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Analysis of Multiclass Pesticide Residues in Tobacco by Gas Chromatography Quadrupole Time-of-Flight Mass Spectrometry Combined with Mini Solid-Phase Extraction

Rui Bie [1,†], Jiguang Zhang [1,†], Yunbai Wang [1], Dongmei Jin [2], Rui Yin [3], Bin Jiang [4] and Jianmin Cao [1,*]

[1] Laboratory of Quality & Safety Risk Assessment for Tobacco, Ministry of Agriculture and Rural Affairs, Tobacco Research Institute of Chinese Academy of Agricultural Sciences, Qingdao 266101, China; 82101202172@caas.cn (R.B.); zhangjiguang@caas.cn (J.Z.); wangyunbai@caas.cn (Y.W.)
[2] Sichuan Tobacco Quality Supervision and Testing Station, Chengdu 610041, China; dongmeijin1979@outlook.com
[3] Ningqiang Branch of Hanzhong Tobacco Company, China National Tobacco Corporation, Ningqiang 724400, China; yinruibsy@outlook.com
[4] Shandong Branch of China National Tobacco Corporation, Jinan 250101, China; jiangbin8077@126.com
* Correspondence: caojianmin@caas.cn
† These authors contributed equally to this work.

Abstract: A screening method using gas chromatography quadrupole time-of-flight mass spectrometry (GC-QTOF/MS) combined with mini solid-phase extraction (mini-SPE) was established for the quantification and validation of multiclass pesticide residues in tobacco. The method was quicker and easier, with sample purity higher than that obtained by traditional SPE and dispersed-SPE. Box-Behnken design, an experimental design for response-surface methodology, was used to optimize the variables affecting the target pesticide recovery. Under the optimized conditions, 92% of the pesticides showed satisfactory recoveries of 70%–120% with precision <20% at spiking levels of 50, 250, and 500 ng/g. The limits of detection and quantification for all the analyses were 0.05–29.9 ng/g and 0.20–98.8 ng/g, respectively. In addition, a screening method based on the retention time and a homebuilt high-resolution mass spectrometry database were established. Under the proposed screening parameters and at spiking levels of 50, 100, and 500 ng/g, 76.6%, 94.7%, and 99.0% multiclass pesticide residues were detected, respectively, using the workflow software. The validated method was successfully applied to the analysis of real tobacco samples. Thus, the combination of mini-SPE and GC-QTOF/MS serves as a suitable method for the quantitative analysis and rapid screening of multiclass pesticide residues in tobacco.

Keywords: mini solid-phase extraction; multiclass pesticide residues; tobacco; gas chromatography quadrupole time-of-flight mass spectrometry

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1. Introduction

Tobacco is a non-food crop, and its production heavily relies on the use of pesticides (including insecticides, herbicides, fungicides, and suckercides). Pesticide residues are the pesticides remaining on tobacco after harvesting. Studies have revealed that pesticides are present in the cigarette smoke, thus exposing both active and passive smokers to pyrolyzed pesticide residues [1,2]. The detection and removal of pesticide residues in tobacco have always been challenging, various countries and international organizations have established maximum residue limits for these residues in tobacco. For example, in 2021, the CORESTA Agro-Chemical Advisory Committee provided guidance residue levels (GRLs) for 117 pesticides and other chemicals in tobacco [3].

Various studies have reported the analysis of multiclass pesticide residues in tobacco by gas chromatography tandem mass spectrometry [4–6] and liquid chromatography

tandem mass spectrometry [7–9]. In particular, gas chromatography quadrupole time-of-flight mass spectrometry (GC-QTOF/MS) has become an effective tool for the quantitative and high-throughput screening of targeted and non-targeted trace-level compounds in complex matrix samples. Thus, this technique has been employed by various researchers for the screening and quantification of pesticide residues in various food matrices [10–13]. However, only a few studies have reported the screening and quantification of multiclass pesticides in tobacco.

Because tobacco is a complex matrix and has high contents of pigments, terpenes, alkaloids, and flavonoids [4], a pretreatment step is required before detection to improve the sensitivity and specificity of the detection method. The pretreatment techniques that have been mainly used in the past decades are QuEChERS (Quick Easy Cheap Effective Rugged Safe) and SPE (Solid Phase Extraction) [4,14–17]. The QuEChERS method is quick, easy, inexpensive, effective, robust, and safe and can be used for the analysis of a large number of samples. However, this method has limited ability to eliminate matrix interferences, thus resulting in contamination. In contrast, SPE has remarkable cleanup efficiency, with higher accuracy and precision; however, this method requires multiple steps, making it a time-consuming, complex, and relatively expensive pretreatment method. Simple extraction methods have been gaining attention recently, among which mini-SPE is more effective owing to its simplicity, high extraction rate, and low consumption of organic solvents. This method has already been used as a pretreatment technique in the analysis of multi-pesticide residues in complex food matrices and spices [18,19]. However, mini-SPE has not yet been applied for the pretreatment of pesticide residues in tobacco. In this study, several important parameters affecting the performance of mini-SPE were optimized. In addition, the chromatograms of the tobacco extract cleaned up by mini-SPE and QuEChERS were compared to determine the cleanup efficiency of mini-SPE. Finally, a method for the screening and quantification of 209 pesticides in tobacco was developed using GC-QTOF/MS coupled with mini-SPE.

2. Material and Methods

2.1. Reagents and Materials

HPLC-grade ethyl acetate (cas: 141-78-6), acetic acid (cas: 64-19-7), acetonitrile (cas: 75-05-8), acetone (cas: 67-64-1), and *n*-hexane (cas: 110-54-3) were purchased from ANPEL Laboratory Technologies Inc. (Shanghai, China). All pesticide reference standards (purity $\geq$ 95%) were obtained from Dr. Ehrenstorfer GmbH (Dr. Ehrenstorfer GmbH, Augsburg, Germany) and the Agro-Environmental Protection Institute, Ministry of Agriculture (Tianjin, China). The CAS numbers of all the pesticides are detailed in Figure S1 in Supplementary Materials. The mini-SPE column was purchased from Agela Technologies, Inc. (Tianjin, China). A schematic diagram of the mini-SPE apparatus is shown in Figure 1.

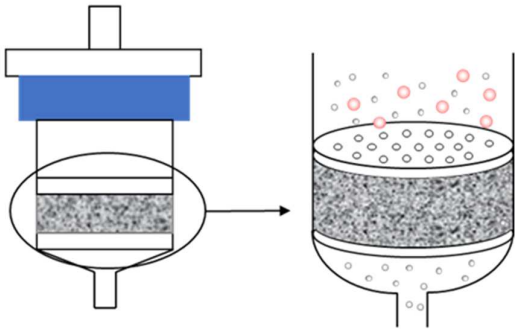

Figure 1. Schematic diagram of the mini-SPE.

2.2. Standard Solution Preparation

Primary stock solutions of each pesticide (1000 μg/mL) and the Mirex internal standard solution (5 μg/mL) were prepared in an *n*-hexane–acetone mixture (1:1, *v*/*v*). Based on the chemical properties and retention times of each pesticide, the 209 pesticides were divided into four groups: I, II, III, and IV. Stock solutions of mixed pesticide standards (1 μg/mL) were also prepared in the same *n*-hexane–acetone mixture (1:1, *v*/*v*). The matrix-matched standards (0.01,0.05, 0.1,0.2,0.5, and 0.8 μg/mL) were prepared by diluting the mixed standards of each analyte with a blank matrix extract solution and a Mirex internal standard solution. All solutions were stored at −20 °C in a refrigerator.

2.3. Sample Preparation

A tobacco sample (1 g) was weighed into a centrifuge tube (50 mL), to which a Mirex internal standard solution (100 μL) and an acetonitrile-0.1% acetic acid solution (10 mL) were added. The centrifuge tube was vortexed at 2000 rpm for 10 min, and then centrifuged at 4000 rpm for 10 min. A 2 mL syringe was used for the mini-SPE column. The supernatant (1 mL) was loaded in the syringe and then slowly released. The effluent was then collected in a 2 mL centrifuge tube, concentrated using a vacuum concentrator at 45 °C, and finally reconstituted in *n*-hexane/acetone mixture (0.5 mL; 1:1, *v*/*v*). After vortexing for 30 s, the reconstituted solution was filtered through a 0.22-μm Nylon membrane prior to GC-QTOF/MS.

To verify the purification efficiency of mini-SPE, the National Standard of the People's Republic of China for the determination of pesticides and metabolites in foods of plant origin, published in 2018, was used for tobacco sample pretreatment. The extraction and cleanup procedures are described in detail in Figure S2 in Supplementary Materials.

2.4. GC-QTOF/MS

In this study, an Agilent 7890B GC system coupled to an Agilent 7200 Q-TOF mass spectrometer (Santa Clara, CA, USA) was used. Two HP-5MS capillary columns (15 m × 250 μm × 0.25 μm; Santa Clara, CA, USA) were connected by a backflush system, which was used at 40.5 min under 50 psi. The oven temperature program was as follows: initial temperature of 60 °C (1 min), increased to 120 °C at 40 °C /min, then to 310 °C at 5 °C /min, and then held for 5 min at 310 °C. The injection volume was 1.0 μL in the splitless mode. The inlet temperature was set to 250 °C. Helium (purity: 99.999%) was used as the carrier gas at a flow rate of 1 mL/min. To correct the retention time drift caused by the change in chromatographic column efficiency, Mirex was used for retention time locking.

Q-TOF/MS was operated in the EI mode with an electron energy of 70 eV. The high-resolution mode of 4 GHz (12000 FWHM), at which the TOF-MS system operates in the full-scan mode (m/z 50–500) at a rate of 5 spectra/s, allows more accurate analyte identification. Internal mass calibration with perfluorotributylamine (PFTBA) was performed before each injection to achieve a precise high-resolution and accurate mass operation. The temperatures of the transfer line, quadrupole, and ion source were maintained at 280 °C, 180 °C, and 230 °C, respectively. The analysis was performed with a solvent delay of 4 min to prevent damage to the filament. Data analysis was performed using Agilent MassHunter Version B.07.06. A mass spectrometry database was created using the Personal Compound Database and Library (PCDL) Manager (Version B.07.00, Agilent, Santa Clara, CA, USA). MassHunter Qualitative Analysis Workflow software (version B.08.00, Agilent, Santa Clara, CA, USA) was used to screen non-targeted pesticides based on a created accurate-mass spectrometry library. Agilent MassHunter quantitative analysis version (version B.09.00, Agilent, Santa Clara, CA, USA) was used for the quantitative determination of the targeted pesticides.

2.5. Experimental Design

Based on our previous single-factor experimental results, three important factors (water volume (A), solvent volume (B), and purification volume (C)) affecting the target pesticide recovery were studied using the Box-Behnken test design with the Design-Expert software (Table 1, version 13, Stat-Ease, Minneapolis, MN, USA).

Table 1. Factors and codes of the sample preparation procedure by the Box-Behnken design.

Factor	Code	Coding Level		
		−1	**0**	**1**
Water volume (mL)	A	0	2	4
Solvent volume (mL)	B	5	10	15
Purification volume (mL)	C	0.8	1.2	1.6

2.6. Analytical Parameters

The proposed method was validated in terms of recovery, linearity, limit of detection (LOD), limit of quantification (LOQ), and precision (coefficient of variation (CV)). The linearity of the method was determined using the matrix-matched standards (10, 50, 100, 200, 500, and 800 ng/mL). Residue-free tobacco samples were added to 50, 250, and 500 ng/g mixed standard stock solutions using three replicates to calculate the average recovery and CV of each pesticide. The LODs and LOQs of the method were calculated at signal-to-noise ratios (S/N) of 3 and 10, respectively.

3. Results and Discussion

3.1. Optimization of Extraction Conditions

The pesticides investigated in this study include organochlorines, organophosphorus, and carbamates, which have large differences in solubility and polarity. Therefore, a solvent with high solubility is needed for a more efficient extraction of the pesticides. To achieve high-efficiency extraction, the amount of matrix compounds co-extracted from the complex tobacco matrix should be as low as possible. According to literature, *n*-hexane–acetone mixture, ethyl acetate, acetonitrile, and acetonitrile–0.1% acetic acid are the most commonly used extraction solvents [20–23]. In this study, the effects of these four solvents on the 209 pesticide residues in tobacco were investigated; the recovery ranges of the target pesticides obtained upon extraction by these solvents are shown in Figure 2. The results showed that when acetonitrile–0.1% acetic acid was used as the extraction solvent, the proportion of pesticides with recoveries in the range of 60–120% was the largest. Moreover, as shown in Figure 3, the use of acetonitrile–0.1% acetic acid as the extraction solvent resulted in significant improvement in the recovery of some carbamates and organophosphorus pesticides with strong polarity, such as mevinphos, disulfoton, and methiocarb and a drift in the retention time was observed. This result was in accordance with that of a previous study [24]. Thus, acetonitrile–0.1% acetic acid was chosen as the optimal extraction solvent.

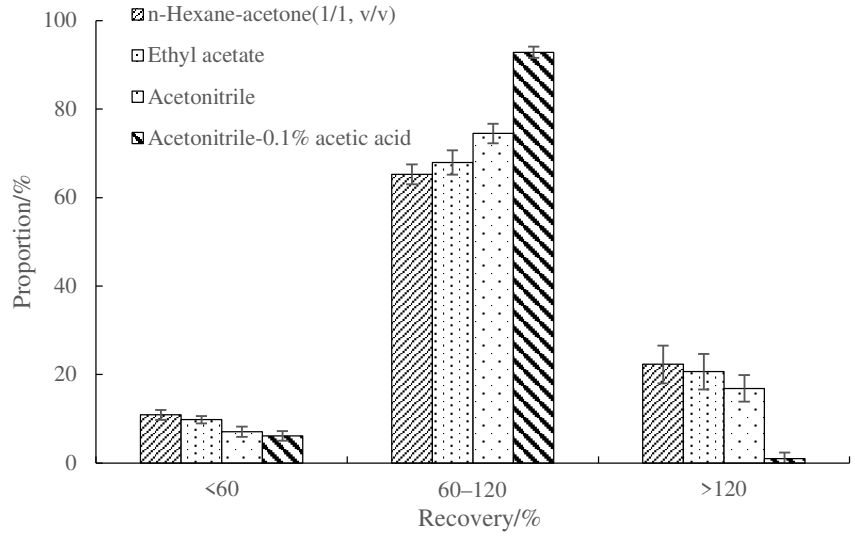

Figure 2. Recovery ranges of pesticides extracted by different solvents.

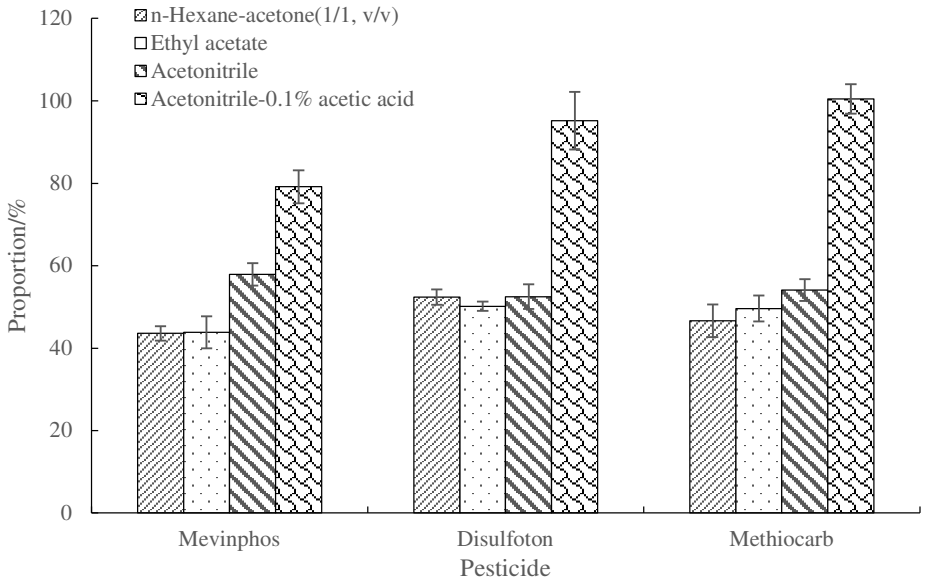

Figure 3. Recovery of three pesticides extracted by different solvents.

3.2. Optimization of Sample Preparation Conditions

According to the analysis of the response surface experimental data using the Design-Expert software, the regression equation indicating the relation of the proportion (Y) of the target pesticide, with a recovery in the range of 60%–120%, with various factors can be expressed by Equation (1):

$$Y = 77.14 - 15.82A - 2.93B - 3.19C - 2.3AB + 1.28AC - 3.06BC + 0.71A^2 - 9.75B^2 - 8.21C^2 \quad (1)$$

The results of ANOVA analysis indicate that the model was extremely significant ($p = 0.0012 < 0.01$), with an insignificant lack of fit ($p = 0.0981 > 0.05$), indicating that the regression equation and actual fitting had a small proportion of abnormal errors. The regression coefficient (R^2) value (0.9451) indicated a good model correlation. The coefficient of variation (7.15%) indicated high experimental stability. Within the selected range of factors, the *p*-values of A, B^2, and C^2 were <0.05, indicating that all factors had a significant impact on the pesticide recovery. Three-dimensional response surface plots of the predicted mode are shown in Figures 4–6.

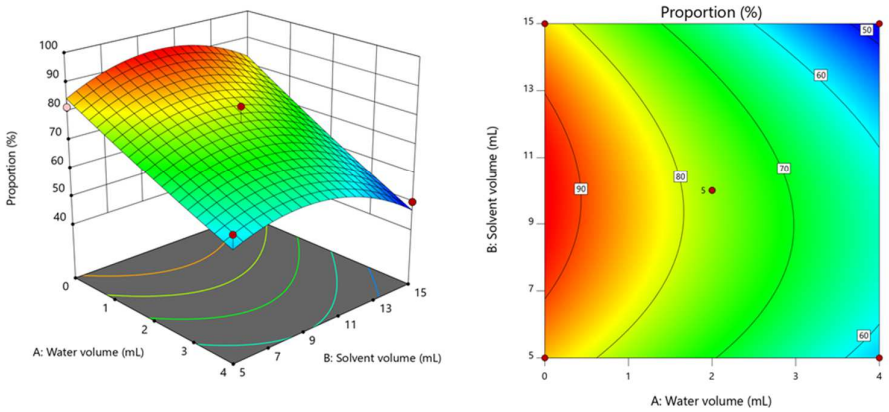

Figure 4. Response surface and contour diagram of R = f (A, B) with a 1.2 mL purification volume.

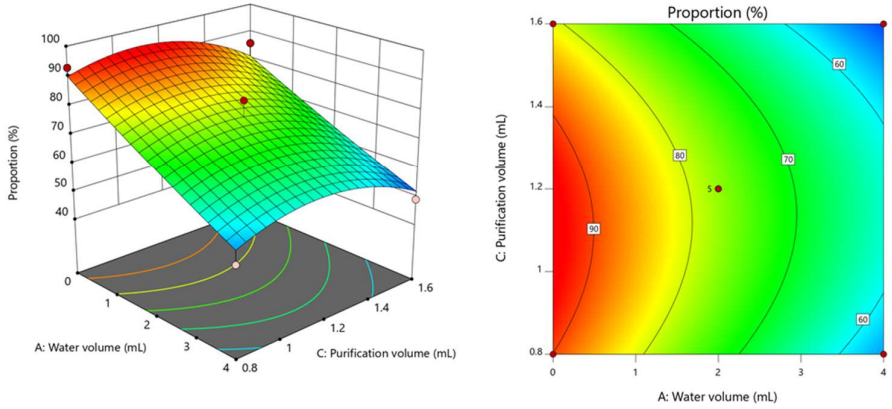

Figure 5. Response surface and contour diagram of R = f (A, C) with a 10 mL solvent volume.

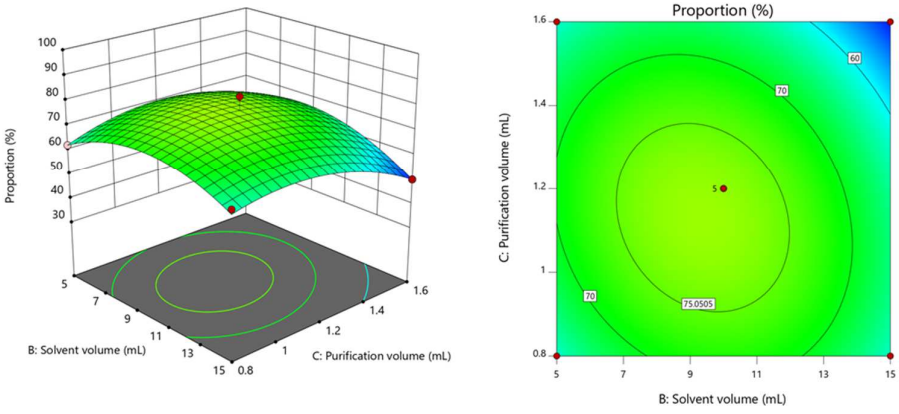

Figure 6. Response surface and contour diagram of R = f (B, C) with a 2 mL water volume.

3.3. Matrix Effects

The nature of the pesticide matrix affects the accuracy and repeatability of the results of GC-MS, and most pesticides exhibit different levels of matrix enhancement. In fact, during sample detection, impurities in the sample can compete with pesticide molecules for the active sites in the mass spectrometer inlet and column head, resulting in an increase of the target molecules. Therefore, the response of analytes with the same content in the matrix solution becomes higher than that in the pure solvent [25,26]. The matrix effect is closely related to the chemical structure and properties of analytes. Generally, the thermal instability, polarity, and hydrogen bonding ability of pesticides have a strong matrix effect in GC. In our previous work, the peak areas of the target pesticides in pure solvents and

matrix solutions were compared at the same concentration, and most pesticides were found to exhibit matrix enhancement effects [5]. Therefore, matrix-matched calibration curves were chosen to nullify the matrix effect.

3.4. Screening Method

Under optimized chromatographic and mass spectrometric conditions, high-resolution mass spectrograms of the 209 pesticides were collected in the full-scan mode and imported to the PCDL software. The name, retention time, molecular formula, accurate mass, CAS number, and structural formula were imported to the PCDL software to establish an accurate mass spectrometry library. In the Agilent MassHunter Qualitative Analysis Workflow software, the homebuilt library was selected, and the search parameters were set as follows: retention time deviation, ±0.15 min; accurate mass deviation, ±20 ppm; minimum qualified fragment number, 2; co-elution matching score, s ±20 ppm. The minimum number of qualified fragment ions measured for each compound and the theoretical value in the library based on the retention time, accurate mass deviation, isotope peak distribution, and abundance ratio were calculated, and a matching score was assigned. Further, the ratio of qualitative and quantitative ions is an important parameter to judge the existence of false positives. The default matching score of qualitative and quantitative ion ratio in the workflow software was ≥75. Therefore, although the co-elution matching score was ≥70, the matching score of qualitative and quantitative ion ratio was <75. The software will provide a warning, indicating the possibility of a false positive. At this point, manual verification is necessary.

The screening method was validated using blank samples spiked with 50, 100, and 500 ng/g pesticides. The screening was performed as described above, and the proportion of pesticides screened at the three concentrations was calculated. The results showed that the proportion of pesticides detected by the workflow software was 76.6%, 94.7%, and 99.0% at the three concentrations, respectively, under the proposed screening parameters. The screening limit of this method was higher than that reported in other studies [27,28], mainly because of the difference between the evaluation method and the pretreatment process. In these studies, a blank matrix matching a mixed standard solution was used for direct injection when the screening limit was evaluated. In this work, the blank samples were spiked with different concentrations of pesticide-mixed standard solutions, and then extracted and purified using the above-mentioned method. This was in accordance with the test requirements for real samples. Owing to the large dilution ratio in the pretreatment process, the final sample concentration detected in the test solution was 0.2 g/mL. During sample analysis, the screening ability of the method can be improved by increasing the concentration ratio.

3.5. Comparison of Cleanup Efficiency of Mini-SPE and d-SPE

The total ion chromatography (TIC) chromatograms of the tobacco extracts obtained by mini-SPE (black) and dispersed-SPE (d-SPE; red) are shown in Figure 7. The mini-SPE-treated sample showed a lower TIC chromatographic baseline, indicating the stronger ability of mini-SPE to remove impurity interferences, especially alkaloids such as nicotine, nicotyrine, and (*R*,*S*)-anatabine. In addition, the ability of mini-SPE to remove megastigmatrienone-I, II, III, and IV, which are important aroma components in tobacco, was stronger, with only a small amount of megastigmatrienones present in the solution after extraction. The two purification methods showed similar abilities for the removal of 4,8,13-duvatriene-1,3-diol, a major glandular trichome secreted by tobacco. In general, mini-SPE can effectively clean up alkaloids, aroma components, and pigments. Moreover, mini-SPE requires few steps and is simple, making it an excellent pretreatment method for rapid detection.

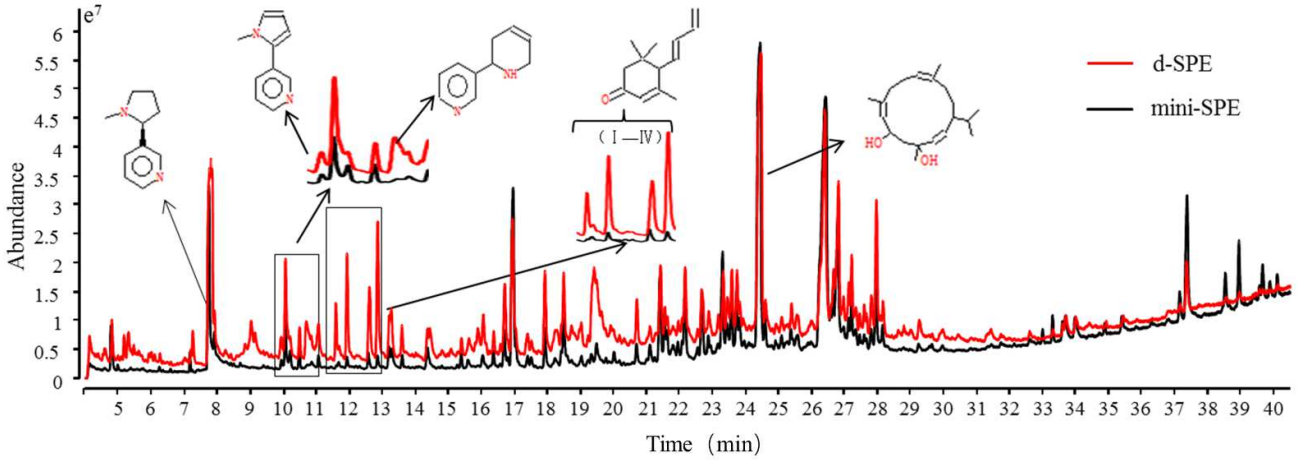

Figure 7. Total ion current (TIC) chromatogram of blank tobacco extract extracted with mini-SPE (black) and with d-SPE (red) method.

3.6. Analytical Parameters of Quantitative Method

The linear regression coefficients (r^2), LOD, LOQ, recovery, and CV values of the 209 pesticides are listed in Table A1 in the Appendix A. The r^2 were higher than 0.995 in the linearity range of 10–800 ng/mL for all the 209 pesticides tested. The LODs for all analyses ranged from 0.05 to 29.8 ng/g, while the LOQs were in the range of 0.2–98.9 ng/g. At spiking levels of 50, 250, and 500 ng/g, the recoveries of the pesticides were 64.2%–122.1%, 66.8%–124.0%, and 63.8%–127.7%, respectively, except for 1,2-dibromo-3-chloropropane, naled, and hexachlorobenzene; the CVs were 0.3%–15.5%, 0.1%–14.3%, and 0.28%–11.9%, respectively. 1,2-Dibromo-3-chloropropane and naled are very unstable and are easily decomposed upon heating [29,30], while other pesticides can decompose in the GC system during the injection process, resulting in a lower recovery of the two pesticides. The recovery of hexachlorobenzene was also very low, which can be attributed to its planar structure, similar to that of the purification material.

3.7. Real Sample Analysis

To demonstrate the applicability of the developed and validated method for the analysis of real samples, seven tobacco samples obtained from three main planting regions in China were analyzed for their pesticide residues. Tobacco samples were prepared according to the method described in Section 2.3. sample preparations, and determined in full scan mode by GC-Q-TOF. Then the screening method was applied to screen the pesticides. There were 12 output results with a screening score greater than 70, involving 7 pesticides, and the qualitative and quantitative ion ratios of all output results were greater than 75. Only 2 of the 7 samples did not detect pesticide residues. Seven pesticides were metalaxyl, triadimefon, triadimenol, dimetachlone, myclobutanil, flumetralin, and cyhalothrin, which are classified as fungicides and insecticides. The detected pesticides were quantified using matrix-matched calibration standards, all of which were below the GRLs set by CORESTA. The results obtained by the proposed method were compared with those obtained by the GC-MS/MS method used in our laboratory [5]. The CV values of the quantitative results obtained using the two methods ranged between 5% and 13.35%.

4. Conclusions

In this study, a simple and rapid sample-preparation method coupled with GC-Q/TOF technique was developed for the screening and quantification of 209 pesticides in tobacco. When this method was evaluated on 209 pesticides in tobacco, 192 of them showed satisfactory recovery and precision at the spiked levels of 50, 250, and 500 ng/g. In the process of sample pretreatment, mini-SPE technology was used to purify tobacco samples for the first time. Compared with the traditional SPE, the samples in mini-SPE can be loaded

and eluted directly, without any activation/equilibration, cleaning, or elution step, which greatly reduced the sample pretreatment time and the amount of organic solvent. Mini-SPE requires few steps, making it an excellent pretreatment method for rapid detection. Moreover, mini-SPE also exhibits good cleanup efficiency, the comparative test showed that mini SPE had stronger ability to remove the pigments and alkaloids than d-SPE. Furthermore, this method was found to be applicable for the analysis of real samples, demonstrating its suitability for sensitive and rapid screening of pesticide residues. The developed method provided accurate and reliable quantitative screening results, was simple and fast, and could be used for the analysis of multiclass pesticide residues in tobacco.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/separations9050104/s1, Figure S1: CAS number, retention time of the 209 pesticides; Figure S2: Sample preparation of d-SPE.

Author Contributions: Conceptualization, Y.W. and J.C.; methodology, R.B. and J.C.; validation, J.Z. and R.Y.; formal analysis, J.C. and J.Z.; investigation, D.J.; data curation, B.J. and R.Y.; writing—original draft preparation, R.B. and J.Z.; writing—review and editing, R.B., J.Z. and J.C. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. The r^2, LOD, LOQ, recovery, and CV values of the 209 pesticides.

Pesticides	r^2	LOD (ng/g)	LOQ (ng/g)	Spiked at 50 ng/g		Spiked at 250 ng/g		Spiked at 500 ng/g	
				Recovery (%)	CV (%)	Recovery (%)	CV (%)	Recovery (%)	CV (%)
1,2-Dibromo-3-chloropropane	0.997	4.5	14.8	40.3	3.6	49.6	5.7	49.3	9.6
Dichlorvos	0.997	4.4	14.6	100.4	7.1	72.7	3.7	80.4	11.8
Disulfoton sulfoxide	0.999	1.4	4.5	96.2	7.0	106.2	1.2	104.3	3.8
Mevinphos(E)	0.999	4.9	16.1	83.3	8.9	75.3	3.0	78.9	9.2
Butylate	0.998	2.2	7.2	71.4	5.4	107.0	7.0	117.1	6.5
Mevinphos(Z)	0.998	6.2	20.6	109.2	2.8	74.9	2.9	77.3	7.6
Pebulate	0.995	8.3	27.2	96.8	10.2	109.8	2.2	111.1	2.1
Methacrifos	0.997	3.3	11.0	110.2	8.9	114.0	3.6	106.3	2.1
Molinate	0.998	3.8	12.7	90.5	3.0	82.0	1.6	107.2	5.1
Isoprocarb	0.998	10.6	35.1	83.0	6.4	80.0	6.3	100.2	8.9
Heptenophos	0.998	3.2	10.4	100.7	10.1	110.1	2.8	120.7	7.6
Chlorphenprop-methyl	0.997	7.1	23.4	91.2	15.5	82.4	6.1	88.6	6.6
Thionazin	0.997	8.1	26.7	95.9	10.6	110.8	9.4	110.9	7.4
Fenobucarb	0.998	4.4	14.5	79.9	11.5	78.6	4.4	101.4	6.8
Propoxur	0.998	3.0	9.9	91.5	12.5	81.8	4.4	113.4	0.3
Demeton-O	0.998	7.2	23.9	88.6	3.8	100.5	4.5	98.2	3.4
Demeton-S-methyl	0.999	9.7	31.9	77.9	9.5	108.1	7.0	89.1	3.8
Cycloate	0.997	2.7	8.9	116.2	3.1	111.9	11.3	108.7	1.3
Ethoprophos	0.999	4.6	15.3	104.5	7.8	119.8	0.7	122.3	3.2
Chlorpropham	0.996	7.5	24.8	70.7	0.3	88.1	12.3	86.4	9.4
Naled	0.996	7.1	23.3	43.8	12.5	50.2	6.4	52.4	5.3
Chlordimeform	0.999	9.5	31.4	73.4	1.5	78.1	6.5	75.3	4.0
Trifluralin	0.995	0.8	2.7	102.6	11.5	121.2	6.1	126.3	9.7
Benfluralin	0.995	1.3	4.3	82.6	6.5	95.8	4.8	111.5	4.5
Cadusafos	0.999	1.5	5.0	99.2	5.4	116.8	3.3	117.6	1.5
Phorate	0.995	0.5	1.6	107.3	8.0	106.6	10.6	106.5	7.7
BHC-alpha	0.998	2.0	6.5	91.4	7.8	115.5	5.0	109.5	7.8
Hexachlorobenzene	0.996	0.3	0.9	27.5	13.6	35.4	5.6	46.5	1.0
Dicloran	0.999	11.2	37.0	73.2	5.5	86.5	4.2	80.5	0.7
Demeton-S	0.999	10.4	34.2	87.4	8.0	88.3	2.1	113.5	7.7
Dimethoate	0.998	9.2	30.5	71.4	4.7	81.4	10.8	76.2	6.9
Carbofuran	0.996	8.4	27.8	99.9	9.9	101.1	5.5	105.5	5.3

Table A1. *Cont.*

Pesticides	r^2	LOD (ng/g)	LOQ (ng/g)	Spiked at 50 ng/g		Spiked at 250 ng/g		Spiked at 500 ng/g	
				Recovery (%)	CV (%)	Recovery (%)	CV (%)	Recovery (%)	CV (%)
Atrazine	0.996	1.7	5.6	87.4	10.8	83.4	2.8	91.2	5.7
BHC-beta	0.999	1.3	4.1	74.1	8.0	95.0	10.2	97.6	6.2
Clomazone	0.998	2.0	6.5	119.2	5.2	114.6	3.7	114.5	4.7
Propazine	0.998	11.6	38.3	94.4	2.4	83.9	9.1	93.9	3.6
Terbumeton	0.996	8.0	26.3	77.7	5.1	78.2	4.4	84.1	3.6
BHC-gamma	0.998	1.3	4.4	104.3	11.8	112.6	11.1	110.1	3.9
Quintozene	0.999	0.1	0.3	71.6	8.1	110.2	7.2	98.0	3.9
Terbufos	0.997	4.5	14.7	99.3	3.4	107.2	2.2	124.8	4.4
Trietazine	0.998	5.5	18.3	73.3	3.2	76.9	3.9	85.7	2.1
Fonofos	0.998	6.7	22.1	110.1	5.6	112.4	2.4	116.8	0.6
Phosphamidon(E)	0.998	11.8	38.8	85.9	6.3	113.2	3.3	97.3	3.3
Diazinon	0.999	5.8	19.1	116.6	9.9	107.1	3.3	110.6	4.0
Disulfoton	0.999	7.5	24.9	102.5	5.5	88.5	6.4	94.6	6.7
BHC-delta	0.995	13.7	45.2	111.1	7.8	103.3	12.1	112.0	5.1
Mexacarbate	0.996	4.3	14.3	94.4	5.5	96.2	4.9	114.2	8.9
Triallate	0.997	1.8	5.8	88.4	5.8	117.1	3.4	116.2	4.1
Tefluthrin	0.996	3.1	10.1	116.5	1.2	116.9	1.5	127.7	3.0
Isazofos	0.997	3.1	10.3	103.3	12.4	115.2	1.6	119.8	4.6
3-Hydroxycarbofuran	0.995	7.7	25.3	108.2	4.9	107.8	1.8	118.9	7.7
Iprobenfos	0.998	3.2	10.6	104.2	5.1	121.3	3.3	124.7	6.0
Pirimicarb	0.998	2.1	6.9	93.1	2.3	108.3	2.6	116.5	1.4
Benfuresate	0.998	4.0	13.3	90.5	8.4	79.5	8.8	85.7	5.1
Phosphamidon(Z)	0.999	6.4	21.2	101.9	3.7	78.3	3.3	76.7	1.3
Propanil	0.997	7.9	26.2	86.6	5.6	76.1	7.6	87.4	8.1
Dimethachlor	0.996	9.2	30.4	76.5	8.1	78.8	6.4	84.9	5.1
Acetochlor	0.998	19.0	62.8	93.8	7.4	110.1	4.9	99.6	2.6
Parathion-methyl	0.996	5.4	18.0	110.2	5.0	99.5	7.3	78.5	1.4
Chlorpyrifos-methyl	0.998	3.6	11.7	94.8	7.2	88.0	2.1	97.9	4.9
Vinclozolin	0.999	6.5	21.4	99.8	6.7	106.0	11.4	91.0	2.6
Simetryn	0.998	14.1	46.4	104.1	11.9	70.0	2.7	72.4	3.2
Carbaryl	0.996	14.5	47.7	73.2	3.5	77.2	2.8	107.4	9.8
Tolclofos-methyl	0.998	6.3	20.9	103.5	7.0	110.9	1.5	113.1	4.2
Heptachlor	0.999	0.4	1.4	104.7	4.7	111.0	7.5	102.2	1.6
Alachlor	0.999	4.3	14.3	100.2	1.0	97.7	8.8	104.5	3.7
Prometryn	0.999	8.4	27.7	121.7	9.3	106.0	4.4	103.1	5.4
Metalaxyl	0.996	3.9	12.8	105.8	8.1	93.7	6.4	116.0	7.3
Fenchlorphos	0.999	6.2	20.4	100.7	6.4	105.3	4.4	117.5	1.6
Prosulfocarb	0.997	5.6	18.3	91.6	6.1	72.3	0.1	104.8	5.1
Demeton-S-methylsulfone	0.996	14.5	47.9	76.4	8.0	85.7	0.8	87.7	1.6
Thiobencarb	0.998	6.7	22.2	98.1	7.6	86.2	9.4	100.4	3.3
Orbencarb	0.998	7.2	23.9	118.0	0.3	92.8	11.6	105.2	5.2
Methiocarb	0.996	2.9	9.5	95.8	7.1	98.1	7.4	104.6	8.8
Fenitrothion	0.998	11.0	36.4	113.7	11.3	113.9	12.8	110.7	3.6
Pentanochlor	0.998	8.0	26.4	100.7	3.7	74.5	2.3	101.3	4.1
Pirimiphos-methyl	0.999	14.5	47.8	108.2	12.0	114.4	3.0	113.2	3.8
Bromacil	0.999	2.3	7.6	88.4	11.8	110.9	12.2	105.1	6.1
Ethofumesate	0.997	8.3	27.5	85.5	1.4	86.0	6.3	88.6	5.3
Aldrin	0.999	6.5	21.6	113.2	1.0	110.8	1.8	107.1	4.4
Malathion	0.998	10.5	34.5	105.6	10.2	109.1	11.5	108.9	7.6
Phorate-sulfone	0.995	8.9	29.5	113.3	5.2	104.2	8.9	124.2	1.5
Metolachlor	0.999	5.4	17.8	107.6	4.2	112.1	1.5	111.4	4.7
Fenthion	0.999	3.9	12.7	99.4	8.6	108.7	8.7	114.8	2.7
Dicofol	0.997	20.3	67.1	94.8	3.1	103.5	0.3	113.1	3.9
Parathion	0.996	7.5	24.9	79.9	3.7	83.9	4.3	99.1	2.5
Thiazopyr	0.998	0.1	0.2	73.8	8.2	100.4	5.4	109.7	8.0
Chlorpyrifos	0.997	4.8	15.7	106.6	9.0	113.0	10.5	120.1	2.6
Triadimefon	0.996	9.6	31.7	105.7	7.9	122.3	2.9	120.6	6.0
Chlorthal-dimethyl	0.999	1.7	5.6	116.3	5.8	108.2	2.2	107.2	1.8
Flufenacet	0.998	9.8	32.3	106.4	9.9	111.1	2.2	108.3	7.5
Dimetachlone	0.999	5.0	16.4	117.7	7.7	82.1	3.8	103.6	5.8
Isocarbophos	0.998	4.4	14.4	118.5	1.1	104.3	6.0	105.1	8.3
Thiamethoxam	0.998	4.8	15.8	108.1	5.9	78.4	12.6	79.8	7.4
Bromophos	0.999	3.1	10.4	116.3	5.4	98.8	7.8	106.3	4.4
Butralin	0.996	2.9	9.6	109.0	5.7	96.7	10.4	103.8	4.2
Diphenamid	0.997	9.0	29.6	115.1	4.2	92.6	8.1	86.3	6.2
Isopropalin	0.995	8.1	26.7	70.0	5.6	78.4	9.1	71.0	4.9
Oxychlordane	0.999	1.8	5.8	103.0	11.5	88.3	5.9	90.9	4.2

Table A1. *Cont.*

Pesticides	r^2	LOD (ng/g)	LOQ (ng/g)	Spiked at 50 ng/g		Spiked at 250 ng/g		Spiked at 500 ng/g	
				Recovery (%)	CV (%)	Recovery (%)	CV (%)	Recovery (%)	CV (%)
trans-Chlorfenvinphos	0.996	2.3	7.7	87.3	11.3	105.0	3.6	99.4	7.9
Heptachlor epoxides (cis-)	0.997	3.6	11.7	106.9	8.4	111.8	11.1	98.7	5.2
Terbufos sulfone	0.997	2.6	8.4	91.9	4.6	114.5	7.0	123.3	1.8
Pendimethalin	0.995	9.6	31.6	105.7	3.4	123.0	3.5	118.1	1.8
Penconazole	0.999	10.0	33.1	114.5	2.2	101.8	4.7	101.1	3.5
Heptachlor epoxides (trans-)	0.998	5.5	18.3	110.8	1.4	98.5	3.1	82.3	6.5
Captan	0.998	10.9	36.1	80.3	6.6	74.5	5.4	86.9	2.0
cis-Chlorfenvinphos	0.998	5.6	18.5	114.3	4.1	117.4	3.3	119.7	0.4
Isofenphos	0.995	5.8	19.2	97.9	7.9	113.6	3.6	118.6	3.8
Quinalphos	0.999	3.3	11.0	88.4	9.3	102.4	3.8	106.4	6.2
Triadimenol	0.997	5.6	18.6	97.1	13.1	105.6	5.9	107.3	5.3
Phenthoate	0.996	7.4	24.3	81.8	8.1	101.7	14.0	109.8	2.4
Folpet	0.999	5.8	19.1	67.6	8.6	68.8	0.8	117.6	1.7
Methoprene	0.995	9.3	30.6	98.5	4.8	109.1	8.1	108.9	6.8
Chlordane-trans	0.998	2.0	6.5	83.5	7.0	115.7	5.9	116.4	2.6
Methidathion	0.995	8.3	27.4	109.8	13.0	124.0	6.5	119.6	1.1
o,p′-DDE	0.995	2.3	7.6	92.0	1.6	109.5	4.4	117.4	1.2
Haloxyfop-methyl	0.996	6.7	22.2	102.2	6.2	106.9	2.9	106.8	10.9
alpha-Endosulfan	0.997	4.6	15.0	83.3	6.1	119.5	1.7	109.6	3.9
Disulfoton-sulfone	0.997	9.3	30.8	118.3	6.5	110.7	10.1	115.2	2.3
Tetrachlorvinphos	0.998	4.3	14.3	90.7	12.5	109.1	9.2	103.6	8.2
Chlordane-cis	0.997	1.6	5.3	74.3	11.3	66.8	3.4	100.6	8.3
Mepanipyrim	0.999	7.9	25.9	68.0	6.5	75.5	0.4	103.9	8.8
Butachlor	0.999	10.2	33.5	109.0	6.5	108.8	5.8	115.1	6.9
Flumetralin	0.999	2.7	8.9	94.7	4.7	109.5	5.6	118.9	1.4
Napropamide	0.999	2.8	9.3	115.3	1.4	108.5	10.6	111.1	6.2
Fenamiphos	0.999	20.9	68.9	92.8	10.4	104.9	10.2	119.9	3.2
Butamifos	0.997	8.1	26.7	101.0	8.2	101.8	9.8	104.5	8.9
Hexaconazole	0.998	1.2	4.0	117.7	4.1	104.9	12.2	112.3	7.2
Imazalil	0.999	14.4	47.5	70.8	6.0	79.2	0.5	87.9	6.7
Prothiofos	0.999	3.5	11.6	102.4	2.1	96.7	8.8	122.3	2.1
Isoprothiolane	0.996	7.5	24.7	76.4	6.3	102.1	11.6	112.2	2.0
Profenofos	0.998	5.2	17.1	83.7	5.9	94.3	10.4	119.2	5.1
Dieldrin	0.998	5.9	19.5	74.8	9.0	100.2	8.0	88.4	8.1
p,p′-DDE	0.999	1.3	4.3	122.1	2.3	111.4	7.8	110.8	6.2
Uniconazole-P	0.997	0.4	1.4	104.8	10.8	93.2	6.6	88.1	6.2
Pretilachlor	0.999	0.8	2.6	98.1	2.3	108.4	0.5	105.5	6.1
Tribufos	0.999	7.4	24.4	116.9	8.5	110.6	10.1	114.1	3.9
Oxadiazon	0.997	9.3	30.5	92.8	7.6	94.2	6.5	101.5	3.3
o,p′-DDD	0.998	1.0	3.1	111.0	4.7	112.6	3.2	115.7	3.1
Myclobutanil	0.996	16.4	54.2	86.9	9.5	81.7	12.4	105.7	3.4
Flamprop-methyl	0.998	2.2	7.4	88.7	4.9	89.5	2.9	92.8	4.2
Buprofezin	0.995	11.3	37.2	80.3	5.4	94.4	6.5	101.5	8.4
Oxyfluorfen	0.998	5.0	16.5	76.4	5.0	102.4	9.9	112.4	4.0
Bupirimate	0.999	11.2	37.1	111.4	7.1	109.2	1.6	110.3	4.7
Thifluzamide	0.999	1.4	4.7	94.3	1.4	113.7	8.3	110.1	1.8
Kresoxim-methyl	0.997	6.9	22.7	82.8	9.1	99.3	7.3	99.5	3.8
Nitrofen	0.998	8.7	28.6	87.1	10.3	98.6	4.4	83.1	5.4
Endrin	0.999	4.8	15.9	90.6	6.2	97.5	8.9	103.3	0.5
Isoxathion	0.999	14.7	48.4	85.1	6.5	77.3	4.4	114.8	9.6
Fluazifop-butyl	0.997	8.0	26.6	67.1	2.7	94.7	10.4	73.2	1.8
beta-Endosulfan	0.999	18.1	59.6	115.9	2.8	96.4	3.5	63.8	6.7
Chlorobenzilate	0.999	7.4	24.4	107.9	10.2	107.5	7.4	106.8	9.2
Fensulfothion	0.999	2.4	7.9	108.3	8.1	77.6	6.6	104.1	2.6
Fenthion sulfoxide	0.998	13.6	44.7	96.3	10.3	107.1	4.6	111.5	2.5
Aclonifen	0.997	1.2	4.0	86.6	9.4	111.3	8.9	99.4	7.1
p,p′-DDD	0.999	2.4	8.0	105.0	2.5	99.9	2.3	104.9	8.2
Fenthion sulfone	0.998	12.8	42.2	86.3	11.4	117.3	10.2	96.3	9.4
o,p′-DDT	0.999	1.0	3.2	104.9	8.0	114.7	3.3	100.1	4.8
Oxadixyl	0.999	12.5	41.2	71.3	0.9	68.3	3.7	70.0	0.4
Ethion	0.997	5.2	17.2	120.8	3.7	119.3	1.1	116.2	4.6
Chlorthiophos	0.996	4.9	16.2	93.4	4.6	108.0	1.2	113.0	5.9
Triazophos	0.997	21.3	70.2	89.4	1.5	99.8	9.8	120.0	4.2
Carbophenothion	0.997	2.8	9.1	94.0	1.1	110.5	11.6	114.8	3.4
Benalaxyl	0.999	6.8	22.3	95.5	4.9	102.1	6.0	106.1	5.6
Endosulfan sulfate	0.998	1.1	3.7	98.3	5.6	106.0	2.1	105.1	3.9

Table A1. *Cont.*

Pesticides	r^2	LOD (ng/g)	LOQ (ng/g)	Spiked at 50 ng/g		Spiked at 250 ng/g		Spiked at 500 ng/g	
				Recovery (%)	CV (%)	Recovery (%)	CV (%)	Recovery (%)	CV (%)
Carfentrazone-ethyl	0.996	9.3	30.6	95.8	8.7	85.4	7.4	95.4	5.4
Propiconazole I	0.999	11.1	36.7	104.9	5.3	90.6	5.0	94.7	11.9
Propiconazole II	0.998	10.3	34.1	97.8	4.5	108.1	7.7	112.9	2.9
p,p′-DDT	0.999	2.8	9.1	81.6	8.2	89.1	8.5	80.7	5.7
Hexazinone	0.996	13.1	43.1	85.4	6.7	73.5	6.6	72.8	8.7
Tebuconazole	0.997	20.2	66.7	92.0	8.8	82.5	9.2	83.6	6.9
Thenylchlor	0.998	6.4	21.1	77.6	1.0	81.7	8.4	70.1	0.5
Triphenyl phosphate	0.999	4.9	16.0	105.0	6.7	81.2	3.8	79.8	6.1
Piperonyl butoxide	0.996	4.8	15.8	117.5	1.8	108.4	2.5	107.7	4.0
Pyributicarb	0.998	8.2	27.0	90.0	0.6	91.1	5.3	98.2	1.8
Benzoylprop-ethyl	0.996	2.4	7.8	86.7	2.0	91.5	6.0	90.9	2.9
Iprodione	0.997	11.7	38.8	74.8	10.3	74.0	0.4	106.3	7.4
Bromopropylate	0.998	3.5	11.7	95.6	8.7	93.1	6.9	103.4	2.7
Carbosulfan	0.998	1.8	5.9	95.9	6.6	108.4	2.2	87.9	10.9
EPN	0.999	13.7	45.1	96.1	11.1	112.9	5.0	114.3	5.9
Picolinafen	0.998	8.9	29.2	71.2	8.9	78.2	2.0	74.3	5.3
Chlorantraniliprole	0.996	10.9	35.9	73.8	3.1	72.3	6.2	73.3	5.2
Bifenthrin	0.997	8.4	27.7	94.8	4.3	104.5	3.4	120.5	3.2
Methoxychlor	0.999	5.0	16.6	86.2	8.0	104.6	3.6	110.4	4.9
Fenamidone	0.999	9.9	32.8	82.7	4.9	101.7	7.2	102.2	6.0
Anilofos	0.996	8.9	29.2	64.2	2.3	96.4	2.1	110.4	4.7
Clomeprop	0.998	4.4	14.4	81.1	8.5	71.3	1.7	76.0	9.8
Tetradifon	0.999	27.6	91.2	83.7	4.9	95.9	4.5	83.2	5.2
Phosalone	0.998	9.6	31.8	86.9	0.4	110.9	5.1	109.2	6.7
Leptophos	0.999	9.5	31.3	72.4	3.3	74.9	7.4	112.8	2.0
Cyhalofop-butyl	0.999	16.7	55.0	98.8	2.2	96.5	6.1	113.4	5.9
Cyhalothrin	0.997	20.1	66.4	101.7	8.7	95.4	7.4	110.7	5.0
Fenarimol	0.997	13.9	46.0	93.0	6.8	96.7	9.0	98.8	3.7
Pyrazophos	0.996	13.9	46.0	114.8	6.8	70.4	6.6	100.7	5.3
Benfuracarb	0.998	13.1	43.2	115.5	1.9	109.3	2.6	110.8	4.0
Fenoxaprop-P-ethyl	0.998	2.5	8.3	103.1	10.8	70.6	3.5	77.3	6.3
Bitertanol	0.996	26.9	88.9	87.4	5.2	96.5	3.8	100.6	1.3
Permethrin-cis	0.996	7.4	24.3	111.1	6.6	112.8	5.1	119.1	5.1
Permethrin-trans	0.997	6.9	22.7	91.4	11.8	110.2	1.2	113.2	5.1
Boscalid	0.998	8.5	28.2	83.8	6.3	84.3	5.3	82.0	3.1
Quizalofop-p-ethyl	0.999	9.6	31.7	101.8	8.7	100.6	6.3	95.7	4.9
Quizalofop-ethyl	0.996	8.9	29.3	110.2	8.7	99.7	9.5	111.6	2.1
Flucythrinate I	0.999	13.6	44.9	89.0	10.1	91.6	10.5	92.0	3.9
Flucythrinate II	0.999	14.4	47.5	114.0	12.3	99.8	6.7	91.4	5.5
Fenvalerate	0.997	29.9	98.8	107.9	8.1	96.1	4.4	91.7	4.7
Deltamethrin	0.999	14.1	46.6	80.3	6.3	93.0	3.3	98.2	6.9
Indoxacarb	0.998	14.2	47.0	90.2	11.5	104.6	14.3	105.0	6.4
Dimethomorph(Z)	0.995	12.6	41.5	87.3	8.0	104.9	6.6	115.0	5.1
Dimethomorph(E)	0.996	14.3	47.1	103.3	7.3	113.8	8.4	98.2	6.9

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