

Analysis of Agrochemical Residues in Tobacco Using QuEChERS Method by GC-MS/MS

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ABSTRACT : This study was performed to apply the more rapid and accurate sample preparation, and the high selectivity and sensitivity of the analyte detection by gas chromatography-triple quadrupole mass spectrometry (GC-MS/MS). QuEChERS (quick, easy, cheap, effective, rugged and safe) method was validated for 49 agrochemicals in the CORESTA Agrochemical Advisory Committee guide and amenable to GC-MS/MS determination. In QuEChERS method, the effects of sorbents (PSA, C₁₈ and GCB) and matrix of the analytes in tobacco types (flue-cured, burley and oriental) were investigated. MS/MS acquisition provided high specificity and selectivity for agrochemicals and low limit of quantification. QuEChERS by using PSA alone and the matrix-matched standards gave good recoveries and RSD values in three types of tobaccos. QuEChERS method was no needed to be complex clean-up procedure and would be used as the fast and easy method for agrochemical residue analysis in tobacco.

Key words : Tobacco, agrochemicals, QuEChERS, GC-MS/MS

Nowadays, public interest in agrochemical residues in foods and related commodities has been increased. This situation has let to regulation setting maximum residue limits (MRLs) (Mueller *et al.*, 1999) of agrochemical residues in agricultural products including tobacco. Thus, the rapid multi-residue determination of wide range of agrochemicals in many samples has been required.

The multi-residue determination of agrochemicals in samples consists of extraction, clean-up and instrumental analysis. The general sample preparation methods based on the conventional liquid-liquid extraction (LLE) (Tahboub *et al.*, 2005) and the automated instrument based extraction technique, pressurized

liquid extraction (PLE; Dionex trade name ASE for accelerated solvent extraction) (Haib *et al.*, 2003), followed by clean-up such as solid-phase extraction (SPE). These methods are complicated and require large amount of solvents. In order to cover these problems, QuEChERS (quick, easy, cheap, effective, rugged and safe) method was firstly established by using the dispersive-SPE (Anastassiades *et al.*, 2003). After these sample preparation procedures, analytes have been analyzed by gas chromatography (GC) or liquid chromatography (LC).

For GC separations, selective detectors (ECD, NPD and FPD) or mass spectrometry (ISO, 2000; Barrio *et al.*, 1994; Dugo *et al.*, 2005; Albero *et al.*, 2004) are popular for detection of agrochemical

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residues. But, recently more sensitive analytical technique is needed to qualify and quantify agrochemical residues because many of modern agrochemicals are either not amenable to GC or not detectable at sufficiently low levels. Instead of these detectors and single mass spectrometry, GC coupled with triple quadrupole mass spectrometry is used for the rapid and sensitive determination of trace-level analytes (Haib *et al.*, 2003; Frenich *et al.*, 2005). Triple quadrupole mass spectrometry can increase the number of co-eluted agrochemicals to be analyzed if it is operated in selected reaction monitoring (SRM) mode that only monitors a few selected products per analyte.

Therefore this study was performed to apply the more rapid and accurate sample preparation of agrochemical residues in tobacco by using QuEChERS method. Also the purpose of this study was to apply triple quadrupole mass spectrometry (MS/MS) for the high selectivity and sensitivity detection of analytes.

MATERIALS AND METHODS

Reagents and Materials

Acetone, *n*-hexane and acetonitrile (pesticide grade) were obtained from JT Baker (USA). All pesticide standards were purchased from Supelco (USA) and Fluka (USA). Sorbents (40 μ m particle size) for dispersive-SPE included primary secondary amine (PSA) obtained from Varian (USA), C₁₈ silica based reverse phase from Merck (USA) and graphitized carbon black (GCB) from Supelco (USA). SPE cartridges containing 1 g of Florisil were purchased from Varian (USA). Anhydrous magnesium sulfate, sodium chloride, trisodium citrate dihydrate and disodium hydrogencitrate sesquihydrate, which were all ACS-grade or better, obtained Sigma and Aldrich (USA).

Three types of tobacco, flue-cured (B10,

Korea), burley (B1T, Korea) and oriental (Basma, Greece) were used in this study.

Standard Preparation

Selected agrochemicals and the internal standard (ISTD, mirex) obtained from Sigma, Supelco and Reidel-de-Haën (USA). Stock standard solutions of individual compounds with concentration 100 μ g/mL were prepared by exact weighing of the powder or liquid and dissolution in 100 mL of acetone, which were then stored in a freezer at -19 $^{\circ}$ C. A multi compounds working standard solution (0.01~0.4 μ g/mL concentration of each compound) were prepared by appropriate dilutions of the stock solutions with acetone and stored in a refrigerator at 4 $^{\circ}$ C.

Sample Preparation

Three types of tobacco are dried in the oven set at 50 $^{\circ}$ C or 2 h to obtain a mass fraction of moisture of approximately 5 % after drying. The tobacco is grounded through a 2 mm mesh, taking care to avoid heating above 50 $^{\circ}$ C. The grounded tobacco is stored in sealed containers and is excluded from light.

Recovery tests carried out 3 spiking levels and 3 replicates. A solution of analytes in acetone was spiked to tobacco to achieve a concentration of 0.05, 0.5, 1 μ g/g for each agrochemical. The extraction procedure was performed as the sample preparation method.

QuEChERS Preparation

Extraction & clean-up : Ground tobacco (2 g) were weighed into a 50 mL centrifuge tube, 10 mL of acetonitrile and 100 μ L of ISTD solution (20 μ g/mL of mirex in acetone) were added and the tube was closed and shaken vigorously by shaker for 1 min. After shaking a mixture of 4 g magnesium sulfate, 1 g sodium chloride, 1 g trisodium citrate dihydrate and 0.5 g disodium hydrogencitrate sesquihydrate were added. The

tube was closed and immediately shaken vigorously by shaker for 1 min and centrifuge for 5 min at 6,000 rpm.

An aliquot of the extract was transferred into a PP-single use centrifugation tube which contains sorbents ; 1) 25 mg of PSA and 150 mg of magnesium sulfate per mL extract, 2) 25 mg of PSA, 25 mg of C₁₈ and 150 mg of magnesium sulfate per mL extract, 3) 25 mg of PSA, 2.5 mg of GCB and 150 mg of magnesium sulfate per mL extract. Tube is shaken vigorously for 30 s and centrifuged. After centrifugation the cleaned extract was transferred into a vial.

Preparation of calibration solutions

To prepare calibration solutions, a blank matrix is necessary. The blank was treated as any other sample, without ISTD solution. An aliquot of the blank extract was fortified with the desired amount of an agrochemical mixture stock solution and a known amount of ISTD solution was added at approximately the same concentration as in the sample extracts.

GC-MS/MS analysis

GC-MS/MS analysis was carried out on a Varian 3800 gas chromatograph/1200L triple quadrupole mass spectrometer equipped with a split/splitless injector and CombiPAL autosampler (CTC Analytics, USA). The data system contains all of the software required for calibration, collection of GC/MS spectra and data processing for qualitative and quantitative analysis.

The chromatographic separation was performed by a VF-5ms capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness, Varian, USA). Helium was used as the carrier gas at flow rate of 1.0 mL/min. Argon was used as the collision gas. The injector temperature was set at 250 °C and 1 μL was injected in undividable mode for 1 min. Samples were analyzed as the

following oven temperature program : initial temperature 50 °C (hold for 3 min), ramp to 150 °C at 20 °C/min and finally ramp to 280 °C at 2 °C/min (hold for 5 min). The manifold, source and transfer line temperature were set at 40 °C, 230 °C and 250 °C respectively.

RESULTS AND DISCUSSION

Optimization of GC-MS/MS conditions

To optimize MS/MS conditions, fragmentation of agrochemicals was triple quadrupole mass spectrometer performed. MS, in the selected ion monitoring and full scanning mode, could not avoid matrix interference. Fragmentation of each analyte was caused by collisions of precursor ions. Product ions of each agrochemical were chosen for the purposes of quantification and reduction of interferences. The product ions chosen were the ions (*m/z*) with high intensity. The optimized MS/MS acquisition was carried out with the transitions reported in Table 1.

MS/MS acquisition could detect the low level of agrochemicals without interference peak. The gas chromatographic separation of the target analytes in SRM (selected reaction monitoring) mode was not very important because this MS/MS acquisition was able to determine several co-eluted analytes at the same time.

Matrix effects and recoveries on sorbent types

Three types of sorbent, such as PSA, C₁₈ and GCB were used to investigate the influences on recovery rate and matrix effect in flue-cured tobacco (Table 2, Fig. 1). C₁₈ was used to remove co-extracted fat and waxes with PSA and magnesium sulfate in the dispersive-SPE step. GCB was used to remove carotenoids or chlorophyll with PSA and magnesium sulfate (4).

PSA alone and additional use of C₁₈ (PSA + C₁₈) showed 35.4 % of matrix effects (less than 20 % signal enhancement and suppression). In

Table 1. SRM transition for the different agrochemicals

Active ingredient	Type*	Precursor ion (m/z)	Product ion (m/z)	CE (eV)	Active ingredient	Type*	Precursor ion (m/z)	Product ion (m/z)	CE (V)
1 Heptenophos	OP	250	124	-10	26 Pendimethalin	DN	252	162	-25
2 Ethoporphos	OP	200	97	-30	27 Chlorfenvinphos	OP	267	159	-25
3 Trifluralin	DN	306	264	-15	28 Phenthoate	OP	274	121	-15
4 Benfluralin	DN	292	160	-25	29 Quinalphos	OP	146	118	-10
5 Phorate	OP	260	75	-10	30 Methidathion	OP	145	85	-10
6 Quintozene	OC	237	143	-30	31 Flumetralin	DB	143	107	-25
7 Terbufos	OP	231	129	-30	32 Prothiofos	OP	309	239	-15
8 Diazinon	OP	179	121	-25	33 Profenofos	OP	337	267	-15
9 Disulfoton	OP	274	88	-10	34 Oxadixyl	AM	163	132	-10
10 Pirimicarb	CB	166	96	-25	35 Ethion	OP	231	129	-25
11 Phosphamidon	OP	264	127	-25	36 Benalaxyl	AM	148	105	-20
12 Chlorpyrifos methyl	OP	286	93	-25	37 Tebuconazole	HC	250	125	-25
13 Tolclofos methyl	OP	265	93	-30	38 <i>cis</i> -Permethrin	PY	183	1530	-15
14 Alachlor	AM	188	130	-30	39 <i>trans</i> -Permethrin	PY	183	153	-20
15 Metalaxyl	AM	206	132	-30	40 Cyfluthrin 1	PY	226	206	-15
16 Fenchlorphos	OP	285	270	-30	41 Cyfluthrin 2	PY	226	199	-10
17 Pirimiphos methyl	OP	305	180	-30	42 Cyfluthrin 3	PY	226	206	-10
18 Fenitrothion	OP	277	109	-25	43 Cyfluthrin 4	PY	226	206	-10
19 Malathion	OP	173	99	-30	44 Flucythrinate 1	PY	199	107	-15
20 Chlorpyrifos	OP	314	258	-30	45 Flucythrinate 2	PY	199	107	-30
21 Fenthion	OP	278	109	-20	46 Deltamethrin 1	PY	253	174	-30
22 Dicofol	OC	139	111	-15	47 Deltamethrin 2	PY	253	174	-15
23 Butralin	DN	266	174	-30	48 Dimethormorph 1	HC	301	301	-5
24 Diphenamid	AM	167	165	-30	49 Dimethormorph 2	HC	301	301	-5
25 Isopropalin	OP	280	238	-10	50 Mirex	ISTD	272	237	-25

* Abbreviations for agrochemical type : OP : organophosphorus, OC : organochlorine, DN : dinitramine, AM : amides, PY : pyrethroids, HC : heterocyclic

the distribution of validated agrochemicals, the additional use of GCB (PSA + GCB) showed the 43.8 % of matrix effect (less than 20 % signal enhancement and suppression).

In the dispersive-SPE clean step, PSA sorbent and anhydrous magnesium sulfate alone was found to remove many matrix co-extractives without affecting agrochemical recoveries. The

additional use of C₁₈ did not affect recoveries, but neither did it provide additional cleanup over PSA alone in tobacco samples. GCB did a good job of removing additional matrix components from the QuEChERS extracts, but unfortunately, it also tended to remove certain agrochemicals, such as terbufos, disulfoton, pirimicarb, metalaxyl and other analytes.

Table 2. Recoveries and relative standard deviation of agrochemicals on sorbent types in flue-cured tobacco by QuEChERS method

Active ingredient	PSA		PSA + C ₁₈		PSA + GCB	
	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)
1 Heptenophos	81.4	7.5	118.7	8.7	122.1	12.1
2 Ethoporphos	118.1	9.6	89.5	6.1	124.7	1.1
3 Trifluralin	100.5	7.0	104.6	11.5	121.7	13.3
4 Benfluralin	81.5	8.1	91.8	7.3	102.3	10.3
5 Phorate	70.9	9.9	100.7	4.8	90.4	11.7
6 Quintozene	82.6	10.5	70.0	15.6	118.6	11.8
7 Terbufos	87.3	8.7	122.2	4.3	65.9	13.6
8 Diazinon	71.9	11.6	113.9	9.7	90.1	8.3
9 Disulfoton	85.6	7.4	111.3	9.0	62.7	9.4
10 Pirimicarb	81.6	7.6	91.2	8.8	74.0	12.3
11 Phosphamidon	104.1	9.5	92.1	8.9	87.9	7.5
12 Chlorpyrifos methyl	83.3	7.4	111.9	11.1	73.3	15.2
13 Tolclofos methyl	94.6	2.9	108.7	12.1	111.6	7.1
14 Alachlor	76.8	5.8	102.3	10.7	122.7	13.6
15 Metalaxyl	106.5	9.7	100.5	9.7	73.3	13.7
16 Fenchlorphos	104.3	3.7	105.5	9.1	83.3	9.5
17 Pirimiphos methyl	111.6	0.7	102.6	12.3	89.8	12.5
18 Fenitrothion	94.8	8.8	117.8	10.4	122.9	10.1
19 Malathion	88.0	11.2	93.1	5.3	86.5	9.4
20 Fenthion	105.1	6.0	104.9	9.4	116.3	8.9
21 Chlorpyrifos	99.2	1.2	57.6	10.0	120.1	7.2
22 Dicofof	107.0	3.2	84.3	1.6	104.9	12.7
23 Butralin	107.9	3.9	92.3	10.2	115.0	7.8
24 Diphenamid	120.1	3.8	111.0	6.8	110.1	9.5
25 Pendimethalin	81.7	2.9	86.2	14.5	89.6	13.4
26 Isopropalin	105.1	6.0	106.2	12.9	129.0	8.8
27 Chlorfenvinphos	102.3	6.9	121.8	3.4	91.6	7.4
28 Phenthoate	98.7	10.9	94.8	11.8	109.6	9.9
29 Quinalphos	98.4	3.5	109.7	10.5	111.3	1.6
30 Methidathion	116.0	7.1	108.9	13.4	101.5	10.8
31 Flumetralin	110.5	5.8	111.6	8.0	120.2	9.0
32 Prothiofos	104.0	6.0	94.5	7.2	113.3	14.7
33 Profenofos	101.7	7.6	113.6	2.5	91.5	8.1
34 Oxadixyl	119.5	9.4	105.5	9.9	101.6	11.5
35 Ethion	117.1	3.0	110.7	7.4	98.0	7.3
36 Benalaxyl	98.9	6.9	97.7	2.0	93.2	8.9
37 Tebuconazole	116.7	6.4	102.8	7.4	78.4	8.7
38 <i>cis</i> -Permethrin	114.5	5.8	71.5	10.9	81.7	13.7
39 <i>trans</i> -Permethrin	117.8	1.5	87.6	12.3	80.8	7.6
40 Cyfluthrin 1	105.6	11.0	94.0	10.7	76.6	15.8
41 Cyfluthrin 2	110.7	7.6	93.9	8.9	77.1	15.4
42 Cyfluthrin 3	100.0	13.1	88.2	1.7	74.7	13.5
43 Cyfluthrin 4	97.2	6.3	109.8	10.8	102.2	19.2
44 Flucythrinate 1	98.0	5.4	95.8	15.7	107.3	14.8
45 Flucythrinate 2	114.2	11.0	113.2	17.4	87.8	9.4
46 Deltamethrin 1	97.4	8.0	109.7	15.5	84.3	14.7
47 Deltamethrin 2	92.4	7.1	139.7	16.5	84.3	11.7
48 Dimethormorph 1	119.5	13.9	119.7	7.9	108.0	10.1
49 Dimethormorph 2	113.5	4.3	114.6	4.7	80.5	8.3

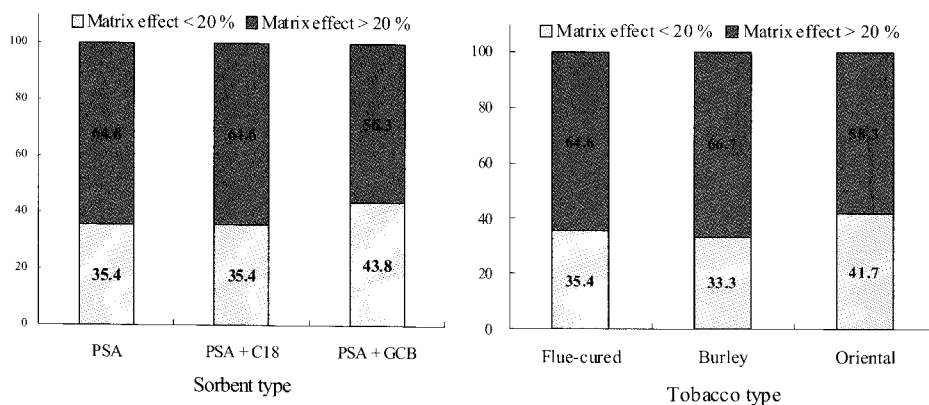


Fig. 1. Influences of sorbent and tobacco types on matrix effects.

Matrix effects and recoveries on tobacco types

Three types of tobacco such as flue-cured, burley and oriental were used to investigate the influences on matrix effects, recovery rates and LOQs by using PSA sorbent in QuEChERS method (Figure 1, Table 3). The matrix effects caused by different types of tobacco were flue-cured 35.4 %, burley 33.3 % and oriental 41.7 % (less than 20 % signal enhancement and suppression) in the distribution of validated agrochemicals, respectively.

Tobacco samples of three types, which prepared QuEChERS by using PSA alone and calculated the matrix-matched standards, showed good recoveries and relative standard deviation (RSD) values. The results of QuEChERS method for the wide range of 49 agrochemicals generally fell within the commonly accepted range of 70~120 % and ≤ 20 % RSD for quantitative agrochemical residue methods (Anspach, 2006). This was previously observed in case of the food matrices (Lehotay *et al.*, 2005). The LOQs of agrochemicals determined by the method were below the guidance residue levels of CORESTA ACAC (CORESTA, 2003).

QuEChERS method requires less sample weight and less organic solvent amount. Also,

QuEChERS method was easy, cheap and fast, and requires less apparatus than the LLE and PLE methods using SPE (Tahboub *et al.*, 2005; Haib *et al.*, 2003). The slightly better clean provided by the SPE technique does not compensate for the better recoveries and practical advantages of dispersive-SPE.

As a result, one type of matrix-matched might be representative for the other types. Nevertheless, for a proper quantification it is necessary for the analyst to know the type of tobacco in advance. QuEChERS method does not require complicated procedure, and it could be a rapid, accurate and effective method for the determination of agrochemical residues in tobacco.

CONCLUSIONS

QuEChERS method carried out to apply the rapid and accurate sample preparation method for the determination of agrochemical residues in tobacco by GC-MS/MS. MS/MS acquisition provided high specificity and selectivity for agrochemicals and low limit of quantification. QuEChERS method showed different recoveries and matrix effects on sorbent types and tobacco types. QuEChERS by using PSA alone and the matrix-matched standards gave good recoveries

Table 3. Recoveries and relative standard deviation (RSD) of agrochemicals on tobacco types by QuEChERS method

Active ingredient	Flue-cured		Burley		Oriental		LOQ (µg/g)
	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)	RSD (%)	
1 Heptenophos	81.4	7.5	106.4	11.5	92.2	7.7	0.040
2 Ethoporphos	118.1	9.6	111.8	9.7	104.3	10.0	0.036
3 Trifluralin	100.5	7.0	75.1	7.5	87.5	5.7	0.032
4 Benfluralin	81.5	8.1	111.9	5.1	91.1	10.4	0.072
5 Phorate	70.9	9.9	114.0	10.0	118.9	7.1	0.024
6 Quintozene	82.6	10.5	92.0	13.2	71.8	12.1	0.120
7 Terbufos	87.3	8.7	87.7	7.4	104.1	7.6	0.039
8 Diazinon	71.9	11.6	110.7	2.7	84.1	12.1	0.054
9 Disulfoton	85.6	7.4	98.2	9.9	81.8	10.9	0.056
10 Pirimicarb	81.6	7.6	99.3	8.4	76.1	7.3	0.080
11 Phosphamidon	104.1	9.5	108.4	8.4	89.2	8.9	0.100
12 Chlorpyrifos methyl	83.3	7.4	100.6	12.5	117.3	13.1	0.040
13 Tolclofos methyl	94.6	2.9	82.1	6.9	111.2	5.9	0.032
14 Alachlor	76.8	5.8	94.0	8.1	89.9	2.1	0.039
15 Metalaxyl	106.5	9.7	99.5	10.5	116.7	9.1	0.019
16 Fenclorpos	104.3	3.7	93.5	8.4	111.5	11.9	0.076
17 Pirimiphos methyl	111.6	0.7	91.6	11.2	92.8	7.3	0.084
18 Fenitrothion	94.8	8.8	85.2	10.9	106.8	9.5	0.080
19 Malathion	88.0	11.2	101.6	6.5	114.0	10.3	0.136
20 Fenthion	105.1	6.0	94.9	8.8	94.4	6.0	0.033
21 Chlorpyrifos	99.2	1.2	75.0	5.5	70.5	10.9	0.080
22 Dicofof	107.0	3.2	113.0	7.0	94.6	5.0	0.030
23 Butralin	107.9	3.9	71.8	9.0	75.6	11.1	0.033
24 Diphenamid	120.1	3.8	117.7	6.8	89.4	7.6	0.086
25 Pendimethalin	81.7	2.9	73.3	5.9	74.0	8.8	0.157
26 Isopropalin	105.1	6.0	98.8	9.6	107.8	7.6	0.015
27 Chlorfenvinphos	102.3	6.9	127.1	11.9	77.0	15.0	0.041
28 Phenthoate	98.7	10.9	119.3	5.4	95.5	9.7	0.026
29 Quinalphos	98.4	3.5	119.0	12.3	82.4	14.8	0.036
30 Methidathion	116.0	7.1	120.2	10.6	98.2	3.6	0.028
31 Flumetralin	110.5	5.8	72.6	5.5	88.2	3.9	0.016
32 Prothiofos	104.0	6.0	101.0	7.4	79.0	8.3	0.100
33 Profenofos	101.7	7.6	102.0	6.6	90.5	8.3	0.080
34 Oxadixyl	119.5	9.4	108.5	7.7	86.0	8.9	0.045
35 Ethion	117.1	3.0	82.2	6.1	87.6	4.8	0.022
36 Benalaxyl	98.9	6.9	102.3	9.3	95.5	7.9	0.032
37 Tebuconazole	116.7	6.4	89.0	10.5	72.9	15.5	0.024
38 <i>cis</i> -Permethrin	114.5	5.8	99.7	9.7	79.4	2.8	0.040
39 <i>trans</i> -Permethrin	117.8	1.5	99.0	5.0	73.7	4.6	0.043
40 Cyfluthrin 1	105.6	11.0	85.8	15.8	95.6	13.2	0.040
41 Cyfluthrin 2	110.7	7.6	126.0	5.1	74.6	10.4	0.040
42 Cyfluthrin 3	100.0	13.1	116.5	11.2	104.2	15.9	0.032
43 Cyfluthrin 4	97.2	6.3	94.5	1.5	85.5	10.3	0.032
44 Flucythrinate 1	98.0	5.4	79.4	6.6	93.3	8.3	0.019
45 Flucythrinate 2	114.2	11.0	108.0	9.5	86.9	8.5	0.015
46 Deltamethrin 1	97.4	8.0	80.9	11.3	91.2	8.5	0.040
47 Deltamethrin 2	92.4	7.1	99.5	16.5	72.0	1.6	0.024
48 Dimethormorph 1	119.5	13.9	96.4	10.9	96.9	4.6	0.040
49 Dimethormorph 2	113.5	4.3	93.8	10.0	99.9	8.4	0.016

and RSD values in flue-cured, burley and oriental tobaccos. The LOQs determined by the QuEChERS method were below the guidance residue level of CORESTA ACAC. As QuEChERS method gave good recoveries, RSD values, low LOQs, it would be used to analytical method for agrochemical residue in tobacco by QuEChERS method and GC-MS/MS.

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