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Development and validation of a combined QuEChERS and HPLC-MS/MS method for trace analysis of ten diamide insecticides in agricultural products†

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Diamide insecticides are being widely registered worldwide, yet most of them lack established maximum residue limits (MRLs) in agricultural products. In this study, we combined a QuEChERS (quick, easy, cheap, efficient, rugged, and safe) extraction method with high-performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS) analysis to simultaneously identify and quantify ten diamide insecticides in seven matrices for the first time. The method was validated in accordance with SANTE/11312/2021 guidelines, including sensitivity, linearity, trueness, and precision. Excellent linearity (R^2 > 0.99) was obtained for all diamide insecticides within the concentration range of 5–1000 μg kg^{-1}. The limit of detection (LOD) and limit of quantification (LOQ) were 0.01–1 μg kg^{-1} and 5 μg kg^{-1}, respectively. The recoveries of the ten diamide insecticides at three levels (5, 100, and 1000 μg kg^{-1}) ranged from 76.6% to 108.2% with good intra-day relative standard deviation (RSD_r) (1.0–13.4%) and inter-day relative standard deviation (RSD_R) (2.3–15.7%). The proposed method was applied to analyze 70 real agricultural product samples, and only six samples contained diamide insecticides. The results demonstrated that the method was both convenient and reliable for detecting diamide insecticides in agricultural products. The method was then applied to analyze agricultural product samples collected in a field trial to estimate the MRLs for the next step.

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1. Introduction

Currently, the pesticides in use are characterized by high selectivity and low environmental impact.[1] Pesticides, including herbicides, fungicides, and insecticides, are essential substances for the prevention and control of weeds, diseases, and pests in agricultural production. However, a study by Carson reported for the first time that extensive use and misuse of pesticides may have negative consequences in 1962.[2] This report has prompted global attention to the impact of pesticides on the environment, leading to the development of a new generation of pesticides that are theoretically less toxic and persistent. At present, the pesticides used have the characteristics of higher selectivity and less environmental impact. However, they are not entirely harmless. Some studies have found that many pesticides and their metabolites were determined in the environment and organisms, such as surface water, groundwater, soil, zebra fish, and earthworm.[3–7] Pesticides can enter the human body through the food chain, water, and air. The pesticides in food commodities have been shown to be toxic to humans and pose a potential threat to human health.[8,9] For the past few years, people have become increasingly concerned about the pesticide residues in food. This problem has also aroused the attention of the government. To protect public health, governments and regulatory agencies around the world have formulated policies to reduce the use of pesticides. However, farmers around the world still use pesticides to reduce losses.[1,7] To protect consumers, many countries have established stringent maximum residue limits (MRLs) for pesticides in various agricultural products. With the continuous development and registration of new pesticides, the default limit was used when an MRL value is not specified. However, the default limit is different in different countries. The default limits are 0.05 and 0.01 mg kg^{-1} in Iran and the European Union (EU), respectively. Meanwhile, these new pesticides lack detection methods in food products. Thus, it is crucial to establish a pesticide analysis method to monitor pesticide residues in food when there are MRLs but no detection methods.

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Pests have a devastating effect on food security across the world. Up to 40% of global crop production is destroyed by pests annually.[10] For crops, including cereals, vegetables, and fruits, pests can lead to a decrease in crop yield and quality.[11] To our knowledge, the use of chemical pesticides is still the main method to reduce losses caused by pests.[12] Thus, the monitoring of pesticide residues in crops is necessary to accomplish with MRLs for new pesticides. And it also helps to ensure food safety and reduce the impact of crop export trade.

Diamide insecticides are the most popular insecticidal products in the market after neonicotinoid insecticides. It is predicted that, in 2024, they will surpass neonicotinoid insecticides and occupy the top position in global insecticide products.[13] Diamide insecticides were developed and registered in 2001. They can be used to control *Lepidoptera*, *Coleopteran*, and *Dipteran* pests and have low toxicity to mammals.[14] Diamide insecticides have been paid more and more attention because of their unique specific structure, high insecticidal activity, and long persistent control. At present, there are ten diamide insecticides around the world, of which 9 have been officially registered and approved for pest control in different countries, and 1 has been temporarily approved by the International Organization for Standardization (ISO). In addition, there are two compounds belonging to the class of phthalimides (flubendiamide and cyhalodiamide), seven compounds belonging to the class of *o*-carboxamidobenzamide (chlorantraniliprole, cyantraniliprole, tetrachlorantraniliprole, tetraniliprole, thiorantraniliprole, cyclaniliprole, and fluchlordiniliprole), and one compound belonging to the class of *m*-formamidobenzamide (broflanilide).[13] Due to the high activity and no cross-resistance with traditional pesticides of diamide insecticides, more than 200 crops have been registered for these insecticides, which have great application prospects. However, diamide insecticides have a long residual period and strong mobility in soil, and long-term and large-scale application may lead to enrichment. The Environmental Protection Agency (EPA) has reported that flubendiamide poses acute and chronic risks to aquatic invertebrates.[13] China only has set MRLs of flubendiamide, chlorantraniliprole, cyantraniliprole, and tetrachlorantraniliprole in crops. There is no corresponding MRL value for the other six diamide insecticides. However, many countries and organizations, such as the EU and Codex Alimentarius Commission (CAC), have stipulated the MRLs for diamide insecticides (except for fluchlordiniliprole) in various foods to ensure food and environmental safety. Furthermore, there are some studies for the determination of these insecticides. Most of them are the methods for analyzing one or several compounds.[14–22] Thus, analyzing these ten diamide insecticides with comprehensive and simultaneous techniques is imperative to provide a technical basis for the routine detection of insecticides in crops (GB 2763-2021, 2021).

Several methods have been validated for the quantitative and qualitative analyses of diamide insecticides, including Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS),[14,15] Liquid Chromatography (LC),[23] Gas Chromatography-Tandem Mass Spectrometry (GC-MS/MS),[24] Gas Chromatography (GC),[25] and electrochemical methods.[26] However, GC and GC-MS/MS are unsuitable for analyzing the ten diamide insecticides as some of them are difficult to vaporize. LC analysis takes a lot of time and has low sensitivity.[27] Compared with previously established methods, the LC-MS/MS method has the best sensitivity and efficiency in trace analysis of diamide insecticides and has been widely used. Therefore, in this study, LC-MS/MS was selected to analyse diamide insecticides. A lot of sample preparation techniques have been reported, including solid-phase extraction (SPE), gel permeation chromatography (GPC), and QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe).[28–31] SPE is labor-intensive and time consuming. GPC requires the use of a large amount of organic solvents, including *n*-hexane and acetone. In recent years, QuEChERS has become a commonly used method in laboratories around the world because of its good extraction efficiency for various compounds and its wide applicability in various matrices.[32,33] Thus, the QuEChERS technique was the first choice in this study to extract the ten diamide insecticides.

There are no defined MRLs for cyhalodiamide, broflanilide, tetraniliprole, thiorantraniliprole, cyclaniliprole, and fluchlordiniliprole in crops in China. This study is the first try to establish the MRLs for these diamide insecticides in vegetables, fruits, and cereals. The aim of the present study was to develop and validate an improved QuEChERS method combined with LC-MS/MS analytical method for simultaneous determination of the ten diamide insecticides in vegetables, fruits, and cereals. The extraction solvent and clean-up process of QuEChERS were investigated to obtain higher recoveries. The LC-MS/MS conditions were also optimized for the qualification and quantitation of each target compound within 6 min. As far as we know, this is the first time that a method for simultaneous determination of the ten diamide insecticides in different matrices has been established. Finally, the developed method was used to determine the residual status of the diamide insecticides in real crop samples.

2. Materials and methods

2.1. Chemicals and reagents

Alta Scientific Co., Ltd, Tianjin, China, was the source of nine certified reference standards of diamide insecticides (flubendiamide, cyhalodiamide, chlorantraniliprole, cyantraniliprole, tetrachlorantraniliprole, tetraniliprole, thiorantraniliprole, cyclaniliprole, and broflanilide), whereas fluchlordiniliprole was obtained from Hailir Pesticides and Chemicals (Qingdao, China). The purity of all analytical standards was more than 97%. Honeywell International Inc. located in New Jersey, USA, provided methanol, acetonitrile, and formic acid, all of LC-MS grade. Anhydrous magnesium sulphate ($MgSO_4$) and sodium chloride (NaCl) were procured from Sinopharm Chemical Reagent Co., Ltd (Beijing, China). The ultrapure water used for the LC mobile phase was obtained successively from a Millipore system (Bedford, MA, USA). Sorbents, 100 g per bottle, including primary secondary amine (PSA), graphitized carbon black (GCB), and octadecylsilane (C18), were provided by Agilent Technologies Inc (Beijing, China). Then, they were weighed by using a precision balance.

Different sorbents based on PSA, C18, and GCB were evaluated: sorbent 1 (50 mg PSA and 150 mg $MgSO_4$), sorbent 2 (50 mg C18 and 150 mg $MgSO_4$), sorbent 3 (5 mg GCB and 150 mg $MgSO_4$), sorbent 4 (50 mg PSA, 5 mg GCB, and 150 mg $MgSO_4$), sorbent 5 (50 mg C18, 5 mg GCB, and 150 mg $MgSO_4$), and sorbent 6 (20 mg PSA, 30 mg C18, and 150 mg $MgSO_4$).

Solutions of the ten diamide insecticides were prepared by weighing 10 mg of the active component of each target insecticide into volumetric flasks and then dissolving them in 10 mL of acetonitrile to obtain a concentration of 1000 mg L^{-1}. The volumetric flasks required ultrasonication for 20 min at 40 °C to dissolve the fluchlordiniliprole. They were sealed and stored at −20 °C in the dark until use. The solutions were stable over one month under these conditions. When ready for use, the solutions were thawed and ultrasound treated at room temperature. Afterwards, the solutions were mixed in equal volumes to obtain a mixed standard solution with a concentration of 100 mg L^{-1}. This solution was used to prepare the working solutions for recovery studies, calibration, and optimization and for matrix-matched calibration. For matrix-matched calibration, standard multi-component solutions were prepared at different concentrations (5, 10, 50, 100, 500, and 1000 μg kg^{-1}) by appropriate dilution of the mixed solution with the extraction blank samples. An individual solution at 100 μg kg^{-1} was prepared to optimize MS parameters. Vegetables and fruits (tomatoes, cucumbers, peppers, cabbages, and apples) were supplied from an organic food store in Zhengzhou. Rice and corn were acquired form the experimental base in Xinxiang, Henan Province, China. The seven matrices were previously checked to ensure that they did not contain the ten diamide insecticides. As expected, no residues of the ten diamide insecticides were detected in seven matrices. All solutions and matrices were stored at −20 °C in the dark until analysis.

2.2. Instrumentation

This study utilized an Agilent 1290 high-performance liquid chromatography (HPLC) system (Agilent Technologies, Inc., Santa Clara, CA, USA). The system consists of three main components, including a column compartment (G1316C), a binary pump (G4220A), and an autosampler (G4226A). Quantitative and qualitative analyses were performed using a triple quadrupole mass spectrometer (QQQ 6460A, Agilent Technologies, Inc., Santa Clara, CA, USA).

An Agilent Poroshell 120 EC-C18 column, 2.1 × 100 mm, 2.7 μm particle diameter, was used to separate the ten diamide insecticides, with a flow rate of 0.30 mL min^{-1}. The mobile phases A and B were water and acetonitrile, respectively. Starting with 10% acetonitrile, the gradient for mobile phase B was established as follows: the mobile phase B was increased to 70% in 1 min. Then, isocratic conditions were kept for 2 min. Afterwards, the mobile phase B was increased to 90% in 2 min. Finally, the mobile phase B was reduced to 10% at 5.1 min (initial conditions) and kept for 0.9 min to ensure that the column was fully re-equilibrated. The running time of the chromatographic system was 6 min. The temperature of the column compartment and autosampler was set at 35 °C and 4 °C, respectively. The injection volume was 5 μL.

Regarding the conditions of the mass spectrometer, dynamic multiple reaction monitoring (MRM) was selected as the acquisition mode. Two MRM ion transitions in each target compound were selected for the quantifier and qualifier. And the high response values were used for quantitative analysis, while low response values were used for qualitative analysis. All samples were analyzed in both positive and negative modes with the following parameters: capillary voltage, 4000 V; drying gas temperature, 350 °C; drying gas flow, 8 L min^{-1}; sheath gas temperature, 350 °C; sheath gas flow, 12 L min^{-1}; nebulizer gas pressure, 35 psi. The fragments voltage and collision energy were also optimized during the infusion of each target analyte (0.1 mg L^{-1}). Table 1 shows all the parameters for the ten diamide insecticides. Instrument control and data acquisition and processing were performed with Agilent MassHunter Workstation software, version B.03.01 (Agilent Technologies, Inc.).

2.3. Sample preparation and extraction procedure

The tomato, cucumber, pepper, cabbage, apple, rice, and corn samples (approximately 1 kg each) were homogenized and stored in a freezer at −20 °C in the dark until analysis. For the extraction, 10 g of blank samples were weighed into centrifuge tubes (50 mL). Then, the mixed standard solution was added to the tubes at three levels. Samples and mixed standard solution were vortexed for 1 min and left for 2 h at room temperature to allow the ten diamide insecticides to penetrate into the matrices. For rice and corn samples, 10 mL of ultrapure water was added to the tube, and the tube was carefully mixed (2 min). Subsequently, 10 mL of acetonitrile was added into all the samples, and the tubes were shaken (10 min). Once done, to induce phase separation, the salting-out process was carried out by adding a concoction of anhydrous $MgSO_4$ (4 g) and NaCl (1 g). The tubes were shaken again (5 min). After that, the tubes were centrifuged at 2077*g* (5 min) to separate the organic phase and obtain the supernatant. For clean-up, the supernatant (1.5 mL) was added to a tube containing different sorbents (50 mg PSA for tomatoes, peppers, and corn; 20 mg PSA and 30 mg C18 for cucumbers, cabbages, apples, and rice) and 150 mg anhydrous $MgSO_4$. The mixture was vigorously mixed and purified for 1 min and then centrifuged at 2400*g* (5 min). 1 mL of the layer-separated solution was filtered using a 0.22 μm nylon filter and detected using HPLC-MS/MS. The scheme for sample extraction and purification procedures is shown in Fig. 1.

2.4. Method validation

The analytical performance was estimated according to the European Union SANTE 11312/2021, including the linearity, specificity, selectivity, trueness and precision, limit of detection (LOD), limit of quantification (LOQ), and matrix effect (ME). The specificity of the proposed analytical method was evaluated by analyzing the tomatoe, cucumber, pepper, cabbage, apple, rice, and corn blank samples. The samples were confirmed to be free of the ten target compounds. For linearity, blank samples

Table 1 Retention times and related MS data of the ten diamide insecticides

Compound	Molecular formula	Ion source	Ion polarity	Precursor ion	Fragments (V)	Product ion	Collision energy (V)	RT (min)
Flubendiamide	$C_{23}H_{22}F_7IN_2O_4S$	ESI^-	$[M-H]^-$	681.0	170	254.1 [a]	30	3.1
						274.0 [b]	10	
Cyhalodiamide	$C_{22}H_{17}ClF_7N_3O_2$	ESI^-	$[M-H]^-$	522.2	140	254.1 [a]	20	3.0
						274.1 [b]	10	
Chlorantraniliprole	$C_{18}H_{14}BrCl_2N_5O_2$	ESI^+	$[M+H]^+$	484.0	90	453.0 [a]	20	2.4
						286.0 [b]	10	
Cyantraniliprole	$C_{19}H_{14}BrClN_6O_2$	ESI^+	$[M+H]^+$	475.0	100	286.0 [a]	10	2.2
						444.1 [b]	18	
Tetrachlorantraniliprole	$C_{17}H_{10}BrCl_4N_5O_2$	ESI^-	$[M-H]^-$	535.8	100	202.0 [a]	10	2.8
						499.9 [b]	10	
Tetraniliprole	$C_{22}H_{16}ClF_{10}N_{10}O_2$	ESI^+	$[M+H]^+$	545.2	110	356.0 [a]	10	2.4
						376.0 [b]	20	
Thiorantraniliprole	$C_{19}H_{15}BrCl_3N_5OS$	ESI^+	$[M+H]^+$	548.0	110	285.9 [a]	10	3.4
						177.3 [b]	30	
Cyclaniliprole	$C_{21}H_{17}Br_2Cl_2N_5O_2$	ESI^-	$[M-H]^-$	599.9	110	255.9 [a]	18	3.0
						257.9 [b]	10	
Broflanilide	$C_{25}H_{14}BrF_{11}N_2O_2$	ESI^+	$[M+H]^+$	665.1	150	625.0 [a]	30	4.0
						555.6 [b]	30	
Fluchlordiniliprole	$C_{17}H_{10}BrCl_3FN_5O_2$	ESI^-	$[M-H]^-$	520.0	100	204.0 [a]	10	2.3
						261.0 [b]	15	

[a] Quantifier. [b] Qualifier.

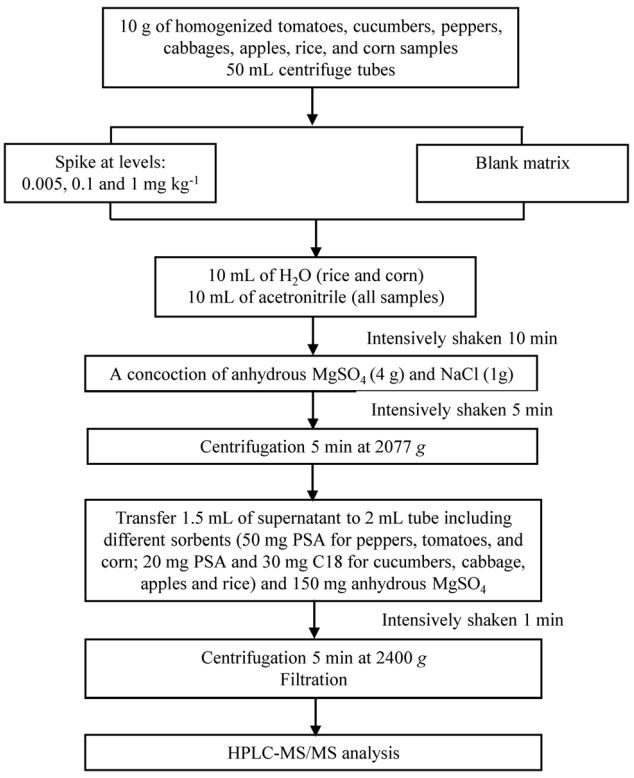

Fig. 1 Workflow of sample preparation.

were spiked with the ten diamide insecticides at different concentrations of 5, 10, 50, 100, 500, and 1000 μg kg^{-1} to obtain the matrix-matched calibration. The selectivity was investigated by comparing the chromatograms of the blank sample and fortified sample to verify whether there is any interference peak around the peak time of the target compound. The trueness and precision were acquired by detecting the target compounds in blank samples spiked with three concentrations (LOQ, 20× LOQ, and 200× LOQ) with five replications and on three different days. The recoveries were used to evaluate the trueness. The relative standard deviations (RSDs), including intra-day and inter-day, were used to evaluate the precision. The LOD was defined as the lowest concentration of the ten target compounds detected in the seven matrices. The LOQ was the lowest spiked concentration of the ten target compounds that met the acceptance criterion for trueness and precision.[15] MEs may affect the quantification of the target compounds. The slope ratio was used to evaluate the ME, according to the following equation:

$$ME\% = \left(\frac{\text{Slope of calibration curve in matrix}}{\text{Slope of calibration curve in solvent}} - 1\right) \times 100\% \quad (1)$$

3. Results and discussion

3.1. Optimization of MS/MS conditions

Optimization of MS/MS conditions for the ten target compounds was done after the injection of individual insecticide standards in negative or positive ESI mode. The precursor ions, fragments, product ions, and collision energy were optimized in MRM transitions for each target compound to achieve the best sensitivity and selectivity. For chlorantraniliprole, cyantraniliprole, tetraniliprole, thiorantraniliprole, and broflanilide, the precursor ions were the ($[M+H]^+$) molecular ions. However, the ($[M-H]^-$) molecular ions were selected as the precursor ions for flubendiamide, cyhalodiamide, tetrachlorantraniliprole, cyclaniliprole, and fluchlordiniliprole. For

each insecticide, the precursor ion and two product ions were selected for qualitative and quantitative analyses. For chlorantraniliprole, thiorantraniliprole, and broflanilide, the product ions with more abundance were used for quantitation. In contrast, the product ions with more abundance were applied for identification of other target compounds. For the ten diamide insecticides (except for tetraniliprole, thiorantraniliprole, and fluchlordiniliprole), the optimization of MS parameters is consistent with other studies.[14,15,19–21] And the MS parameters of tetraniliprole, thiorantraniliprole, and fluchlordiniliprole did not provide useful information in the current study. The optimized parameters for the ten target compounds are presented in Table 1.

Many studies have found that the composition of the mobile phase in HPLC-MS/MS analysis could affect the peak shape, retention time, and peak area of the target analytes.[14,33] In the present study, the chromatographic separation of the ten diamide insecticides was carried out using an injection of 100 μg kg^{-1} mixed standard solution. Four commonly used mobile phase compositions (acetonitrile and water, acetonitrile and 0.1% formic acid aqueous solution, methanol and water, and methanol and 0.1% formic acid aqueous solution) were compared to acquire better peak shapes and sensitivities of the target analytes. Compared with acetonitrile and water, methanol and water delayed the retention time and produced a poorer peak shape for some analytes (peak splitting and tailing). Acetonitrile and water, as well as acetonitrile and 0.1% formic acid aqueous solution, can produce better peak shapes for the target compounds, and the overall time was reduced. As observed in Fig. 2, the mobile phase of acetonitrile and 0.1% formic acid aqueous solution produced a lower peak area than acetonitrile and water. In addition, some target compounds were determined in negative ESI mode. Thus, the mobile phase of acetonitrile and water was selected to acquire the best peak shapes and sensitivities. Under the optimized MS and chromatography conditions, typical MRM chromatograms of the ten diamide insecticides in acetonitrile and black samples are shown in Fig. S1–S3.† No interferences were found at the retention times of the target compounds, and the analysis times were shorter than 6 min.

3.2. Optimization of the extraction and clean-up procedure

The pesticide residues in agricultural products have drawn the attention of governments and consumers. They may be a potential threat to human health.[34] Thus, the application of reliable sample pre-treatment technologies to detect pesticide residues in foods is critical. It is well known that the moisture content of cereals is less than 15%.[35] And the QuEChERS method is suitable for the extraction of samples with high water content, such as most fruits and vegetables.[36] Therefore, the analysis of pesticide residues in cereal samples is a difficult task. In order to solve this problem, an appropriate volume of water should be added to improve the sample moisture content. In this study, some parameters, including the water volume, extraction solvent, and different combinations of sorbents, were optimized to acquire the optimal extraction effect of the QuEChERS method.

First, the volume of water was optimized. Some studies have found that adding an appropriate volume of water can improve the extraction efficiency of pesticides in dry samples.[37–39] Different volumes (5, 10, and 20 mL) of water were added to compare the extraction effect. The extraction effect with 10 mL and 20 mL of water was better than that with 5 mL of water. However, there was no difference in the extraction effect between 10 mL and 20 mL of water. In addition, using 20 mL water required adding more $MgSO_4$. Hence, taken together, 10 mL water was added in rice and corn before the QuEChERS extraction.

Besides, the extraction solvents were optimized. The extraction solvent had a significant effect on the recoveries of the

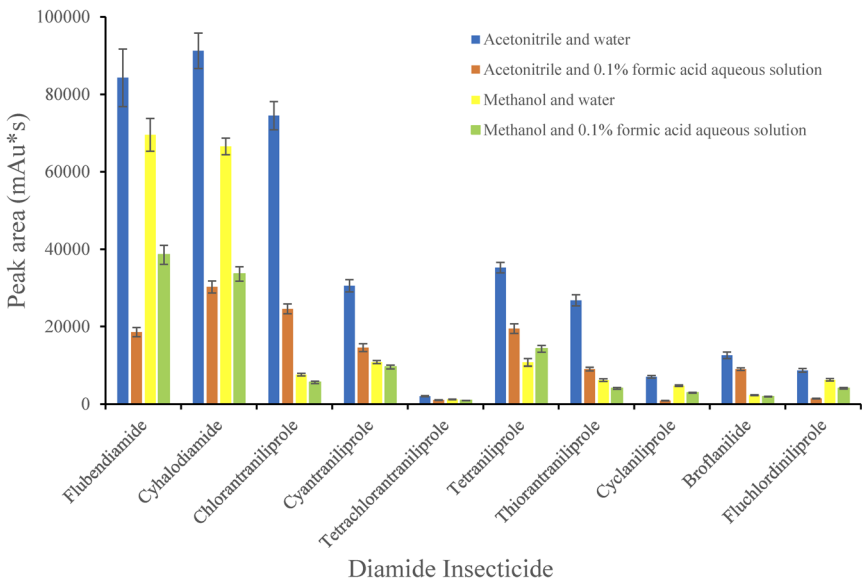

Fig. 2 The peak area of the ten diamide insecticides (at 0.01 mg L^{-1} concentration using four different mobile phase compositions).

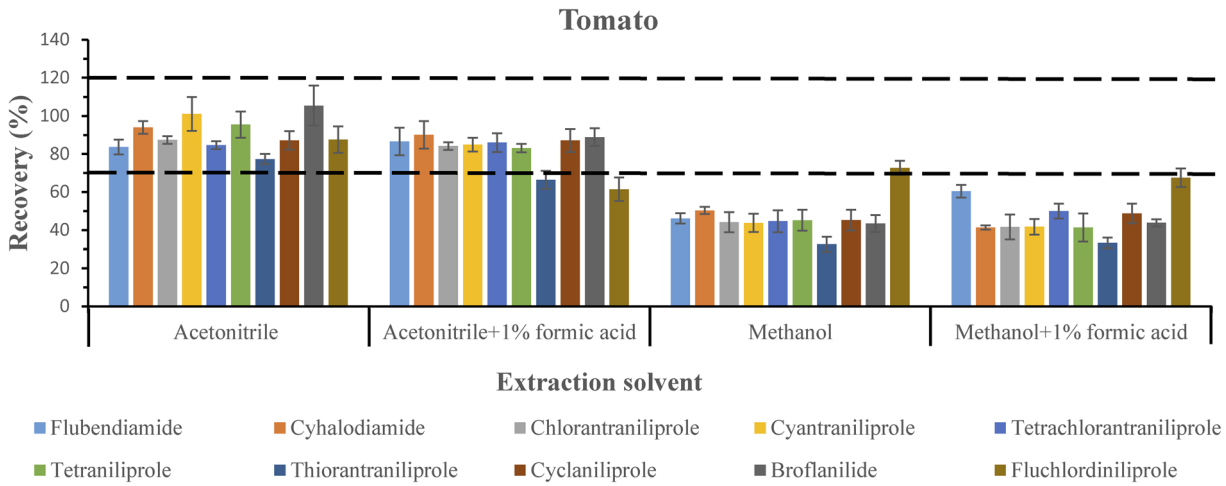

Fig. 3 Effect of different types of extraction solvents for the targeted compounds in the tomato matrix at 10 μg kg^{-1} level ($n = 3$).

target analytes in the samples, especially for the complex matrices. Acetonitrile and methanol were frequently used to extract pesticide residues from food samples.[7,28] In addition, for multi-residue analysis, the use of acid may protect the base-sensitive pesticides and improve the extraction efficiency.[40] In the current study, the extraction effects of four extraction solvents (methanol, acidified methanol (1% formic acid), acetonitrile, and acidified acetonitrile (1% formic acid)) were compared. Tomato was chosen as the representative of the blank sample, which was spiked with 10 μg kg^{-1} mixed standard solution. Then, the tomato samples were extracted and purified according to the methods mentioned in Section 2.3. As shown in Fig. 3, the recoveries of the ten target compounds were satisfactory when acetonitrile was used as the extraction solvent. 1% formic acid and acetonitrile also produced a remarkable recovery efficiency of the ten target compounds except for thiorantraniliprole and fluchlordiniliprole. However, the recovery was below 70% when methanol and acidified methanol were used. Thus, acetonitrile was selected to extract the target analytes from the seven matrices.

Finally, different sorbents were compared and optimized to reduce the interferences. PSA, C18, and GCB were often used to remove interfering substances in various complex matrices.[41] Vegetables, fruits, and cereals contained a lot of interferences, such as fats, proteins, pigments, fatty acids, and sugars. Some researchers have found that using PSA can remove sugars, organic acids, and other polar components; using C18 can remove fats, lipids, and other non-polar organic compounds; using GCB can remove polyphenols, chlorophyll, carotenoids, and other visible pigments.[42–44] Nevertheless, some studies also found that a single sorbent might not be able to fully purify the samples.[15,43,45] In addition, several studies have proved that the combination of PSA with other sorbents (C18 and GCB) can improve the removal efficiency for the extracts of many matrices.[33,35,46] The purification effect of each sorbent was compared by mixing them with 150 mg anhydrous $MgSO_4$. In the current study, the purification effects of six different types of sorbents (sorbent 1 : 50 mg PSA; sorbent 2 : 50 mg C18; sorbent 3 : 5 mg GCB; sorbent 4 : 50 mg PSA + 5 mg GCB; sorbent 5 : 50 mg C18 + 5 mg GCB; sorbent 6 : 20 mg PSA + 30 mg C18) were tested, and the results are shown in Fig. 4. In the tomato matrix, the average recoveries of the ten diamide insecticides were acceptable (70–120%) under the use of six different sorbents. In the pepper matrix, the average recoveries of target insecticides were 70–120% under the use of 50 mg PSA. In the cucumber, cabbage, and apple samples, the recovery and RSD were both satisfactory when 50 mg PSA or 20 mg PSA + 30 mg C18 were used. In the rice matrix, the average recoveries of each target compound were satisfactory with the use of 50 mg C18 or 20 mg PSA + 30 mg C18. In the corn matrix, only when 50 mg PSA was used, the recoveries of the ten diamide insecticides were within the acceptable range. For GCB, the recoveries of compounds 1–9 were <70%. PSA and C18 presented good recoveries for most compounds in all matrices. Possibly, GCB absorbed some target compounds in addition to polyphenols, chlorophyll, and carotenoids, resulting in low recoveries. Some studies also found that the recoveries of some pesticides were relatively low when GCB was used.[15,35,44] In addition, C18 was relatively cheaper than PSA. And considering other factors, including the recoveries, matrix effect, and purification effect, 50 mg PSA was selected for tomato, pepper, and corn extracts, while 20 mg PSA + 30 mg C18 was selected as the most appropriate absorbent for cucumber, cabbage, apple, and rice extracts in this study.

3.3. Method performance

Under the above optimized experimental conditions, the performance of the developed method was evaluated in line with the SANTE 11312/2021 guidelines.[1] The specificity, linearity, LOD, LOQ, precision, and trueness (recoveries) of the ten diamide insecticides were studied. Satisfactory linearity, recovery, trueness, and precision were obtained.

3.3.1. Specificity. The seven matrices (tomato, cucumber, pepper, cabbage, apple, rice, and corn) were extracted and purified using the abovementioned method to obtain analytical

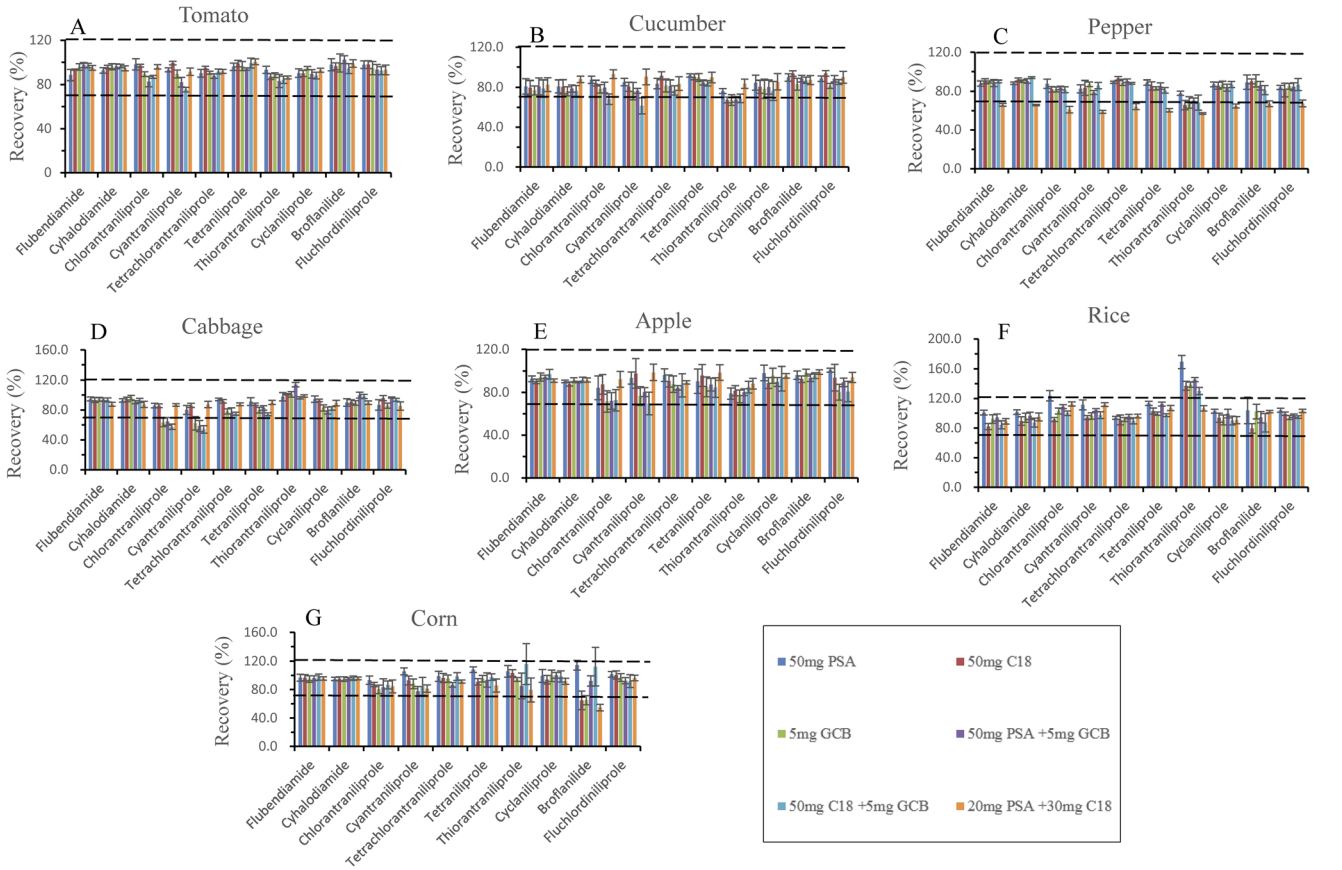

Fig. 4 Comparison of recoveries of the ten diamide insecticides with different sorbents in different matrices at 100 μg kg^{-1} concentration.

sample solutions from the blank food samples and diamide-fortified samples. As shown in Fig. S1–S3,† exemplified by the apple matrix, none of the ten compounds exhibited interference peaks at the retention times, suggesting that the developed method has a high degree of specificity.

3.3.2. Linearity and limits of detection and quantification. Reliable linearity for the ten diamide insecticides was obtained in acetonitrile and the seven matrices by plotting the peak areas (y) against the corresponding concentrations (x). The calibration curves of each target compound in acetonitrile and the blank matrix extract (tomato, cucumber, pepper, cabbage, apple, rice, and corn) were established over six concentrations (ranging from 5 to 1000 μg kg^{-1}), with high correlation coefficients $R^2 > 0.99$ in all cases for all target compounds (Table 2). Method sensitivity was measured from LODs and LOQs for each target compound. LODs were defined as the lowest concentration of the ten target compounds detected in the seven matrices. LODs oscillated from 0.01 μg kg^{-1} to 1 μg kg^{-1} in tomato, 0.05 μg kg^{-1} to 1 μg kg^{-1} in cucumber, 0.1 μg kg^{-1} to 1 μg kg^{-1} in pepper and rice, 0.05 μg kg^{-1} to 0.5 μg kg^{-1} in cabbage and apple, and 0.2 μg kg^{-1} to 1 μg kg^{-1} in corn, where >92.9% of LOD values was below 1 μg kg^{-1} (Table 2). The validated LOQs were the lowest spiked level with acceptable recovery, 5 μg kg^{-1} in this method. In terms of MRLs in China and EU, all LOQs for each target compound in this method met the requirements in all matrices. These results suggest that the sensitivity of the developed method met the daily detection requirements for the ten diamide insecticides in vegetables, fruits, and cereals.

3.3.3. Trueness and precision. The recovery tests were performed to evaluate the trueness and precision of the developed method. The trueness and precision were expressed as the recovery rate and RSD, respectively. The trueness and precision experiments were performed at three concentrations (LOQ, 20 x LOQ, and 200 x LOQ) with five replications on seven blank matrix samples (tomato, cucumber, pepper, cabbage, apple, rice, and corn). After spiking the mixed solutions, 2 h of standing time was allowed to assure that the ten diamide insecticides were fully absorbed by the samples. Then, they were extracted and purified in accordance with the methods presented in Section 2.3. As presented in Table 3, the ten diamide insecticides gave excellent mean recoveries ($n = 15$) in the range of 96.6–107.5% for tomato, 77.0–104.9% for cucumber, 80.3–106.2% for pepper, 86.0–104.9% for cabbage, 86.2–108.2% for apple, 86.3–108.1% for rice, and 86.3–100.7% for corn. The precision of the developed method was evaluated by repeatability studies. It was calculated and expressed as the RSD. The intra-day RSD was calculated by analyzing five samples spiked with the ten diamide insecticides at three fortification levels on a single day ($n = 5$). The inter-day RSD was calculated by analyzing the ten diamide insecticides in the same sample over three consecutive days ($n = 15$). For the three spiked levels, intra-day RSDs of all the target compounds ranged from 1.8% to

Table 2 Calibration equations, R^2, LOD, and LOQ of the studied the ten diamide insecticides in food matrices[a]

Compound	Matrix	Regression equation	R^2	Matrix effect[b] (%)	LOD (μg kg^{-1})	LOQ (μg kg^{-1})	MRL (mg kg^{-1}) EU	MRL (mg kg^{-1}) China
Flubendiamide	Acetonitrile	$y = 3734.6x + 85749.9$	0.9971	—	—	—	—	—
	Tomato	$y = 3468.3x + 110137.8$	0.9928	−7.13	0.2	5	2	2
	Cucumber	$y = 3094.7x + 80240.6$	0.9953	−17.13	0.2	5	0.2	—
	Pepper	$y = 3427.5x + 116214.7$	0.9925	−8.22	0.5	5	0.7	0.7
	Cabbage	$y = 3162.2x + 98408.8$	0.9944	−15.33	0.1	5	0.01	0.2
	Apple	$y = 2189.3x + 70385.5$	0.9932	−41.38	0.1	5	0.9	0.8[c]
	Rice	$y = 2046.4x + 66135.2$	0.9920	−45.20	0.2	5	0.3	0.01
	Corn	$y = 3361.5x + 137129.6$	0.9928	−9.99	0.2	5	0.02	0.02
Cyhalodiamide	Acetonitrile	$y = 3640.0x + 89277.5$	0.9951	—	—	—	—	—
	Tomato	$y = 3551.2x + 118457.6$	0.9929	−2.44	0.05	5	—	—
	Cucumber	$y = 3418.5x + 82004.5$	0.9943	−6.09	0.05	5	—	—
	Pepper	$y = 3591.3x + 121914.1$	0.9922	−1.34	0.05	5	—	—
	Cabbage	$y = 3350.7x + 100639.1$	0.9927	−7.95	0.05	5	—	—
	Apple	$y = 2438.7x + 76483.3$	0.9936	−33.00	0.05	5	—	—
	Rice	$y = 2544.2x + 62167.1$	0.9960	−30.10	0.1	5	—	—
	Corn	$y = 3195.5x + 53609.5$	0.9975	12.21	0.1	5	—	—
Chlorantraniliprole	Acetonitrile	$y = 8931.9x + 128703.9$	0.9926	—	—	—	—	—
	Tomato	$y = 1766.4x + 37707.1$	0.9985	−80.22	0.01	5	0.6	0.6[c]
	Cucumber	$y = 3182.7x + 79694.7$	0.9940	−64.37	0.05	5	0.3	0.6[c]
	Pepper	$y = 1418.7x + 20912.9$	0.9979	−84.12	0.1	5	1	0.6[c]
	Cabbage	$y = 4602.1x + 122165.2$	0.9929	−48.48	0.05	5	20	2[c]
	Apple	$y = 5142.5x + 114771.6$	0.9964	−42.43	0.05	5	0.4	2[c]
	Rice	$y = 3773.15x + 66200.7$	0.9947	−57.76	0.1	5	0.4	0.04[c]
	Corn	$y = 1411.9x - 2723.8$	0.9991	−84.19	0.1	5	0.01[c]	0.02
Cyantraniliprole	Acetonitrile	$y = 1549.3x + 34837.1$	0.9961	—	—	—	—	—
	Tomato	$y = 474.4x + 6639.8$	0.9964	−69.38	0.5	5	1	0.2[c]
	Cucumber	$y = 678.0x + 1988.9$	0.9978	−56.24	0.5	5	0.4	0.2[c]
	Pepper	$y = 494.1x + 6585.7$	0.9970	−68.11	0.5	5	1.5	1[c]
	Cabbage	$y = 1055.4x + 16146.3$	0.9964	−31.88	0.2	5	30	0.5[c]
	Apple	$y = 1216.7x + 24539.2$	0.9952	−21.47	0.1	5	0.8	0.8[c]
	Rice	$y = 825.8x + 12185.5$	0.9943	−46.70	0.2	5	0.01[c]	0.2[c]
	Corn	$y = 153.0x - 145.3$	0.9997	−90.12	1	5	0.01[c]	—
Tetrachlorantraniliprole	Acetonitrile	$y = 228.9x + 178.4$	0.9987	—	—	—	—	—
	Tomato	$y = 362.5x + 8862.4$	0.9954	58.37	0.5	5	—	—
	Cucumber	$y = 256.7x + 6186.1$	0.9943	12.15	0.5	5	—	—
	Pepper	$y = 319.9x + 10312.5$	0.9927	39.76	0.5	5	—	—
	Cabbage	$y = 315.9x + 7534.2$	0.9947	38.01	0.5	5	—	3[c]
	Apple	$y = 228.6x + 5034.2$	0.9969	−0.13	0.5	5	—	—
	Rice	$y = 233.0x + 2880.5$	0.9966	1.79	0.5	5	—	0.5[c]
	Corn	$y = 350.9x + 10361.0$	0.9952	53.30	0.2	5	—	0.05[c]
Tetraniliprole	Acetonitrile	$y = 1317.2x + 49033.2$	0.9921	—	—	—	—	—
	Tomato	$y = 334.4x + 8344.0$	0.9916	−74.61	0.5	5	—	—
	Cucumber	$y = 813.6x + 23177.1$	0.9933	−38.23	0.2	5	—	—
	Pepper	$y = 351.2x + 7281.2$	0.9949	−73.34	0.5	5	—	—
	Cabbage	$y = 946.5x + 24973.8$	0.9944	−28.14	0.2	5	—	—
	Apple	$y = 1782.2x + 65293.3$	0.9913	35.30	0.1	5	—	—
	Rice	$y = 893.8x + 23618.7$	0.9934	−32.14	0.2	5	—	—
	Corn	$y = 189.2x + 1394.7$	0.9968	−85.64	0.2	5	—	—
Thiorantraniliprole	Acetonitrile	$y = 4274.0x + 28115.6$	0.9941	—	—	—	—	—
	Tomato	$y = 1330.0x - 6051.3$	0.9946	−68.88	0.5	5	—	—
	Cucumber	$y = 2223.6x + 7059.0$	0.9984	−47.97	0.2	5	—	—
	Pepper	$y = 1034.6x - 7046.0$	0.9926	−75.79	0.5	5	—	—
	Cabbage	$y = 2895.3x + 37204.8$	0.9967	−32.26	0.1	5	—	—
	Apple	$y = 2340.0x + 27481.9$	0.9970	−45.25	0.1	5	—	—
	Rice	$y = 1832.5x - 3485.7$	0.9998	−57.12	0.2	5	—	—
	Corn	$y = 732.1x + 3967.9$	0.9995	−82.87	0.2	5	—	—
Cyclaniliprole	Acetonitrile	$y = 274.6x + 6862.8$	0.9943	—	—	—	—	—
	Tomato	$y = 246.6x + 6873.3$	0.9927	−10.20	0.5	5	0.01[c]	—
	Cucumber	$y = 174.5x + 3086.9$	0.9955	−36.45	0.5	5	0.01[c]	—
	Pepper	$y = 226.3x + 7591.4$	0.9918	−17.59	0.5	5	0.01[c]	—
	Cabbage	$y = 191.7x + 6152.4$	0.9933	−30.19	0.5	5	0.01[c]	—

Table 2 (*Contd.*)

Compound	Matrix	Regression equation	R^2	Matrix effect[b] (%)	LOD (μg kg^{-1})	LOQ (μg kg^{-1})	MRL (mg kg^{-1}) EU	MRL (mg kg^{-1}) China
	Apple	$y = 146.7x + 3931.3$	0.9930	−46.58	0.5	5	0.01[c]	—
	Rice	$y = 119.3x + 2468.5$	0.9977	−56.55	1	5	0.01[c]	—
	Corn	$y = 247.0x + 8879.9$	0.9939	−10.05	0.2	5	0.01[c]	—
Broflanilide	Acetonitrile	$y = 786.4x + 15560.3$	0.9967	—	—	—	—	—
	Tomato	$y = 533.9x + 1206.8$	0.9987	−32.11	1	5	—	—
	Cucumber	$y = 601.5x + 3261.8$	0.9953	−23.51	1	5	—	—
	Pepper	$y = 415.8x - 103.7$	0.9988	−47.13	1	5	—	—
	Cabbage	$y = 822.4x + 11928.1$	0.9972	4.58	0.5	5	—	—
	Apple	$y = 533.1x + 9980.3$	0.9934	−32.21	0.5	5	—	—
	Rice	$y = 401.2x + 838.8$	0.9993	−48.98	1	5	—	—
	Corn	$y = 229.1x + 1194.2$	0.9984	70.87	0.5	5	—	—
Fluchlordiniliprole	Acetonitrile	$y = 722.8x + 6443.5$	0.9973	—	—	—	—	—
	Tomato	$y = 176.4x + 7130.3$	0.9930	−75.59	0.2	5	—	—
	Cucumber	$y = 487.8x + 810.9$	0.9998	−32.51	0.5	5	—	—
	Pepper	$y = 168.2x + 6463.7$	0.9925	−76.73	0.2	5	—	—
	Cabbage	$y = 449.7x + 11374.7$	0.9950	−37.78	0.5	5	—	—
	Apple	$y = 383.4x + 3760.7$	0.9978	−46.96	0.5	5	—	—
	Rice	$y = 153.6x + 4472.9$	0.9953	−78.75	0.2	5	—	—
	Corn	$y = 159.2x + 6362.2$	0.9929	−77.97	0.2	5	—	—

[a] The calibration ranges of all the target compounds are 1–1000 μg L^{-1}. [b] Matrix effect (%) = ((slope matrix/slope solvent) − 1) ×100. [c] Temporary maximum residue limit.

9.5% for tomato, 1.0% to 11.0% for cucumber, 1.0% to 11.0% for pepper, 1.1% to 7.9% for cabbage, 1.4% to 13.4% for apple, 1.2% to 10.8% for rice, and 1.4% to 11.3% for corn. Regarding inter-day RSD, the values ranged from 2.3% to 13.2% for tomato, 2.3% to 9.7% for cucumber, 2.7% to 12.6% for pepper, 2.5% to 10.8% for cabbage, 3.0% to 15.7% for apple, 4.2% to 15.3% for rice, and 3.2% to 13.7% for corn. The trueness and precision of this method for all the target compounds are presented in Table 3. The results reflect the commendable trueness and precision of the proposed method for all the matrices studied.

3.3.4. Matrix effects. According to eqn (1), the MEs for all target compounds in the seven matrices were calculated. Generally speaking, ME (%) could be categorized as negligible (−10% to 10%), soft (−20% to −10% or 10–20%), medium (−50% to −20% or 20–50%), and strong (<−50% or > 50%).[15,47] After optimizing the QuEChERS extraction and purification, the MEs for the ten diamide insecticides in the seven matrices were calculated, and the results are shown in Table 2. The results showed that only some of the analytes' ME in some matrices was between −10% and 10% and can be ignored. In addition, most compounds presented different degrees of signal suppression (except for tetrachlorantraniliprole) in the seven matrices. Tetrachlorantraniliprole showed signal enhancement in all seven matrices except apple. The ten diamide insecticides (except for flubendiamide, cyhalodiamide, and tetrachlorantraniliprole) in tomato, cucumber, pepper, rice, and corn had the most obvious signal inhibition, 80.22%, 64.37%, 84.12%, 78.75%, and 90.12%, respectively. The ME values for all target compounds ranged from −80.22% to 58.37% in tomato, −64.37% to 12.15% in cucumber, −84.12% to 39.76% in pepper, −48.48% to 38.01% in cabbage, −46.96% to 35.30% in apple, −78.75% to 1.79% in rice, and −84.19% to 53.3% in corn, indicating ion suppression or enhancement. The results also implied that the ME of most target compounds in the seven matrices still existed despite the inclusion of the clean-up procedure.

Extracts of vegetable, fruit, and cereal matrices generally contained a lot of components, such as fats, proteins, pigments, fatty acids, and sugars. These compounds can increase the surface tension of the droplets and the viscosity of the sample, resulting in a decrease in the evaporation efficiency of the ten diamide insecticides.[48,49] As is known to all, the occurrence of matrix effects should be calculated when LC-MS with ESI analysis was used to co-elute sample constituents. The ME can enhance or suppress analyte signals depending on the level of ion inhibition and may also lead to inaccurate quantitative results. The evaluation of ME was very important for LC-MS/MS analysis because it can affect the trueness and sensitivity of the proposed method.[35] Therefore, to evaluate the influence of the ESI source, the ME was calculated by comparing the slopes acquired in matrix spiked calibration and those acquired in standard solution calibration. The negative and positive results suggest that the ion signal was suppressed and enhanced, respectively. As mentioned in previous studies, to obtain accurate results, the matrix-matched standard calibration was used for quantification.[7,35,50] Thus, in the current study, this method was utilized to compensate the ME for quantitative analysis. All the above results show the potential of the developed QuEChERS and HPLC-MS/MS methods to detect the ten diamide insecticides for food safety analysis.

Table 3 Recoveries ($n = 15$, %), RSD_r[a] and RSD_R[b] (%) for matrix-spiked samples

	Sorbent	50 mg PSA			20 mg PSA + 30 mg C18			50 mg PSA			20 mg PSA + 30 mg C18			20 mg PSA + 30 mg C18			20 mg PSA + 30 mg C18			50 mg PSA		
	Spiked level	Tomato			Cucumber			Pepper			Cabbage			Apple			Rice			Corn		
Compound	($\mu g\ kg^{-1}$)	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]	Recovery	RSD_r[a]	RSD_R[b]
Flubendiamide	5	99.4	7.9	7.1	91.5	2.1	3.4	96.1	1.2	7.0	86.0	5.6	9.5	98.9	3.9	13.1	98.3	7.2	14.4	87.2	1.7	3.2
	100	103.2	6.1	7.5	90.2	6.6	9.7	91.7	2.3	6.5	92.9	6.7	5.6	99.2	4.1	14.0	90.3	1.8	8.6	96.1	2.9	9.0
	1000	106.0	4.5	5.5	89.4	9.0	6.8	93.6	1.5	9.3	90.1	2.4	5.5	102.8	2.3	7.4	86.3	6.3	8.3	100.7	6.6	8.5
Cyhalodiamide	5	100.2	6.5	6.8	88.7	2.5	7.5	96.1	1.3	3.8	86.4	6.3	9.2	108.2	3.0	9.5	95.1	3.3	12.8	90.7	3.4	3.6
	100	103.9	2.8	8.4	90.5	3.4	7.3	93.9	2.4	3.0	93.2	7.9	8.5	100.1	12.3	15.7	89.7	4.2	7.6	97.4	2.0	6.0
	1000	104.2	4.3	11.5	86.1	9.5	9.0	97.0	1.8	5.7	91.1	2.2	5.6	101.4	2.9	8.7	90.1	5.4	7.3	100.2	2.7	7.5
Chlorantraniliprole	5	93.2	3.6	13.2	104.9	3.0	4.1	99.1	3.1	6.5	91.8	2.9	10.8	88.3	10.8	7.7	94.9	8.4	13.8	93.0	4.1	9.8
	100	102.2	9.5	9.2	90.6	1.3	2.3	88.3	8.9	7.3	94.9	1.6	3.8	94.2	7.8	11.2	91.3	4.7	5.4	89.2	4.4	9.3
	1000	91.7	6.1	10.6	90.4	3.4	8.3	87.7	1.6	3.6	99.8	1.1	3.9	100.5	3.6	4.3	92.5	2.3	5.1	87.3	8.2	8.5
Cyantraniliprole	5	94.6	8.6	7.4	92.1	3.5	4.7	93.8	6.3	7.2	89.0	2.2	8.9	99.1	7.4	8.7	95.8	7.2	12.3	88.3	7.3	7.8
	100	93.8	7.3	6.2	85.5	2.4	7.3	83.4	4.0	6.3	93.3	2.0	3.4	92.5	6.2	10.4	89.9	4.0	6.3	95.5	8.7	8.2
	1000	89.6	1.8	5.8	87.1	3.2	3.7	88.3	1.1	4.9	96.0	1.3	2.9	97.7	2.7	4.9	88.0	2.5	4.2	98.5	5.4	8.8
Tetra chlorantraniliprole	5	94.4	5.2	3.5	96.0	1.2	5.0	92.9	2.3	7.6	86.1	4.5	9.0	99.9	1.7	9.3	97.2	4.0	15.3	88.4	4.9	7.8
	100	97.2	6.9	9.5	92.1	6.0	8.3	95.9	1.8	2.7	96.0	4.9	5.7	98.0	13.4	12.9	106.5	2.6	5.8	88.3	2.7	5.0
	1000	96.7	2.7	7.2	91.9	6.8	7.5	100.6	3.9	4.0	90.8	1.8	4.0	99.4	1.5	6.1	108.1	1.2	6.3	99.7	1.4	3.2
Tetraniliprole	5	93.8	6.1	10.1	99.3	1.8	7.0	97.3	5.7	12.6	97.7	4.7	9.1	89.7	9.7	9.1	99.1	5.7	13.4	95.0	6.0	10.3
	100	97.1	5.9	8.6	95.3	2.1	4.4	92.3	11.0	10.5	94.1	5.6	6.7	93.0	9.5	12.5	95.7	4.7	4.9	100.4	3.5	13.7
	1000	93.1	5.3	6.8	95.5	4.4	5.1	93.9	1.5	9.8	95.8	4.4	7.6	96.8	2.4	5.1	95.3	1.3	7.0	90.1	7.2	11.2
Thiorantraniliprole	5	76.6	4.1	4.6	77.0	4.8	5.8	93.5	5.1	9.9	86.0	2.9	6.4	90.9	4.7	5.3	87.7	8.3	9.9	88.5	3.1	7.7
	100	93.7	4.2	5.4	85.7	1.0	2.9	80.3	7.1	6.8	89.3	1.8	9.6	86.2	1.6	8.7	91.0	2.8	6.7	94.1	5.3	6.2
	1000	91.6	2.1	2.3	88.8	1.5	4.3	91.0	2.6	11.1	99.1	1.4	8.2	96.0	1.4	4.2	90.2	7.4	8.5	96.9	1.5	6.3
Cyclaniliprole	5	94.8	5.9	8.2	91.5	2.5	6.0	93.5	3.6	8.4	91.5	4.9	6.2	101.7	5.7	6.7	91.0	10.8	12.9	86.3	9.0	9.8
	100	101.1	6.0	9.1	86.2	7.4	7.8	96.9	2.8	4.1	94.7	4.1	4.2	93.6	9.5	14.4	91.6	2.0	7.2	90.1	3.1	10.4
	1000	107.5	6.9	9.5	84.6	8.5	8.6	106.2	2.7	6.5	87.3	1.3	2.5	101.0	2.3	7.5	101.0	3.3	5.0	99.8	5.8	11.4
Broflanilide	5	90.4	5.0	6.4	96.3	3.4	7.5	99.0	5.4	9.0	86.9	4.9	9.1	96.1	3.5	9.6	94.6	10.5	7.6	86.7	5.4	6.1
	100	83.7	3.6	9.0	90.3	1.1	6.1	84.8	1.8	8.2	94.6	1.7	4.3	98.9	1.6	5.5	96.2	3.3	7.0	90.3	11.3	8.7
	1000	83.0	3.4	8.0	97.7	1.4	7.8	90.2	5.0	5.5	96.0	4.2	7.4	101.1	2.8	5.3	88.0	2.5	4.7	89.7	5.2	6.5
Fluchlordiniliprole	5	95.8	4.2	4.6	87.5	3.9	9.0	93.5	5.1	93.5	93.2	2.4	9.9	92.2	5.2	7.7	97.5	6.9	7.2	92.1	3.3	7.6
	100	89.8	4.7	5.2	89.2	5.7	5.4	92.4	2.9	92.4	97.1	1.9	9.2	104.2	2.3	11.9	97.8	1.4	4.6	98.0	5.9	9.8
	1000	92.6	2.9	4.0	97.6	11.0	7.9	8.2	5.2	6.4	95.3	7.0	10.7	98.1	2.7	3.0	95.9	2.5	6.8	89.5	4.4	5.1

[a] RSD_r: intra-day ($n = 5$), which is the RSD for repeatability. [b] RSD_R: inter-day ($n = 15$), which is the RSD for reproducibility.

3.4. Comparison with the literature methods

The analytical performance of the proposed method was further evaluated by comparing with previous literature methods used for the determination of the ten diamide insecticides in terms of several parameters, including LOD, LOQ, analysis time, and RSD. As shown in Table S1,† the literature methods usually studied 1–2 of the ten diamide insecticides, with only five studies covering 5–6 of them. In contrast, this developed method included ten diamide insecticides, and 3–4 of them had no analytical methods for vegetables, fruits or cereals. It is worth noting that the LC or LC-MS methods in the previously reported literature showed relatively high LOQs.[22,51–56] For example, LOQs for tetraniliprole, chlorantraniliprole, and flubendiamide in literature methods were 50 μg kg^{-1}, 60 μg kg^{-1}, and 50 μg kg^{-1}, respectively. Whereas in the method proposed herein, the LOQ was 5 μg kg^{-1} in all seven matrices. Similarly, analysis times for LC and LC-MS of these compounds were longer in the literature methods than in the developed method. For example, the analysis times for cyantraniliprole, chlorantraniliprole, flubendiamide, and tetraniliprole in literature methods were 40 min, 12.5 min, 20 min, and 15 min,[51,52,55,57] respectively, while the analysis times were shorter than 6 min in the developed method. The LODs were defined as the lowest concentration of the ten target compounds detected in the seven matrices. The values of LOD in the proposed method were comparable to those in literature methods for the determination of the ten diamide insecticides. Most of the reported literature studies also used LC-MS/MS to detect diamide insecticides, except that LOQs of cyantraniliprole in Zhang's method, chlorantraniliprole in Telo's method, tetraniliprole in Ma's method, and fluchlordiniliprole in Wu's method are lower than those of the proposed method.[21,22,58,59] The LOQs of the ten diamide insecticides in other literature LC-MS/MS methods are higher than or equal to the values of the proposed method. In addition, the analytical methods for the simultaneous determination of the ten diamide insecticides have not been reported. The sample matrix of the proposed method, including vegetables, fruits, and cereals, is comprehensive and meets the requirements of pesticide residue supervision. Given the above, the sensitivity and precision of the developed method were better than or equal to the values in the literature methods. The proposed method is easy, inexpensive, and rapid, and it is suitable for daily detection of the ten diamide insecticides in agricultural products.

3.5. Application to real samples

Unreasonable use of pesticides can affect crop growth and food safety and pollute the environment. In the current study, seventy real samples (10 per matrix) were bought from the local markets in Zhengzhou, Henan Province (China), and analyzed in accordance with the previously mentioned method (Section 2.3) to detect the pesticide residue and evaluate the effectiveness and applicability of the developed method. Two pepper samples, one apple sample, one rice sample, and one corn sample were found to contain chlorantraniliprole in the range of 0.86–7.4 μg kg^{-1}. Cyantraniliprole was detected in one positive rice sample, and the concentration was 8.1 μg kg^{-1}. No positive samples were detected for the other diamide insecticides. In order to ensure food safety and protect the environment, many countries have established legal and monitoring measures to control the use of pesticides. In addition, they also have established the MRLs of these compounds in food. The concentration of chlorantraniliprole and cyantraniliprole in some of the samples was far lower than MRLs established by the EU and China. The MRLs of chlorantraniliprole in pepper, apple, rice, and corn are 1000 μg kg^{-1} (EU) and 600 μg kg^{-1} (China), 400 μg kg^{-1} (EU) and 2000 μg kg^{-1} (China), 400 μg kg^{-1} (EU) and 500 μg kg^{-1} (China), and 10 μg kg^{-1} (EU) and 20 μg kg^{-1} (China), respectively. The MRLs of cyantraniliprole in rice in the EU and China are 10 μg kg^{-1} and 200 μg kg^{-1}, respectively. The frequency and concentration of diamide insecticide residues in food were found to be low. Chlorantraniliprole and cyantraniliprole were the major residual contaminants detected. The results also imply that the developed method could obtain satisfactory results during the analysis of real samples. The residual diamide insecticides in food matrices are unlikely to pose a threat to consumer health. However, some of the new diamide insecticides mentioned in the current study are being registered worldwide for use against pests. Therefore, monitoring the residues of these diamide insecticides in agricultural products should be strengthened.

4. Conclusions

A sensitive, simple, and reliable method based on QuEChERS extraction and HPLC-MS/MS analysis was developed to detect and quantify ten diamide insecticides, which are being widely registered worldwide with most of them not regulated with MRLs in agricultural products, in seven representative plant origin foods (tomatoes, cucumbers, peppers, cabbages, apples, rice, and corn). The effects of extraction solvent, sorbent combination, mobile phase composition and proportions were carefully studied. The LODs and LOQs were 0.01–1 μg kg^{-1} and 5 μg kg^{-1}, respectively. The correlation coefficients R^2 were > 0.99. The recoveries ranged from 76.6% to 108.2%. RSD_r and RSD_R ranged from 1.0% to 13.4% and 2.3% to 15.7%, respectively. The results indicated that the proposed method had high sensitivity, good linearity, satisfactory recoveries and repeatability. This method has been successfully applied to the detection of the ten diamide insecticides in real samples. Chlorantraniliprole and cyantraniliprole were detected in agricultural products, and their concentrations were far lower the MRLs established by the EU and China. The residual diamide insecticides in food matrices are unlikely to pose potential risk to consumer health. In a word, the newly proposed method can be applied to monitor the ten diamide insecticide residues in vegetables, fruits, and cereals and can provide an effective reference for the research and formulation of MRLs of cyhalodiamide, tetrachlorantraniliprole, tetraniliprole, thiorantraniliprole, cyclaniliprole, broflanilide, and fluchlordiniliprole in agricultural products. It is worth noting that the universality of the QuEChERS method and the multi-residue analysis of

HPLC-MS/MS can allow this developed method to be expanded to more pesticides and matrices.

Data availability

Data will be made available on request.

Author contributions

Fajun Tian: methodology, writing – original draft, writing – review & editing, investigation. Zhenzhen Zhou: investigation, validation. Junfeng Lu: investigation, software. Chengkui Qiao: software. Caixia Wang: investigation. Tao Pang: investigation. Linlin Guo: validation. Jun Li: validation. Rongli Pang: visualization. Hanzhong Xie: writing – review & editing, conceptualization.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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