. The proposed approach can be difficult for GC–QqQ-MS, as it requires using a narrow mass tolerance window on the QqQ-MS and could lead to a decrease in sensitivity or missing target ions.

Nonpolar pesticides (e.g., organochlorines) with low solubility tend to be strongly adsorbed by sediment, requiring aggressive extraction technologies such as pressurized liquid extraction (PLE), Soxhlet, or ultrasound/microwave-assisted extraction to extract pesticide residues from soil or sediment matrices prior to GC–QqQ-MS analysis. Luo *et al*. [23] employed PLE and GC–QqQ-MS to determine 12 pyrethroids in soils. Camino-Sánchez [24] developed a method for the simultaneous determination of PCBs, PAHs, PBDEs, and pesticides in marine sediments using PLE extraction, stirring bar concentration, and GC–QqQ-MS analysis. Sánchez-Avila [25] used ultrasound-assisted extraction and GC–QqQ-MS to analyze PAHs, PCBs, PBDEs, APS, and pesticides in sediments. These results reveal GC–QqQ-MS can perform target analysis for a wide range of chemical contaminants with excellent sensitivity and selectivity.

Pitarch *et al*. conducted a series of studies to evaluate the potential of GC–QqQ-MS for monitoring the occurrence of PAHs, PCBs, PBDEs, octyl/nonylphenols, and pesticides in wastewaters [26,27]. Water samples were prepared using simple solid-phase extraction (SPE) cleanup and concentration procedures. More than 50 chemical contaminants could be detected below 25 ng/mL using GC–QqQ-MS. The analytical strategy proposed using GC–QqQ-MS and LC–QqQ-MS for targeted pesticides and GC-TOF and LC-TOF for nontargeted analysis of chemical contaminants in wastewater [27]. Results of the study provide valuable information for wastewater treatment and emphasize the challenging aspects of determining a wide range of organic pollutants with varying physicochemical properties. A summary of GC–QqQ-MS methods for different environmental samples are listed in Table 1 (#1–10), including instrument parameters, sample preparation procedures, target pesticides, and sample matrices.

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
1	Pesticides, PCBs, PAHs, PBDEs, octyl/ nonylphenols	Wastewater	1. 100 mL water sample + 1 mL of surrogate mixture (5 IS) 2. SPE cartridge (C18) cleanup 3. Cartridge was dried by passing air and pesticides eluted using 5 mL ethyl acetate:DCM (50:50) 4. Collected extract evaporated to dryness and redissolved in 1 mL of hexane	An Agilent 6890N GC coupled with a Quattro Micro QqQ-MS A fused silica HP-5MS capillary column (30 m × 0.25 mm i.d. × 0.25 μm) EI, positive; CI, negative; 1 μL injection, splitless injection mode, ~42 min run time Carrier gas: helium; collision gas: nitrogen	[26]
2	PAHs, octyl/ nonylphenols, PCBs, pesticides, PBDEs	Wastewater	1. 100 mL water sample + 1 mL of surrogate mixture (5 IS) 2. SPE cartridge (C18) cleanup 3. Cartridge was dried by passing air and pesticides eluted using 5 mL ethyl acetate:DCM (50:50) 4. Collected extract evaporated to dryness and redissolved in 1 mL of hexane	An Agilent 6890N GC coupled with a Quattro Micro QqQ-MS A fused silica HP-5MS capillary column (30 m × 0.25 mm i.d. × 0.25 μm) EI, positive, 1 μL injection, splitless injection mode, ~42 min run time Carrier gas: helium; collision gas: nitrogen	[27]
3	20 pesticides	Soil	1. 5 g soil sample + 10 mL water or 5 g soil sample + 10 mL 1.0 M aqueous Na_2-EDTA solution for 30 min 2. 10 mL acetonitrile + acetic acid mixture (99:1, v/v) added to the centrifuge tube containing the hydrated sample	A Varian CP-3800 GC coupled with a Varian 1200 QqQ-MS A Zebron ZB-50 capillary column (30 m × 0.25 mm × 0.25 μm) EI, positive, 3 μL injection, splitless injection mode, 25 min run time Carrier gas: helium; collision gas: argon	[28]

			3. Salting out with addition of 4 g anhydrous $MgSO_4$ (4.0 g) and $NaAc{\cdot}3H_2O$ (1.7 g) 4. Centrifugation and acetonitrile layer used for cleanup 5. Concentrated acetonitrile extract to 1 mL and then mixed with water (1 mL) and *n*-hexane (5 mL) 6. Concentrated hexane extract to dryness + IS 7. Redissolved in 1 m hexane for GC–QqQ-MS analysis		
4	32 endocrine disrupting compounds and pesticides	Water	1. Conditioned SPE cartridge using 7 mL of ethyl acetate, 7 mL of methanol, 7 mL of Milli-Q water at 1 mL/min 2. 500 mL sample passed through the cartridge at 5 mL/min 3. Rinsed the cartridge with 5 mL water and dried by vacuum pressure for 60 min 4. Eluted pesticides with $2\times$ 2.5 mL of methanol and 2×2.5 mL acetonitrile at 1 mL/min 5. Extracts were evaporated to dryness and resuspended until a final volume of 500 µL in methanol	A Shimadzu GC-QP2010 coupled with a Shimadzu QP 2010 QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) EI, positive, 1 µL injection, 34.5 min run time Carrier gas: helium; collision gas: argon	[29]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
5	Pyrethroids	Soils	1. 10 g soil sample extracted using PLE. DCM, acetone, 50% DCM in acetone (selected), or 50% DCM in ethyl acetate was evaluated as extraction solvent 2. Extracts concentrated to near dryness and redissolved in *n*-hexane (1 mL) 3. The PLE extracts were cleaned up using SPE. Graphitized-carbon black (GCB) cartridge (selected), Florisil cartridge, silica cartridge, or C18 cartridge was evaluated	An Agilent 6890N GC coupled with a Waters Micromass Quattro Micro QqQ-MS A DB-5 capillary column (30 m × 0.25 mm × 0.25 μm) EI, positive, 25 min run time; carrier gas: helium; collision gas: argon	[23]
6	PCBs, PAHs, PBDEs, pesticides	Marine sediment	1. 10 g dried sample was extracted using PLE (methanol, 80 °C, 1000 psi, 10 min) 2. After extraction, volume was adjusted to 50 mL using methanol 3. 10 mL extracts from step 2 + 200 mL deionized water extracted using stir-bar sorptive extraction (Twisters) for 12 h 4. Addition of 60 g NaCl and extracted for another 12 h 5. Twisters were analyzed using the thermal desorption unit and GC–QqQ-MS	An Agilent 7890 GC coupled with an Agilent 7000B QqQ-MS A fused silica HP-5MS capillary column (30 m × 0.25 mm i.d. × 0.25 μm) EI, positive, ~42 min run time Carrier gas: helium; collision gas: nitrogen	[24]

7	40 pesticides	Airborne	1. The PM10 filters extracted MAE (50 °C for 20 min, using a power of 1200 W, and 30 mL of ethyl acetate) 2. 20 L of nonane (keeper) added to the extract and concentrated with Turbo Vap 500 3. Extracts were redissolved with 750 µL of dichloromethane prior to GPC cleanup 4. GPC cleanup 5. Collection fractions evaporated to dryness and redissolved with 1 mL of hexane prior to GC–QqQ-MS analysis	A Trace GC Ultra coupled with a Thermo-Finnigan TSQ Quantum A TR-5MS capillary column (30 m × 0.25 mm i.d. × 0.25 µm) EI, positive, 1 µL injection, splitless injection mode, 36.6 min run time Carrier gas: helium; collision gas: nitrogen	[22]
8	16 PAHs, 5 PEs, 7 PCBs, 6 PBDEs, 6 APs, 3 OCs, BPA	Seawater, river water, wastewater treatment plant (WWTP) effluents, sediments, mussels	Water samples SPE using Oasis HLB cartridges and eluting with dichloromethane/hexane (1:1, v/v) and dichloromethane/acetone (1:1, v/v) Mussels and sediments Ultrasound-assisted extraction using DCM as solvent	An Agilent 7890A GC coupled with an Agilent 70000 A QqQ-MS A 15 m HP-5MS capillary column used to detect BDE 209 A HP-5MS capillary column (30 m × 0.25 mm × 0.25 µm) used to detect PAHs, PCBs EI, positive, 1 µL injection, ∼60 min run time Carrier gas: helium; collision gas: nitrogen	[25]
9	12 pyrethroids	Water, sediment, milk	Water 1. 20 mL unfiltered water fortified with surrogates 2. Extracted using sonication and 1 mL DCM for 5 min	An Agilent 7890A GC coupled with 7000A QqQ-M A DB-5MS capillary column (15 m × 0.25 mm × 0.1 µm) containing 5% phenyl methyl siloxane	[30]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
			3. Organic phase evaporated and redissolved with 100 µL ethyl acetate Sediment 1. 1 g sediment fortified with surrogate standards 2. Extracted twice with 20 mL of hexane/dichloromethane (2:1) 3. Cleaned up using a Florisil cartridge 4. Eluted with 25 mL of ethyl acetate, evaporated and redissolved with 100 µL ethyl acetate	EI, positive; CI, negative; 3 µL injection, splitless injection mode; 20 min run time Carrier gas: helium; collision gas nitrogen; NCI:ammonium	
10	77 pesticides	Natural spring water, tap, and commercial mineral waters	Solid phase microextraction (SPME) 1. 14 mL sample (+IS) extracted by immersion of a StableFlex 65 µm PDMS-DVB fiber (60 min, 70 °C, sample agitation at 500 rpm, addition of NaCl, pH adjusted to 6) 2. Desorption of the pesticides at 250 °C for 5 min in the split–splitless injector and held for 4 min at the split ratio at 100:1 3. The fiber baked out for 10 min at 250 °C	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, SPME fibers or 10 µL injection (HF-LPME), split injection mode, 27 min run time Carrier gas: helium; collision gas: argon	[31]

			Hollow fiber liquid phase microextraction (HF-LPME) 1. A syringe plunger inserted into the hollow fiber soaked with 1-octanol:dihexyl ether (75:25, v/v; 1 min), and then placed into a 15 mL screw top vial containing 14 mL of sample 2. Addition of NaCl to adjust the ionic strength and adjusted 3. Shook the vial for 90 min at 90 rpm 4. The fiber transferred on a 2 mL vial containing 1.5 mL of cyclohexane and agitated for 5 min at 30 rmp 5. The extract passed through $MgSO_4$ and evaporated to dryness 6. The residue redissolved with 250 µL of cyclohexane and 5 µL of a solution of parathion ethyl d-10 (IS) for GC–QqQ-MS/MS analysis		
11	12 pesticides, metabolites	Baby foods of fruit and rice, fish and pasta, and potato and pork	1. 10 g sample + 10 mL acetonitrile, anhydrous magnesium sulfate (4 g), sodium chloride (1 g) 2. Addition of volumetric standard (delta-hexachlorocyclohexane, -HCH) 3. Centrifugation and transferred 1 mL supernatant for dispersive cleanup with PSA sorbent (50 mg), anhydrous $MgSO_4$ (150 mg), C18 sorbent (100–300 mg) 4. Centrifugation and supernatant used for GC–QqQ-MS analysis	A Varian CP-3800 GC coupled with a Varian 1200 QqQ-MS A Zebron ZB-50 capillary column (30 m × 0.25 mm × 0.25 µm) EI, positive, 8 µL injection, LVI, 21.5 min run time Carrier gas: helium; collision gas: argon	[32]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
12	130 pesticides	Vegetables	1. 5 g sample + 10 mL ethyl acetate 2. Extract filtered with a cartridge containing glass wool and 3 g anhydrous sodium sulfate 3. Filtered extract was evaporated to dryness and redissolved in 1 mL cyclohexane 4. Screen 1 MRM; reanalyzed nonnegative samples using 2–3 MRMs	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 μL injection, splitless injection mode, 11.6 min run time Carrier gas: helium; collision gas: argon	[14]
13	130 pesticides	Cucumbers	1. 5 g sample + 10 mL of ethyl acetate 2. Filtration with a home-made cartridge containing a glass wool plug and 3 g of anhydrous sodium sulfate 3. Evaporation of the solvent and redissolved residue with 1000 mL of cyclohexane	A Varian 3800 GC coupled with Varian 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 μL injection, split injection mode, 11.6 min run time Carrier gas: helium; collision gas: argon	[33]
14	78 pesticides	Tomato, onion	1. 20 g sample + 40 mL ethyl acetate 2. Salt out with 20 g of anhydrous sodium sulfate 3. Dispersive cleanup of 10 mL extract from step 2 + 0.25 g NH_2 adsorbent and 1.5 g anhydrous magnesium sulfate 4. 1 mL aliquot + IS for GC–MS/MS analysis	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 μm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 μL injection, splitless injection mode, 30.3 min run time Carrier gas: helium; collision gas: argon	[34]

15	151 pesticides	Strawberry	1. 10 g sample + 10 mL acetonitrile 2. Salt out with anhydrous NaCl (1 g) and anhydrous $MgSO_4$ (4 g) 3. Centrifuged and 1 mL upper layer used for dispersive cleanup with 25 mg of PSA and 150 mg of $MgSO_4$	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 μL injection, splitless injection mode, 20.5 min run time Carrier gas: helium; collision gas: argon	[35]
16	129 pesticides	Lettuce and other green leafy vegetables	1. 10 g sample + 10 mL acetonitrile + IS 2. Salt out 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride 3. Dispersive cleanup of an aliquot of the extract using 150 mg anhydrous magnesium sulfate, 25 mg PSA, and 12.5 mg GCB per mL acetonitrile extract 4. Acidification of an aliquot of the supernatant (1.5 mL) with 50 μL of 5% formic acid in acetonitrile (v/v) 5. The extract was evaporated and redissolved in toluene prior to GC–MS/MS analysis. The sample concentration in the final extract was 1 g/mL	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 μm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 μL injection, splitless injection mode, 30.3 min run time Carrier gas: helium; collision gas: argon	[36]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
17	140 pesticides	Cucumber, orange	1. 10 g sample + 10 mL acetonitrile 2. Salt out with anhydrous NaCl (1 g) and anhydrous $MgSO_4$ (4 g) 3. Centrifuged and 1 mL upper layer used for dispersive cleanup with 25 mg of PSA and 150 mg of $MgSO_4$	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 μL injection, splitless injection mode, 13.3 min run time Carrier gas: helium; collision gas: argon	[37]
18	12 pesticides	Orange, cucumber	1. 15 g sample + 50 mL ethyl acetate and 10 g of anhydrous sodium sulfate 2. Extract was filtered through a porous plate funnel to a spherical flask 3. Evaporation of the extract to nearly dryness and residue was redissolved in 5 mL of a cyclohexane + IS 4. 1 mL extract from step 3 diluted to 2 mL	A Varian 3800 GC coupled with 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI positive, 10 μL injection, splitless injection mode, 18.5 min run time Carrier gas: helium; collision gas: argon	[38]
19	167 OHs, OPs, pyrethroids	Fruit and vegetables	1. 15 g sample + 15 mL ACN (salt-out extraction) + IS 2. Solid-phase dispersive cleanup with octadecyl-bonded silica (C18) 3. Graphitized carbon black/primary–secondary amine (GCB/PSA) sorbents and toluene	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (5 m × 0.25 mm i.d.)	[39]

			4. Concentrated 6 mL extracts from step 3 to ~100 µL 5. Reconstitution to 1.0 mL using toluene for GC–MS/MS analysis	EI, positive, 1 µL injection, splitless injection mode, 45 min run time Carrier gas: helium; collision gas: argon	
20	130 pesticides	Fruits and vegetables (orange, nectarine, and spinach)	Accelerated solvent extraction (ASE) 1. 7 g diatomaceous earth + 10 g of triturated sample and then homogenized in a mortar 2. The content was transferred to a 33-mL extraction cell + IS 3. Ethyl acetate was selected as extraction solvent and the extraction temperature, pressure 70 °C, and 1500 psi. The preheating and static times, 2 and 3 min; the contact solvent time was 5 min, with a flush volume of 60% and executing two cycles 4. Extracts (~50 mL) evaporated to ~35 mL and salt out with 2 g anhydrous sodium sulfate, volume adjusted to 50 mL 5. 10 mL of ASE extracts evaporated to dryness and redissolved with 0.5 mL ethyl acetate GPC (only for spinach samples) 1. ASE extracted concentrated to 2 mL with ethyl acetate 2. 1 mL aliquot injected into the GPC system and eluted with cyclohexane–ethyl acetate (1:1, v/v) 3. Collected fraction time (14.5–21.0 min) evaporated to dryness and residue redissolved with 1 mL of ethyl acetate	An Agilent 6890N GC coupled to a Quattro Micro QqQ-MS A HP-5MS fused silica capillary column (30 m × 0.25 mm × 0.25 µm) EI, positive, 1 µL injection, splitless injection mode, 38 min run time Carrier gas: helium; collision gas: argon	[40]

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TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
21	160 pesticides	Wines	1. 10 g of wine + 10 mL ACN + IS 2. Salt out with 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride 3. A 5 mL aliquot of the acetonitrile extract dispersive cleanup with 0.75 g anhydrous magnesium sulfate, 0.125 g PSA and 0.250 g C18 4. A 1.5 mL aliquot of the acetonitrile extract + 50 µL of 5% formic acid in acetonitrile (v/v) 5. Extract was evaporated to dryness and reconstituted in 1.5 mL toluene prior to GC–QqQ–MS/MS analysis	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 µm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 µL injection, splitless injection mode, 30.3 min run time Carrier gas: helium; collision gas: argon	[41]
22	140 pesticides	Carrots, tomatoes, and strawberries	Citrated buffered QuEChERS 1. 10 g sample + 10 mL acetonitrile salt-out with 4 g anhydrous magnesium sulfate, 1 g sodium chloride, 1 g trisodium citrate dihydrate, and 0.5 g disodium hydrogen citrate sesquihydrate	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 µm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 µL injection, splitless injection mode, 30.3 min run time	[42]

			2. Dispersive cleanup: 5 mL aliquot + 125 mg PSA and 750 mg anhydrous magnesium sulfate 3. 1.5 mL aliquot of the upper layer + 50 µL 5% formic acid in acetonitrile 4. For the analysis by GC/MS/MS, the extract was evaporated and reconstituted in 1.5 mL toluene	Carrier gas: helium; collision gas: argon	
23	150 pesticides	Fruits and vegetables	1. 15 g sample + 15 mL of MeCN with 1% HOAc + IS 2. Salt out with 6 g of anhydrous $MgSO_4$ and 1.5 g of anhydrous NaOAc 3. 1 mL of MeCN extract for d-SPE cleanup with 150 mg anhydrous $MgSO_4$, 50 mg PSA, 50 mg C18, 7.5 mg GCB 4. 0.5 mL of the extract + add 50 µL QC and analyte protectants mixture and 50 µL MeCN	An Agilent 7890A GC coupled with 7000A QqQ-MS An Rti-5 ms analytical column (10 m × 0.53 mm × 1 µm) coupled to a 3 m × 0.15 mm i.d. HydroGuard noncoated restriction capillary (3 m × 0.15 mm i.d.). A virtual column length entered into the GC configuration (3.13 m × 0.15 mm i.d.) EI positive, 5 µL injection, splitless injection mode; 9.5 min run time Carrier gas: helium; collision gas: nitrogen	[43]
24	25 pesticides	Apple, orange, tomato, carrot	1. 15 g sample + 15 mL acetonitrile 2. Salt out with anhydrous NaCl (1.5 g) and anhydrous $MgSO_4$ (6 g) 3. Centrifuged and 1 mL upper layer used for dispersive cleanup with 50 mg of PSA, 150 mg of $MgSO_4$ and (50 mg C18 for orange) 4. 500 µL extract + 1 mL toluene 5. Evaporated to ~300 µL and adjusted to 500 µL with toluene	An Agilent 7890 GC system coupled to a Quattro Micro QqQ-MS, EI An Agilent 7890A GC system coupled to a Xevo TQ-S QqQ-MS, CI A DB-5 MS column (30 m × 0.25 mm × 0.5 µm) 1 µL injection, splitless injection mode, 22.2 min run time Carrier gas: helium; collision gas: nitrogen	[44]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
25	42 pesticides	Tobacco	1. 7.5 g ground tobacco + IS 2. Extracted using PLE (100 °C; 100 atm; heating time: 5 min; static extraction time: 3 min; flush volume: 60% of extraction cell volume; purge: N_2, 60 s; number of cycles: 3) 3. Concentrated PLE extracts to 1 mL 4. SPE cleanup Low polarity pesticides: 0.1 mL concentrated extract loaded onto a Florisil cartridge; elutes loaded on silicagel cartridge Intermediate- and/or high-polarity pesticides: 0.1 mL concentrated extract loaded onto a silicagel cartridge *N*-methylcarbamate: 0.1 mL concentrated extract loaded onto an aminopropyl cartridge	A HP-6890 GC coupled with a A TSQ-7000 QqQ-MS A HP capillary column (30 m × 0.25 mm × 0.25 μm) EI, positive; CI, negative, splitless injection mode, ~38 min run time Carrier gas: helium; collision gas: argon; CI reagent gas: methane (one MRM transition for each pesticide)	[45]
26	122 pesticides	Dry cereal and animal feeds	1. 5 g sample + 10 mL water + 15 mL ACN + IS 2. Salt out with 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 μm) coupled with a guard column (2 m × 0.53 mm i.d.)	[46]

			3. A 7.5 mL aliquot of the supernatant dispersive cleanup with 0.75 g anhydrous magnesium sulfate, 0.5 g C18, and 0.125 g PSA 4. A 3 mL aliquot of the supernatant + 50 µL of 5% formic acid in acetonitrile (v/v) 5. Evaporated to dryness and redissolved in 1.5 mL toluene prior to GC–MS/MS analysis	EI, positive, 5 µL injection, splitless mode, 30.3 min run time Carrier gas: helium; collision gas: argon	
27	140 pesticides	Dry cereal and animal feeds	1. 5 g sample + 10 mL water + 15 mL acetonitrile + IS 2. Salt out with 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride 3. Freeze out for 2 h or overnight) at −26 °C 4. Dispersive cleanup 100 mg anhydrous magnesium sulfate, 75 mg C18, 20 mg PSA per mL acetonitrile extract 5. Acidification with 15 µL of 5% formic acid in acetonitrile per mL of extract 6. The extract was evaporated under a stream of nitrogen and the residue was redissolved in toluene + second IS 7. The sample concentration in the final extracts was 0.66 g/mL	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 µm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 µL injection, splitless injection mode, 30.3 min run time Carrier gas: helium; collision gas: argon	[47]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
28	168 OHs, OPs, pyrethroids	Dried powdered ginseng	1. 2 g sample + 10 H_2O + IS 2. Addition 20 mL ACN or 2:1:1 acetone/cyclohexane/ethyl acetate 3. Solid-phase dispersive cleanup with octadecyl-bonded silica (C18) 4. Concentration 15 mL of extracts from step 3 to 1 mL 5. SPE graphitized carbon black/ primary–secondary amine sorbents and eluted using acetone:toluene (3:1) 6. Concentration elutes from step 5 to ~100 μL 7. Reconstitution to 1.0 mL using toluene for GC–MS/MS analysis	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 1 μL injection, splitless injection mode; 45 min run time Carrier gas: helium; collision gas: argon	[48]
29	140 pesticides	Cereal samples (wheat, rye, barley, oats, maize, buckwheat, etc.) and various animal feeds	Procedure A 1. 5 g sample + 10 mL water were added + IS 2. Extracted with 15 mL acetonitrile (salt out with 0.5 g disodium hydrogen citrate sesquihydrate,1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride) 3. Hand shaken and centrifuged and an aliquot of acetonitrile supernatant (7.5 mL) was transferred to a 15 mL disposable screw-capped	A Varian CP-3800 GC coupled with a Varian 1200L QqQ-MS A DB-5 MS column (30 m × 0.25 mm × 0.5 μm) coupled with a guard column (2 m × 0.53 mm i.d.) EI, positive, 5 μL injection; splitless injection mode, 33.33 min run time Carrier gas: helium; collision: argon	[49]

4. Dispersive-SPE agents (125 mg PSA, 500 mg C18, and 750 mg $MgSO_4$
5. 3 mL extract evaporated to dryness and residue dissolved using 1.5 mL toluene

Procedure B

1. 5 g sample + 10 mL water were added + IS
2. Extracted using 15 mL acetonitrile
3. Salt out 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride were added
4. An aliquot of acetonitrile supernatant was transferred into a glass test tube and stored for at least 2 h (or overnight) in a freezer (−26 °C)
5. Dispersive-SPE agents (150 mg PSA, 550 mg C18, and 750 mg $MgSO_4$) with an aliquot of the extract (7.5 mL)
6. An aliquot of sample extract (3 mL) was evaporated and reconstituted in 1.5 mL toluene for GC–MS/MS analysis

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
		Procedure C 1. 5 g sample + 25 mL water/acetonitrile mixture (2:3, v/v) + IS 2. Salt out with 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride were added 3. An aliquot of acetonitrile supernatant (7.5 mL) cleanup with dispersive-SPE agents (150 mg PSA, 550 mg C18, 75 mg GCB, and 750 mg $MgSO_4$) 4. An aliquot of sample extract (3 mL) was transferred to a glass tube, evaporated and reconstituted in 1.5 mL toluene for GC–MS/MS analysis Procedure D 1. 5 g sample + 25 mL water/acetonitrile mixture (2:3, v/v) + IS 2. Salt out with 0.5 g disodium hydrogen citrate sesquihydrate, 1 g trisodium citrate dihydrate, 4 g anhydrous magnesium sulfate, and 1 g sodium chloride were added 3. An aliquot of acetonitrile supernatant (7.5 mL) cleaned up		

			with dispersive-SPE agents (550 mg PSA, 375 mg C18, and 750 mg $MgSO_4$) 4. An aliquot of sample extract (3 mL) was transferred to a glass tube, evaporated, and reconstituted in 1.5 mL toluene for GC–MS/MS analysis		
30	135 pesticides	Green and black dry tea leaves and stalks	Procedure A 1. 2 g tea sample + 10 mL water 2. Extracted with 10 mL MeCN (salt out 4 g anhydrous $MgSO_4$ and 1 g NaCl) 3. Centrifuged and used 1 mL extract for partitioning with 1 mL hexane + 5 mL 20% NaCl (w/w) solution 4. A part of hexane layer used for GC–MS/MS analysis Procedure B 1. 2 g tea sample + 10 mL water 2. Extracted with 10 mL MeCN 1% HOAc (salt out 4 g anhydrous $MgSO_4$ and 1.7 g $NaOAc.3H_2O$) 3. Centrifuged and used 1 mL extract for partitioning with 1 mL hexane + 5 mL 20% NaCl (w/w) solution 4. A part of hexane layer used for GC–MS/MS analysis Procedure C 1. 2 g tea sample + 10 mL water	An Agilent 7890A GC coupled with an Agilent 7000B QqQ-MS A HP-5 ms Ultra Inert column (15 m × 0.25 mm × 0.25 µm) coupled with a DB-5 ms Ultra Inert column (0.50 m × 0.15 mm × 0.15 µm) EI, positive, 2 µL injection, splitless injection mode, 20 min run time Carrier gas: helium; collision gas: nitrogen	[50]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
		2. Extracted with 10 mL MeCN 1% HOAc (salt out 4 g anhydrous $MgSO_4$, 1 g NaCl, 1 g $Na_3Citr{\cdot}2H_2O$, and 0.5 g $Na_2HCitr{\cdot}1.5H_2O$) 3. Centrifuged and used 1 mL extract for partitioning with 1 mL hexane + 5 mL 20% NaCl (w/w) solution 4. A part of hexane layer used for GC–MS/MS analysis Procedure D 1. 5 g tea sample + 15 mL MeCN 2. Extracted with an Ultra-turrax macerator at 15,000 rpm for 1 min twice 3. The MeCN extract was purified using LLE 1 mL hexane and 5 mL 20% NaCl (w/w) solution 4. A part of hexane layer used for GC–MS/MS analysis		

32	19 OPs	Fats and oils	1. 25 g sample dissolved with GPC mobile phase (ethyl acetate–cyclohexane, 1:1, v/v) to 10 mL 2. 1 ml was cleaned up by GPC, collecting the fraction eluting between 14.5 and 24.5 min 3. The GPC fraction was evaporated to near dryness 4. Residue was dissolved with 1 mL hexane + IS	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 4 µL injection, splitless injection mode, 24 min run time Carrier gas: helium; collision gas: argon	[51]
33	Isofenphos, famfur, mirex, p,p-DDT, thionazin, gamma-lindane	Meat	1. 5 g sample extracted with 20 mL ethyl acetate 2. Extract filtered with a cartridge containing glass wool and 3 g anhydrous Na_2SO_4 3. Filtered extract was evaporated to dryness and redissolved in 5 mL cyclohexane–ethyl acetate (1:1, v:v) 4. 2 mL was cleaned up using GPC 5. Collected GPC fraction was evaporated to dryness and dissolved with 1 mL cyclohexane	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 µL injection, split injection mode, 11.6 min run time Carrier gas: helium; collision gas: argon	[52]
34	45 OCs, OPs	Muscle of chicken, pork, and lamb	A. Polytron extraction 1. 5 g sample drenched with 3 × 20 mL ethyl acetate and salted out with 3 g of anhydrous Na_2SO_4 using a Polytron PT2100 2. Filtered the extract and evaporated to almost dryness 3. Redissolved residue with 5 mL of mixed cyclohexane–ethyl acetate (1:1 v/v) and used 2 mL into GPC	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 µL injection, split injection mode, 11.6 min run time Carrier gas: helium; collision gas: argon	[53]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
		Soxhlet extraction 1. 5 g sample extracted with 150 mL of ethyl acetate or 6 h 2. Evaporated the extract to almost dryness 3. Residue was redissolved with 5 mL of a mixed cyclohexane–ethyl acetate (1:1 v/v) and used 2 mL into GPC ASE 1. 5 g sample freeze-dried at 0.1–0.2 mbar for 8 h and mixed with 7 g Hydromatrix 2. Extracted at 120 °C; 1800 psi; 11 min; ethyl acetate 60 mL 3. Evaporated extract to almost dryness 4. Residue was redissolved with 5 mL of mixed cyclohexane–ethyl acetate (1:1 v/v) and used 2 mL for GPC GPC 1. Cyclohexane–ethyl acetate (1:1 v/v) in isocratic mode, flow rate was 5 mL/min, collected fractions 15–22 min 2. Evaporated the collected fraction to dryness 3. Residue was redissolved with 950 µL cyclohexane and 50 µL of IS (caffeine)		

35	57 pesticides	Hen eggs	1. 0.5-g homogenized egg + 2.0 g of C18 sorbent (previously washed with two volumes each of *n*-hexane, dichloromethane and methanol) and 1 g of anhydrous $MgSO_4$ 2. SPE (2g Florisil) cleanup 3. The SPE cartridge was eluted with 1.5 mL of ACN saturated in *n*-hexane (85:15, v/v) and 8.5 mL of EtAc (3 + 3 + 2.5 mL) 4. The extract was evaporated to near dryness and the residue was redissolved with 950 L of cyclohexane + IS	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 1 μL injection, splitless injection mode, 17.7 min run time Carrier gas: helium; collision gas: argon	[54]
36	34 OCs and OPs	Animal livers	A. Polytron extraction 1. 5 g sample drenched with 3 × 20 mL ethyl acetate and salted out with 3 g of anhydrous Na_2SO_4 using a Polytron PT2100 2. Filtered the extract and evaporated to almost dryness 3. Redissolved residue with 5 mL of mixed cyclohexane–ethyl acetate (1:1 v/v) and used 2 mL into GPC 4. Collected GPC fraction evaporated to dryness and redissolved using 975 μL cyclohexane and 25 μL IS MSPD 1. 0.5 g liver sample blended with 2.0 g C18 2. SPE extraction (2 g Florisil) and eluted using 10 mL ethyl acetate 3. Evaporated extract and redissolved with 975 μL cyclohexane and 25 μL IS	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 1 μL injection, splitless injection mode, 16.6 min run time Carrier gas: helium; collision gas: argon	[55]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
37	OPs	Fish feeds	1. 10 g fish feed samples extracted by the Soxtec system to generate fat extracts 2. 0.5 g of fat extracts + 3 mL hexane 3. SPE cleanup with an Extrelut cartridge and the pesticides were eluted with 3 × 5 mL portions of acetonitrile/*n*-hexane (80/20, v/v) 4. Extracts + 4 mL methanol evaporated and redissolved 1 mL of *n*-hexane 5. SPE cleanup with a Bond Elut PCB column 6. Elutes from step 5 were evaporated to dryness and the residue was dissolved in 1 mL of *n*-hexane. The dilution factor was two (HCB as the internal standard, which is used to check the cleanup steps. A minimum recovery of 70% for HCB guarantees the absence of procedural errors and/or instrumental failures that can compromise the analysis)	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 μm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 1 μL injection, splitless injection mode, 40 min run time Carrier gas: helium; collision gas: argon	[56]

38	12 pyrethroids	Milk	1. 1 g milk+IS extracted twice with 20 mL hexane/dichloromethane (2:1) 2. SPE cleanup C18 cartridge in tandem with basic alumina cartridge 3. Pyrethroids were eluted with 30 mL of acetonitrile 4. Elutes were evaporated and redissolved with 100 µL ethyl acetate	An Agilent 7890A GC coupled with 7000A QqQ-M A DB-5MS capillary column (15 m × 0.25 mm × 0.1 µm) containing 5% phenyl methyl siloxane EI, positive; CI, negative; 3 µL injection, splitless injection mode; 20 min run time Carrier gas: helium; collision gas nitrogen; NCI:ammonium	[30]
39	100 pesticides	Olive oil	Procedure 1 1. 4 g olive oil dissolved in 20 mL *n*-hexane 2. Extracted using 20 mL ACN saturated with *n*-hexane twice 3. Acetonitrile phase collected and evaporated to almost dryness and dissolved with 5 mL ethyl acetate-cyclohexane (1:1) 4. 2.5 mL was used for GPC cleanup 5. Evaporated collected GPC fraction to dryness 6. Dissolved the residue with 1 mL cyclohexane Procedure 2 1. 1 g olive oil dissolved with 8 mL ethyl acetate–cyclohexane, 1:1, v/v 2. 2.5 mL was used for GPC cleanup 3. Evaporated collected GPC fraction to dryness 4. Dissolved the residue with 1 mL cyclohexane	A Varian CP-3800 GC coupled with a 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 5 µL injection, splitless injection mode, 19 min run time Carrier gas: helium; collision gas: argon	[57]

Continued

TABLE 1 Applications of GC–QqQ-MS for Pesticide Analysis—Cont'd

	Pesticide	Matrix	Sample Preparation	GC–QqQ-MS	References
40	19 OCs, OPs, pyrethroids	Vegetables, eggs	Vegetables 1. 10 g sample extracted with 10 mL acetonitrile (1% HAc) 2. Salt out with anhydrous NaAc (1 g) and anhydrous $MgSO_4$ (4 g) 3. 1 mL extract dispersive cleanup PSA (25 mg) and anhydrous $MgSO_4$ (150 mg) 4. Evaporated 800 µL extract to dryness and redissolved with cyclohexane 400 µL Eggs 1. 0.5 g egg blended with C18 sorbent (2.0 g) anhydrous $MgSO_4$ (1.0 g) were added 2. SPE (2 g Florisil) and eluted with 1.5 mL acetonitrile saturated with hexane and 8.5 mL ethyl acetate 3. Evaporated the extract to near dryness and redissolved with 975 µL of cyclohexane and 25 µL IS	A Varian 3800 GC coupled with a Varian 1200L QqQ-MS A Varian VF-5 fused silica capillary column (30 m × 0.25 mm × 0.25 µm) coupled with a deactivated guard column (2 m × 0.25 mm i.d.) EI, positive, 10 µL injection, splitless injection mode; 20.5 min run time Carrier gas: helium; collision gas: argon	[58]

3.2 Determination of Pesticides in Food Samples

For simplicity, food sample matrices can be categorized as dry foods (e.g., animal feeds, dry botanicals, grains, cereals, etc.), high water content foods (e.g., fresh produce and vegetables), and fatty foods (meat, oil, animal organs, etc.). Depending on the sample matrices, different sample preparation techniques are required to obtain satisfactory results in the GC–QqQ-MS analysis of pesticides in these food matrices.

3.2.1 High Water Content Food Samples

Typically, pesticide residues in fresh produce have been analyzed with gas chromatography equipped with element selective detectors such as ECD, FPD, PFPD, etc. Since the 1980s, many of these detectors have been replaced by GC–MS/SIM as the main instrument of analysis and the element selective detectors are used complementarily for pesticides not suitable for MS because of poor ionization. However, recently, GC–QqQ-MS is beginning to replace GC–MS-SIM because of the improved selectivity and sensitivity. Table 1 (#11–25) includes different GC–QqQ-MS methods, targeting fresh produce, primarily fruits, and vegetables. In general, these methods start with an organic solvent extraction procedure, followed by SPE cartridge or dispersive SPE (d-SPE) cleanup using different sorbents (e.g., C18, graphitized carbon black, primary–secondary amines, etc.), followed by GC–QqQ-MS analysis.

QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) and its subsequent modifications were first applied to pesticide analysis in fresh produce samples [59–61]. The QuEChERS procedure is an efficient salt-out organic extraction followed by dispersive solid extraction cleanup in a test tube. Compared to conventional salt-out extraction methods [62–64], QuEChERS uses less lab glassware, smaller sample size (10–15 g), and less extraction solvent (10–15 mL). The method provides satisfactory recoveries (70–120%) for a wide range of pesticides, including polar pesticides such as methamidophos and acephate. The success of QuEChERS was partially due to its introduction at the time that QqQ-MS technology was becoming popular in pesticide laboratories.

Wong *et al.* [39] compared the instrument performance of GC–QqQ-MS and GC–MS-SIM using samples prepared by an acetonitrile extraction procedure based on QuEChERS and Fillon's method [65]. Their results demonstrate that GC–QqQ-MS outperforms GC–MS-SIM in terms of sensitivity and selectivity. GC–QqQ-MS detects 90% of the 168 target pesticides fortified into 10 different fresh produce and vegetables at 10 and 25 ng/g. The corresponding recoveries range from 70% to 120% with RSD $<20\%$, while GC–MS-SIM could only detect $<80\%$ of the pesticides at the same fortification concentrations. Koesukwiwat *et al.* [43] developed a low-pressure GC–QqQ-MS method for a fast analysis of 150 pesticides. Using a 10 m, 0.53 mm i.d., 1 μm film analytical column, a 3 m, 0.15 mm i.d. capillary at

the inlet, and a rapid oven temperature ramp rate, the method can separate and detect the 150 pesticides within 6.5 min. Though average peak width is just 2–3 s, the method takes advantage of fast data acquisition capability of the GC–QqQ-MS by setting dwell times to 2.5 ms and arranging the number of transitions in each segment to achieve at least eight data points per peak. Cervera *et al*. [40] developed a method that can detect 130 pesticides in vegetables and fruits using accelerated solvent extraction and GC–QqQ-MS. Only spinach extracts underwent GPC cleanup procedure. No cleanup was applied to orange or nectarine samples. Even though recoveries were between 70% and 120% and RSDs were <20%, matrix enhancement was observed in all tested samples for the majority of pesticides investigated. Pesticides had to be quantitated using matrix-matched calibration standards. The observation of signal enhancement reported in this study underlines the importance of evaluating matrix effects.

3.2.2 Fatty Food Samples

In fatty foods, the major interferences include lipids, sterols, waxes, saturated/unsaturated fatty acids, as well as fatty acid esters and proteins. It requires significant efforts to defat the samples by different extraction and cleanup procedures. With fat content <20% (e.g., milk), samples can be prepared using QuEChERS. For samples with fat content >20%, GPC is a commonly used cleanup technology. Garrido Frenich *et al*. [58] compared the performance of ion trap-MS and QqQ-MS using solvent, high water content, and fatty food samples. In the cucumber (high water content) or solvent samples, the two instruments generated similar intraday precision, linearity, and sensitivity. The QqQ-MS provided better sensitivity in egg matrix, suggesting that, for complex matrices, QqQ-MS can better separate target analytes from matrix inferences. Different from the QqQ-MS, the ion trap uses its storage feature to perform MS/MS in time by sequentially storing precursor ions, fragmenting them, and then scanning out the product ions using the same ion storage compartment. In comparison, the selection of precursor ions, fragmentation, and detection of product ions happen in different devices in QqQ-MS. When operating in SRM mode, QqQ-MS has a faster data acquisition rate so that it can monitor more concurrent ions [35,66]. This has been a very desirable feature for improving pesticide screening capacity.

3.2.3 Dry Food Samples

Pesticides have been monitored in dry foods such as medicinal plants, herbs, dietary supplements, and grains. Water content in these matrices is <1%. Compared to fatty samples or high water content samples, dry food samples have more concentrated matrix per mass unit. When analyzing dry food samples, smaller sample sizes compared to high moisture foods are used. A large sample size will lead to more matrix components, requiring additional cleanup

efforts. In order to improve extraction efficiency, hydration is often employed for sample swelling so that enclosed pesticides could be extracted. Cajka *et al.* [50] evaluated four different sample preparation procedures that could be coupled with GC–QqQ-MS for the detection of pesticides in dry tea samples. Compared to a method using GC–MS-SIM [67], Cajka's method achieved satisfactory recoveries (70–120%) for the majority of 135 target pesticides using much less sample cleanup.

The use of GC–QqQ-MS can help identify pesticides from complex matrices such as dry ginseng powder. Due to matrix interference, two BHC isomers could not be identified using GC–MS-SIM, but using GC–QqQ-MS, the four isomers are clearly separated and identified without any difficulty [48]. The presence of ε-BHC could not be confirmed due to the lack of reference standard.

This is best demonstrated in Figure 1 where the presence of incurred BHC residues in dried ginseng powder (*Panax quinquefolius*) was determined by two extraction methods (acetonitrile, ACN, and 2:1:1 acetone/cyclohexane/ethyl acetate, ACE) and analyzed by either GC–QqQ-MS (A) or GC–MS-SIM (B). From Figure 1A, GC–QqQ-MS shows the presence and separation of α-, β-, γ-, δ-, and ε-BHC isomers by the two transitions, 181 → 146 (primary, quantitation) and 219 → 183 (secondary, qualifier). Transition ratios 181 → 146/219 → 183 of the two extraction procedures showed that the two procedures are similar. GC–MS-SIM (Figure 1B), on the other hand, shows

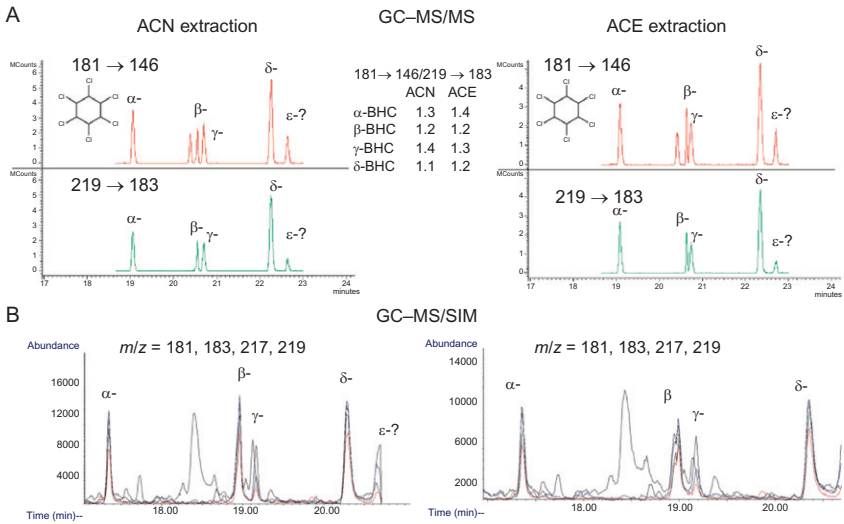

FIGURE 1 BHC residues in dried ginseng powder by (A) GC–QqQ-MS versus (B) GC–MS-SIM.

interferences in the screening and identification of the β- and γ-BHC isomers using *m/z* 181, 183, 217, and 219 (modified from Ref. [48]). Additional studies of dry foods are listed in Table 1 (#25–40).

4 CHALLENGING ISSUES OF GC–QqQ-MS

GC–QqQ-MS only can be applied to semivolatile, nonpolar, and thermally stable pesticides that are amenable to the analysis. When analyzing polar, thermally labile, and low-volatility pesticides, researchers have to use LC–MS for the same selectivity and sensitivity [68]. It is impossible to directly introduce pesticides such as macrocyclic lactones, carbamates, or neonicotinoids into QqQ-MS via GC conditions. Even for pesticides which could be introduced into QqQ-MS, their on-column masses (sensitivity) are limited due to the sample capacity of GC injection system.

The GC–QqQ-MS analysis could also suffer from matrix effects. Two types of matrix effects might occur and have to be addressed. One is signal suppression or enhancement and the other is isobaric interferences (spectral interferences) [69–71]. Overlapping spectral peaks mask the peaks of interest and can provide false-positive or -negative results. Common solutions to signal alteration include matrix-matched calibration standards, stable isotope dilution, standard addition, or addition of analyte protectants. Stable isotope dilution cannot be applied universally to multiresidue pesticide analysis in foods due to the large number of standards required, which may not be available and will greatly increase the cost. When quantitating several pesticides in a single sample, standard addition becomes very impractical and challenging to perform. Changing chromatographic conditions, more cleanup, orthogonal analysis, or high-resolution mass spectrometry (HRMS) could be used to address the issues related to isobar interference. For multiresidue pesticide analysis, there is no perfect solution to matrix effects because each analyte might be affected differently by the matrices.

Compared to GC–MS full scan or GC–MS SIM methods, GC–QqQ-MS methods that use two MRM data acquisitions within a specific RT window provide better selectivity and SNR of the target analytes in extracted ion chromatograms [39,72]. This approach is sufficient to fulfill the requirement of EU Directive 2002/657/EC [17,73] for identification of pesticide residues. Because in the course of GC–QqQ-MS analysis mass spectral fragmentation patterns are dependent on instrument, analyte concentration, and matrix effects, there are challenges using RT, two or more MRM transitions, and their relative ion intensity ratios for identification of target analytes. These include the selection of nonspecific transitions that may be the same as that of a coeluting matrix compound, inconsistent ion ratios in different matrices, or the weak response of the second MRM transition at low intensity, which could lead to false-positive/negative identification [74,75].

Ionization plays a vital role in MS. The majority of existing GC–QqQ-MS instruments uses the standard electron impact ionization (EI) source. Compared to other ionization sources such as electrospray ionization (ESI), EI is a "hard" ionization technology, using standardized conditions (e.g., 70 eV) to ionize target analyte molecules in gas phase. In the course of ionization, many fragments could be generated and molecular ions either do not have enough abundance or are absent, a fact which forces nonmolecular ions (fragments) to be chosen as precursor ions for MS/MS transitions. This raises the concerns for identification. Additionally, when molecular ions are absent, based on full scan spectra, it could be challenging and time consuming to choose multiple precursor ions for collision experiments. For example (see Figure 2), if the molecular ion (*m/z* 315) of dichlorfenthion presents with reasonable abundance, it would be much easier to choose *m/z* 315 than choose between *m/z* 279, 251, and 223 for an appropriate precursor ion. These issues prompted the need for alternative or new ionization technologies to improve existing GC–QqQ-MS methods.

Chemical ionization (CI) has been used as an alternative to EI [76,77]. Molecular ions could be generated with satisfactory abundance using CI, especially when analyzing halogenated compounds. Unlike EI, CI does not have standardized ionization conditions, which will introduce another level of complexity to the GC–QqQ-MS methods, because different reagent gases (e.g., methane, ammonia, iso-butane) and corresponding pressures can be selected and "optimized" to adjust the proton-donating ability of the reagent gas relative to the proton affinity of analytes with the ionization energies used in the analysis. New ionization technologies for GC–MS such as atmospheric pressure chemical ionization (APCI) [44] and supersonic molecular beams (SMBs) ionization [78,79] have been reported but commercially limited or unavailable. Only a few pesticides or food matrices have been tested using those new ionization technologies. Without extensive studies to evaluate the applicability of APCI or SMB, EI will continue to be the main ionization source used for GC–QqQ-MS.

Once a GC–QqQ-MS method becomes validated in a single laboratory, it is difficult to transfer the method to other laboratories. Table 2 indicates that selected MRM transitions are user dependent. The optimal parameters

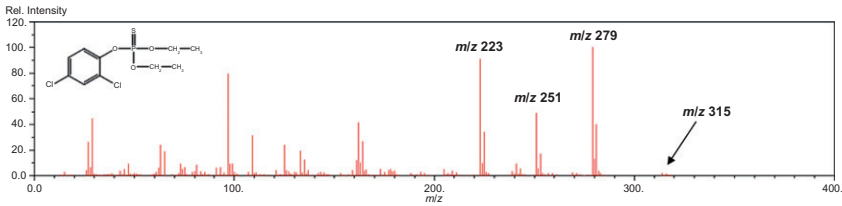

FIGURE 2 EI spectrum of dichlorfenthion. Source: *http://webbook.nist.gov/chemistry*.

TABLE 2 Comparison of QqQ-MS Parameters on Different Platforms

	MRM Transitions (Collision Energy)			
	Platform 1	*Platform 2*	*Platform 3*	*Platform 4*
Captan	149 → 79 (10 eV)	264 → 79 (10 eV)	149 → 105 (2 eV)	149 → 70 (8 eV)
	79 → 77 (10 eV)	NA	149 → 70 (12 eV)	149 → 105 (8 eV)
Cyhalothrin-lambda	181 → 152 (25 eV)	197 → 141 (10 eV)	208 → 181 (8 eV)	181 → 152 (23 eV)
	197 → 141 (15 eV)	197 → 161 (5 eV)	197 → 141 (10 eV)	208 → 181 (10 eV)
Diazinon	304 → 179 (15 eV)	304 → 179 (10 eV)	199 → 93 (16 eV)	304 → 179 (15 eV)
	179 → 137 (20 eV)	304 → 162 (10 eV)	304 → 179 (12 eV)	199 → 193 (15 eV)
Deltamethrin	181 → 152 (25 eV)	253 → 174 (10 eV)	253 → 174 (8 eV)	253 → 172 (18 eV)
	181 → 127 (25 eV)	253 → 172 (5 eV)	253 → 93 (14 eV)	253 → 93 (18 eV)
Collision gas	Nitrogen	Argon	Argon	Argon
EI source temp (°C)	320	270	250	250
References	[43]	[47]	[80]	[81]

NA, not available.

suggested by different platforms are not comparable. One cannot directly transfer one set of parameters from one GC–QqQ-MS system to another. One advantage of GC–MS is the standardized ionization so that spectra are largely transferrable among instrument platforms allowing easy library searching. GC–QqQ-MS measures a set of MRM transitions generated using conditions that are mostly nonstandardized, so the universal aspect of the EI spectrum is lost. It is clear that on different platforms, investigators have optimized different conditions for the same pesticides.

5 FUTURE OF GC–QqQ-MS

Regardless of its high capital cost and time-consuming method development requirements, GC–QqQ-MS would relieve researchers from conventional laborious sample preparation or cleanup procedures. Indeed, a large number

of pesticides have been analyzed using modified QuEChERS and GC–QqQ-MS in fresh produces and vegetables. However, increasing numbers of traditional pesticides such as carbamates and phenyl ureas and newly registered pesticides are not amenable to GC analysis, indicating a shrinking user base of GC-related technologies. A recent study shows that in some botanical matrices, approximately only 100 of the 312 target pesticides could be detected below 40 ng/g using GC–QqQ-MS [81]. This suggests that botanicals are difficult matrices and that GC–MS systems have limited capacity. Without additional sample cleanup or concentration, GC–QqQ-MS lacks the ability to separate the target analytes from isobaric interferences in those tested matrices. This limited capability with respect to analyzing pesticides in dry botanicals restricts the applicability of GC–QqQ-MS. It is not surprising that HRMS has been proposed and evaluated as an alternative to resolve isobaric interferences from analytes. Instruments equipped with new ionization sources such as LC–MS with APPI, ESI, or APCI, and especially LC–HRMS, can analyze pesticides that used to be only amenable to GC with comparable sensitivity. Without any significant improvement in the ionization source, selectivity, or decrease in cost, GC–QqQ-MS will be gradually replaced by other technologies that can perform pesticide analysis in a more practical, efficient, and cost-effective manner.

ABBREVIATIONS

APCI	atmospheric pressure chemical ionization
APPI	atmospheric pressure photo ionization
ECD	electron capture detector
EI	electron ionization
ESI	electrospray ionization
FPD	flame photometric detector
GC	gas chromatography
GC–MS	gas chromatography–mass spectrometry
GC–MS-SIM	gas chromatography–mass spectrometry single ion monitoring
GC–QqQ-MS	gas chromatography–triple quadrupole mass spectrometry
GPC	gel permeation chromatography
HRMS	high-resolution mass spectrometry
LC	liquid chromatography
LC–MS	liquid chromatography–mass spectrometry
LOD	limit of detection
LOQ	limit of quantitation
MRLs	maximum residue limits
MRM	multiple reaction monitoring
PAHs	polycyclic aromatic hydrocarbons

PBDEs	polybrominated diphenyl ethers
PCBs	polychlorinated biphenyls
PFPD	pulsed flame photometric detector
PLE	pressurized liquid extraction
PM	particulate matter
SMB	supersonic molecular beam
sMRM	supersonic molecular beam-scheduled multireaction monitoring
SNR	signal-to-noise ratio
SPE	solid-phase extraction
SRM	selected reaction monitoring
TOF-MS	time-of-flight mass spectrometry

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