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Chapter

Gas Chromatographic-Mass Spectrometric Detection of Pesticide Residues in Grapes

Mahadev C. Khetagoudar, Mahadev B. Chetti and Dinesh C. Bilehal

Abstract

GC-MS/MS method has been developed and validated for the determination and quantification of 35 multi-class pesticide residues in grape samples. Pesticides are selected from different families including organochlorines, organophosphorus, carbamates, pyrethroids, triazines, triazoles, pyrazoles, etc. The QuEChERS-dSPE (dispersive solid-phase extraction) method was used for the extraction of residues of pesticide. An extra cleanup step was included with the help of a primary secondary amine (PSA) and graphitized carbon black (GCB). Recoveries ranged from 70 to 100% with 14% relative standard deviation (RSD). Other parameters such as precision, recoveries, limit of detection (LOD), limit of quantification (LOQ), and linearity were also studied. Finally, the proposed analytical method was successfully employed for the determination of residues of pesticide in grape samples.

Keywords: residues of pesticide, QuEChERS-dSPE, GC-MS/MS

1. Introduction

In India, a large quantity of pesticides is used for the cultivation of grapes mainly for the management of various diseases and pests. Due to the stringent rules set by the various developed countries on food safety standards and the regulations on quality parameters, we find that the residues of the pesticides in food are gaining a lot of attention. Keeping in view the problem of residues of pesticides, the present study was conducted on grape (*Vitis vinifera* L.) of Bijapur District for the qualitative and quantitative analysis of pesticides by GC-MS/MS (gas chromatography coupled to mass spectrometry).

In recent years, the production and marketing of food have gained topmost priority. This in turn has given rise for the implementation of better agricultural practices and has also prompted a substantial increase in the importance given to pesticide residues and related aspects. It is important to analyze large numbers of samples for residues of pesticide in the food due to their control and regulatory issues. Analytical procedures for pesticide residues are usually time-consuming and costly. For this reason multiresidue methods have been devised and regularly applied in regulating pesticide monitoring programmes [1, 2].

There is a difficulty in developing a method for the residue analysis mainly due to wider nature of polarity, volatility and solubility of different pesticides [3].

In relation with different pesticide classes, various methodologies using gas chromatography with numerous detectors, like thermal conductivity detector (TCD), nitrogen-phosphorus detector (NPD), electron capture detector (ECD) and flame photometric detector (FPD), have been implemented [4]. Further several methods have been developed for accurate quantification of residues of pesticides in various consumable food products or commodities. All these seem to be much complicated because of the use of large quantity of inert gases which are quite costly and consuming [5, 6]. Therefore, there is a need to develop new methods in the preparation of the sample and the requisite quantification parameters.

QuEChERS which is a novel quick, easy, cheap, effective, rugged, and safe method for preparation of samples in pesticide residue analysis [7] was used. QuEChERS methodology has been devised in the year 2003 for the multiresidue analysis of pesticides in different matrices, and now it is a universally accepted method. In this procedure extraction was performed with acetonitrile solvent initially and then partitioning step was carried out using salt mixture. A small amount of extract was further cleaned by using dispersive solid-phase extraction (dSPE) method. Finally, extract was used for the determination of pesticide residues using GC-MS/MS. This method has several advantages; firstly, sample throughput is very high; secondly, it does not use chlorinated solvents; and thirdly, a very small quantity of solvents is needed which in turn provides a very high recovery percentage for broad-spectrum volatility and polarity range of pesticide molecules. Even though this method was developed recently, it has been widely accepted by the international community of pesticide residue analysts. There have been several publications on this topic often replacing the original method with newer and better ones [8–12].

Chromatographic system (gas chromatography or liquid chromatography) attached to mass spectrometry (MS/MS) determination provides us with a method for identifying and quantifying several pesticides in different food matrices [13]. Simple extraction procedure along with very limited cleanup technologies has been employed as a result of the use of more sensitive and selective MS/MS detection. Martinez Vidal et al. used gas chromatography-mass spectroscopy (GC-MS/MS) with ethyl acetate for extraction of 130 multi-class pesticides [14]. Pihlström et al. slightly modified GC-MS/MS procedure [15]. Hetherton et al. reported the use of LC-MS/MS and acetonitrile extraction for the analysis of 73 pesticides in lettuce and oranges [16]. Pang et al. used both liquid chromatography and gas chromatography attached to mass spectrometry for the simultaneous determination of 336 pesticides in vegetables and fruits [17, 18] and 440 pesticide residues in wine, fruit juice, and honey using solid-phase extraction (SPE) cleanup [7].

Grape (*Vitis vinifera* L.) is one of the most important fruit crops cultivated in the subtropical regions of India (60,000 ha). The states, namely Maharashtra, Karnataka, Andhra Pradesh, Tamil Nadu, Punjab, and Haryana, are the grape-growing regions in India. Amongst them, Maharashtra and Karnataka rank first and second in terms of area and productivity, respectively. Grapes cultivated in Maharashtra and Karnataka are mainly exported to Europe, the Middle East and to some extent West Asia. As a result, a large quantity of pesticides is used in their cultivation. This is mainly due to the presence of heavy insect pest infestation. Excess usage of pesticides often results in the accumulation of pesticides on the fruit chnd causes various health hazards and is also more prone for rejection in the international market.

This paper explains an effective and simple experimental procedure for extraction of sample by employing QuEChERS (slightly modified) method and the use of gas chromatographic system with mass spectrometric determination for 35 pesticide residues in grape samples.

2. Experimental

2.1 Apparatus

a. GC-MS/MS instrument: gas chromatograph (Agilent 6890N) with auto-sampler and a triple quadrupole mass spectrometer (Quattro Micro RAB120 Waters) detector was used for the analysis of the pesticides studied. MassLynx Solution software was used for the instrument control and data analysis.

b. Low-volume concentrator: Turbovap (Caliper Life Sciences, USA) with inert nitrogen was used for the evaporation of the solvent.

c. Chopper and homogenizer: vegetable chopper was used for chopping, and a homogenizer (Heidolph) was used for proper mixing of the fruit samples.

d. Centrifuge: centrifuge (Sigma 3K 10) was used for both 2 and 50 ml polypropylene tubes.

e. Weighing balance: weighing balance (Sartorius) was used to weigh the chopped samples and preparation of reference standard reagents.

2.2 Reagents

a. Ethyl acetate and acetic acid (glacial): ethyl acetate and acetic acid (glacial) of sufficient quality for pesticide residue analysis were procured from Sigma-Aldrich.

b. Sodium acetate and magnesium sulfate: reagent-grade anhydrous sodium acetate and magnesium sulfate were procured from Merck (India).

c. Certified reference materials (CRMs): certified reference materials of pesticides were procured from Sigma-Aldrich/Riedel-de-Haen (Zwijndrecht, The Netherlands). The individual stock solutions of 1000 ppm were prepared in toluene and hexane (1:1), and working standards containing 35 pesticides at different concentration levels were prepared in ethyl acetate.

d. Primary secondary amine (PSA): SPE sorbent PSA (40 μm, Bondesil PSA) was purchased from Agilent Technologies (Bangalore, India).

e. Grape samples: grape samples (2 kg each) were collected from the field in Vijayapura district (Karnataka state).

2.3 Residue extraction and cleanup step

The method of preparation of the sample for multiresidue pesticide analysis in grapes involved the following steps: (1) crush 2 kg grape samples under ambient conditions and then 200 g of sample further homogenized for 2 min for proper mixing; (2) accurately weigh a 10 ± 0.1 g of this sample into each 50 ml

Sl. no.	Reference standards	t_M (min)	MRM		CE	Fortification levels (mg/kg)		LOD (mg/kg)
			Pre. ion	Prod. ion		0.02	0.05	
1	DEET	7.06	119	65	21	90 (7)	95 (12)	0.001
2	Propiconazole	7.65	69	41	6	88 (14)	92 (11)	0.01
3	Phorate	7.85	260	75	5	69 (9)	75 (12)	0.002
4	Carbofuran	8.35	164	149	8	78 (4)	84 (7)	0.002
5	Atrazine	8.45	215	58	8	95 (7)	99 (5)	0.005
6	Lindane	9.16	184	145	10	90 (5)	95 (8)	0.001
7	Diazinon	9.74	179	137	17	79 (16)	87 (12)	0.0005
8	Chlorothalonil	9.95	266	133	26	84 (16)	86 (9)	0.004
9	Metalaxyl	10.37	206	59	8	74 (9)	76 (13)	0.002
10	Fenitrothion	10.64	125	79	11	89 (9)	91 (4)	0.002
11	Malathion	10.70	173	99	10	91 (7)	89 (11)	0.003
12	Aldrin	11.54	263	193	22	91 (7)	89 (11)	0.003
13	Fenthion	11.99	278	109	12	80 (11)	92 (15)	0.005
14	Chlorpyrifos	12.05	197	169	16	93 (8)	96 (7)	0.0005
15	Parathion	12.39	291	109	10	83 (6)	95 (12)	0.003
16	Triadimefon	12.77	208	181	6	88 (9)	91 (10)	0.006
17	Pendimethalin	13.39	252	162	16	95 (3)	98 (13)	0.005
18	Captan	13.95	79	51	20	72 (10)	79 (8)	0.002
19	Phenthoate	14.19	274	121	16	88 (4)	90 (6)	0.0005
20	2,4-DDT	14.61	146	118	7	70 (15)	82 (10)	0.00001
21	Alpha-endosulfan	14.95	241	170	25	70 (12)	82 (9)	0.004
22	Butachlor	15.29	176	146	20	94 (8)	99 (13)	0.001
23	Profenofos	15.76	337	267	8	73 (11)	78 (6)	0.005
24	2,4-DDD	16.34	235	165	16	95 (11)	98 (9)	0.00001
25	Endrin	16.85	263	193	22	83 (6)	86 (5)	0.005
26	Chlorfenapyr	17.15	247	75	17	76 (5)	78 (13)	0.02
27	Beta-endosulfan	17.41	241	170	25	70 (14)	87 (9)	0.005
28	Quinalphos	17.87	235	165	15	98 (9)	100 (5)	0.003
29	Ethion	17.89	231	129	18	91 (14)	96 (10)	0.0001
30	Triazophos	18.72	161	77	19	72 (5)	79 (10)	0.005
31	Iprodione	18.91	314	245	10	87 (7)	90 (4)	0.02
32	Beta-cyfluthrin	19.63	165	127	5	96 (15)	99 (8)	0.01
33	Alpha-cypermethrin	20.17	163	127	6	91 (11)	95 (8)	0.005
34	Fenvalerate	20.72	167	125	8	89 (9)	94 (3)	0.005
35	Deltamethrin	21.73	181	152	18	70 (15)	78 (11)	0.008

t_M, retention time; MRM, multiple reaction monitoring; CE, collision energy; LOD, limit of detection; LOQ, limit of quantification.

Table 1.
Experimental condition of the optimized GC-MS/MS method parameters, retention time (min), MRM, average recovery (%) and RSD (in parenthesis) of grape samples (n = 4) at two concentration levels.

polypropylene tubes; (3) add 10 ± 0.1 ml acetonitrile (1% acetic acid) to the polypropylene tubes; (4) homogenize the sample at 3000–5000 rpm for 2–3 min. Add 1.5 g sodium acetate and 6 g $MgSO_4$ (anhydrous), and mix it by shaking gently and centrifuging at 3000 rpm for 3 min to separate the organic layer; (5) 1 ml of extract is then taken in a separate dSPE (dispersive solid-phase extraction) tube, and 50 mg PSA and 140 mg magnesium sulfate are then added to it; (6) extracts were then centrifuged at 5000 rpm for 1 min; (7) 1 ml of the supernatant was then transferred to a small glass tube and the solvent was then evaporated using turbo evaporator which was set at 45°C and 20 psi inert nitrogen gas flow; and (8) the final step was the reconstitution of the sample with a 1 ml of ethyl acetate for analysis and confirmation of residues by gas chromatography-mass spectrometry (GC-MS/MS) (24).

GC-MS/MS analysis. A gas chromatography (Agilent 6890N) with mass spectrometer (Waters, Boston, USA) and an auto-sampler (Agilent 7683) with electron ionization (EI+) mode were used. Separation of analytes was carried out using HP-5MS column (30 m, 0.25 μm internal diameter, 0.25 μm film thickness) (J&W Scientific). The oven temperature was increased as follows: 50°C (1 min), 25°C/min up to 150°C and increased to 10°C/min to 280°C (4 min hold). Split-less injection of 1 μl was carried out with an injector temperature maintained at 280°C and hold time of 1 min. The carrier gas that was used was helium (99.999%) at flow rate of 1.3 ml/min. The interface temperature was maintained at 250°C.

Electron ionization (EI+) mode was selected (4 min solvent delay); the source temperature was set at 250°C. The gas argon (purity 99.99%) was used as collision gas which is used to collide with ions after ionization. The dwell time per channel was between 0.05 and 0.1 s. QuantLynx was used to process the data obtained from calibration of CRMs and also from grape fruit extract.

Heptacosa (perfluorotributylamine) was used to calibrate the mass spectrometer. **Table 1** explains the particular ions of quantification for the MRM mode and retention times (t_M) for the residue analysis of individual substances.

3. Validation study

In this method, for the fulfillment of validation criterion, single-laboratory approach was used. The following validation parameters were used.

3.1 Linearity

Five calibration levels (1 and 200 ng/mL) were used for constructing the calibration curve by using pure solvent and matrix. The concentration of a pesticide residue can be calculated based upon the calibration curve. The prerequisite for this method is that the peak area should fall within the linear range of the curve. Then the concentration can be calculated on basis of the slope of the calibration curve using the regression equation:

$$Y = mX + C \qquad (1)$$

where Y = peak area, X = concentration, m = slope of the curve and C = constant.

3.2 Selectivity

It was determined by elimination of noise at the retention time of the compound, which is performed by fixing two transitions of MS/MS for individual molecule of analyte by considering the adequate precursor and product ions.

3.3 Sensitivity

Detection limit (LOD) in the chromatogram was calculated by using peak signal of the analyte molecule concentration to the three times background noise in the chromatogram. The quantification limit (LOQ) in the chromatogram was set as the lowest concentration with very good recovery range (65–100%) and precision (RSD ≤ 20%). The ion ratio (Q/q) was used for the criterion of confirmation in positive samples. The Q/q is the ratio of the intensity quantification (Q) and confirmation transition (q) (**Table 1**).

Typical S/N acceptance criteria: LOD—3:1 and LOQ—10:1.

4. Results and discussion

4.1 Method validation

All the 35 certified reference materials of pesticides were determined in a single chromatographic window of 22 min run time (**Figure 1**). For most of the compounds, the R^2 values (correlation coefficients) of the calibration curve were >0.99 for both pure solvent-based and matrix-matched samples. The recovery of all of the compounds was found to be 70–100% with RSD below 14%. **Figure 2** shows chromatograms of typical pesticide peak shapes. The grape sample extracts were slightly yellow because of the co-extraction of carotenoids in the ethyl acetate. It was found that a two-step homogenization procedure significantly increased the precision of analysis. It was also observed that the use of high-speed homogenization process
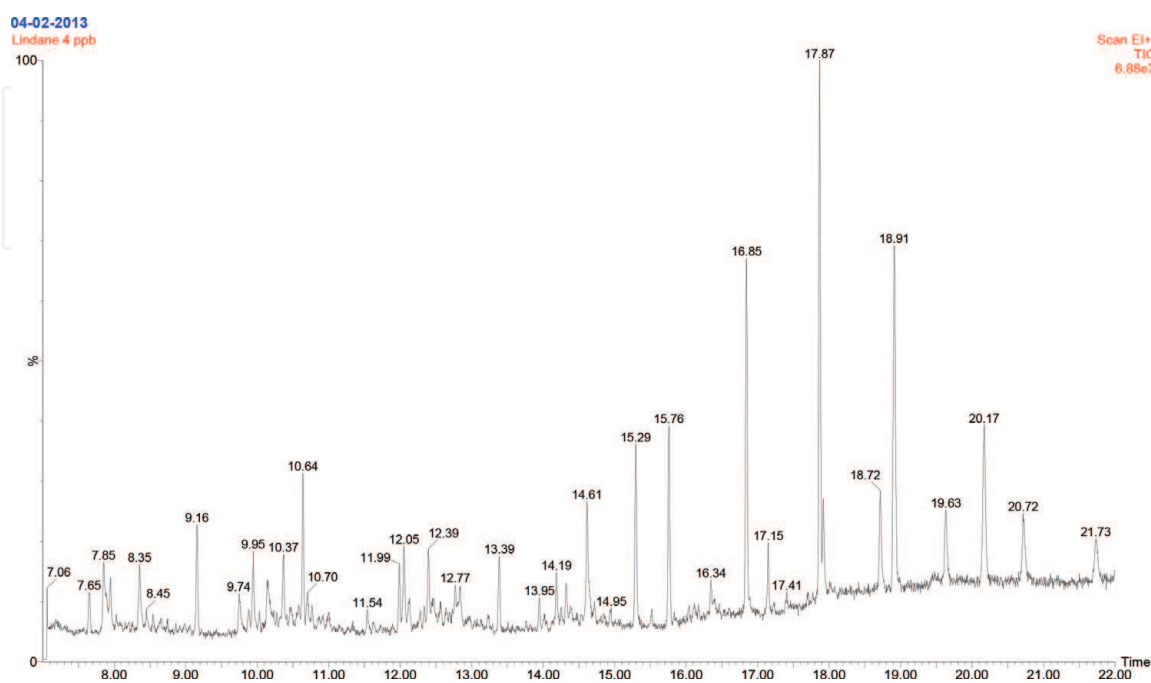
Figure 1.
Total ion chromatogram of 35 certified reference standards.
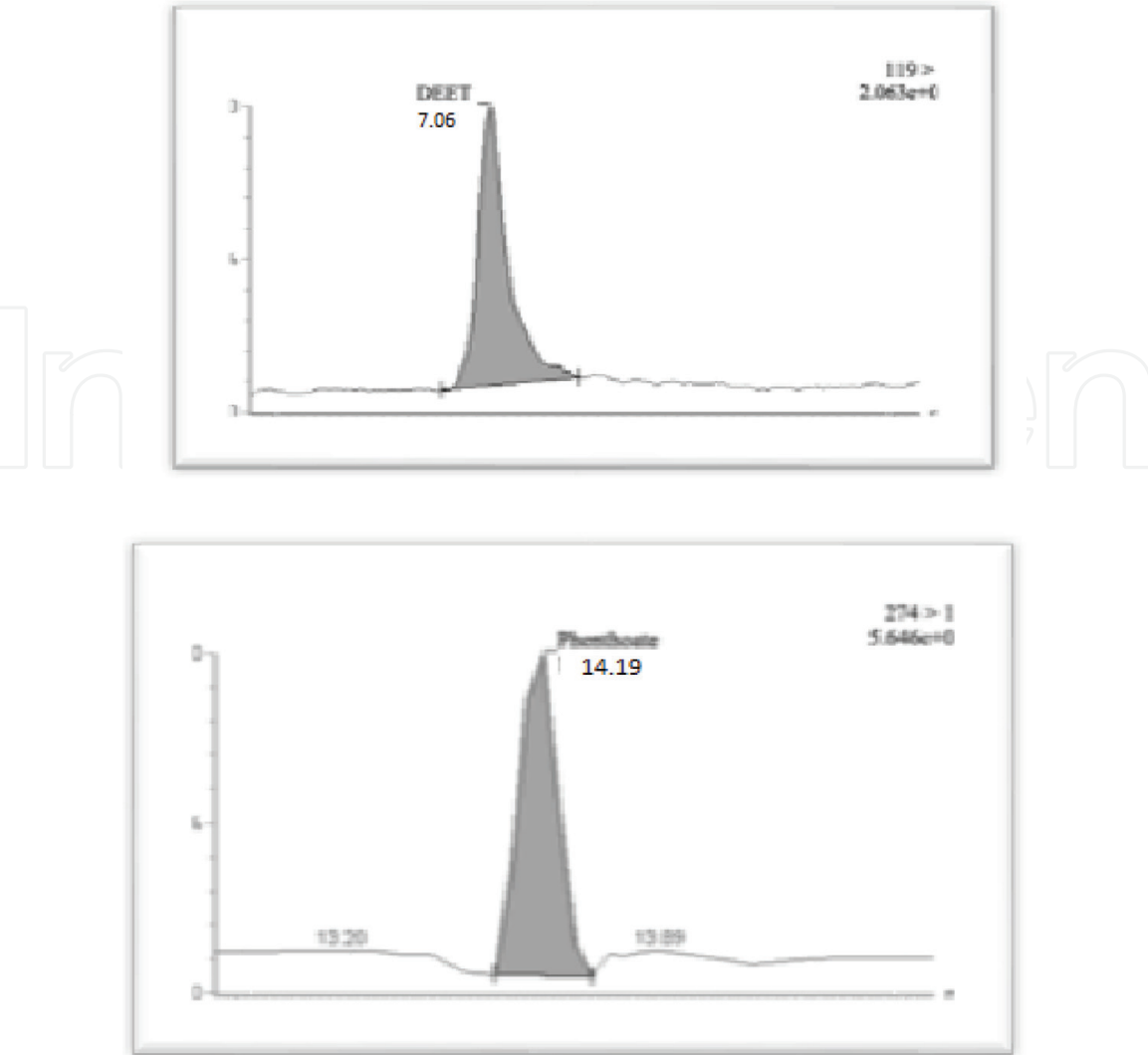
Figure 2.
Chromatograms showing DEET and phenthoate peak shapes.

for precooled sample did not necessarily increase the temperature of the system above 10°C and thereby proved very useful for maintaining the stability of the phthalimides such as captan.

4.2 Recovery experiments of spiked samples

Usually, the extraction and cleanup procedure removes the matrix co-extractives then separates all of the analytes from the matrix. The same does not holds good in most of the matrices during the pesticide residue analysis. As a result, the actual recovery experiments were performed on grape samples. The separated peaks with their t_M (retention times) are summarized in **Table 1**. Using the linear regression equation recoveries of individual pesticides with different levels of spiking along with replicates were calculated in grape matrix. **Table 1** gives the average recoveries for all spiked pesticide standards at each spiked level in grape samples. All the tested 35 pesticides displayed a recovery range between 70 and 100% which is quite acceptable. RSD (relative standard deviation) was used to express the reproducibility, and most of the RSD values were found to be less than 14%. Recovery study is conducted using a control sample and at least two fortification levels with three replications. The formula for arriving percentage recovery for method validation is as follows:

$$\text{Residue (ppm)} = \frac{\text{Area of sample}}{\text{Area of std}} \times \frac{\text{Final vol (ml)}}{\text{Vol injected (μl)}} \times \frac{\text{Std conc (ng)}}{\text{Wt of the sample (g)}} \times \frac{100}{\text{Fortification level}} \qquad (2)$$

In QuEChERS method the use of acetonitrile has several advantages, mainly addition of salt separates it from water without using nonpolar solvents, mutual compatibility with dispersive solid-phase extraction and very good separation/matching with gas and liquid chromatography. The anhydrous $MgSO_4$ tends to form lumps. Shaking the tubes of the centrifuge on adding the salt mixture for 1 min or more, it was observed that the formation of lumps was eliminated. Next, adding the salt to all of the samples, it was also found that the one-minute extractions of the entire batch could be run parallelly. Dispersive solid-phase extraction with primary secondary amine eliminated the color pigments, acidic components and sugars [10, 11]. Apart from this, sugars, lipids and waxes were removed by freezing which helped in increasing the efficiency of GC analysis [12].

5. Applicability of the developed method

5.1 Sampling

Grape samples were collected from farmers' fields in Vijayapura district in Karnataka. These areas are very popular for the production of grapes, and we see an excessive use of pesticides. The developed analytical method was used for the determination of residues of pesticides in grape samples and that were analyzed in triplicate. The results confirmed that the grape samples contained pesticide residues well above the prescribed level, viz. carbofuran, fenvalerate, triazophos, and endrin (**Table 2**). Grapes which were analyzed in the present study mainly contributed to the major dietary intakes of the citizens in India.

Sl. no.	Name of the pesticides	MRLs exceeded samples	Residue content (ppm)	EU MRLs (ppm)
1	Carbofuran	9	0.14	0.02
2	Fenvalerate	6	0.33	0.02
3	Triazophos	4	0.13	0.01
4	Endrin	5	0.04	0.01

EU, the European Union; MRL, maximum residue limit.

Table 2.
Analytical results of grape sample analysis collected from Vijayapura district (n = 100).

6. Conclusion

Grapes contaminated with residues of pesticides pose a major health hazard. Therefore we have developed effective method for the detection of contaminated grapes. Hence, for the simultaneous confirmation and quantification of 35 pesticides in grape samples, a mulitresidue method has been developed and validated. For multi-class pesticide residue determination, GC-MS/MS with triple quadrupole analyzer played an important role. Within 22 min of run time, all the closely eluted and co-eluted peaks were separated with higher sensitivity. The two MRM transitions, one for confirmation another for quantification, achieved very good

sensitivity and selectivity for possible safe identification by the use of Q/q ratio parameter. The limit of detection was lower than the MRL prescribed. Solid-phase extraction with acetonitrile solvent was employed. Finally, the method was successfully validated for two concentrations, viz. 0.02 and 0.05 mg/kg grape sample. The validated method reduces the overall cost of analysis and also offers low-uncertainty measurement. Further, this method was successfully employed for the analysis of real-world grape samples.

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Conflicts of interest

There are no conflicts of interest to declare.

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