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Screening of pesticide residues in Traditional Chinese Medicines using modified QuEChERS sample preparation procedure and LC-MS/MS analysis

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ABSTRACT

A robust and high-throughput method was developed for the determination of 108 pesticide residues in Traditional Chinese Medicines (TCMs) simultaneously using a combination of UHPLC-MS/MS analysis and the modified QuEChERS method. Extraction was carried out in acetonitrile containing 0.75% (v/v) acetic acid with ultrasonication for 15 min; $MgSO_4$ and C18 were used as the dispersive-solid phase extraction sorbents. The method exhibited good linearity ($r^2 > 0.9901$), in addition to good selectivity, precision and repeatability. More than 92% of pesticides exhibited high rates or recovery in the 70–120% range. This method showed high sensitivity, with Limits of Quantitation in the 0.01–20 ng/mL range in Cortex Moutan, and 0.01–50 ng/mL in the other TCMs. The method was employed for the analysis of 39 real samples from different habitats, and pesticides were detected in 92.3% of the samples, with 26 pesticides being detected in these three TCMs. More than four pesticides were detected in a third of the samples. Among them, tebuconazole was detected in all the three TCMs with 0.22–22.02 μg/kg concentration, which was lower than the provisions in GB 2763-2019 (50 μg/kg). In addition, the paclobutrazol detection rate in *Ophiopogon japonicus* was 100%, and the detected concentrations of 9 samples exceeded the Maximum Residue Levels defined for vegetables (50 μg/kg). Considering there are no regulations that govern the limits of pesticide residues in the three TCMs in China, we recommend the acceleration of efforts to introduce appropriate regulations.

1. Introduction

Traditional Chinese Medicine (TCM) has a long history in China and is gaining popularity globally for the treatment of various diseases. The tuberous roots of *Ophiopogon japonicus* (Thunb.) Ker-Gawl. (Liliaceae), called Maidong in Chinese and mainly produced in the Sichuan Province, are a popular TCM. It is used to treat acute cough, numerous cardiovascular diseases and sore throats with relatively few side effects [1–3]. The rhizomes of *Polygonatum odoratum (Mill.) Druce*, called Yuzhu in Chinese, which are mainly produced in the Hunan Province, are used to treat fever, dry cough, heart disease, diabetes, tuberculosis, etc. Cortex Moutan, the bark of *Paeonia suffruticosa* Andr, which is called Mudanpi in Chinese, and is produced mainly in the Anhui Province, promotes blood circulation and resolves blood stasis. Previous studies have reported that 65–80% of the global population prefer treatments based on medicinal plant products over chemical treatments [4,5]. In addition to their medicinal effects, *O. japonicus* and *P. odoratum* are incorporated widely in daily diets in China.

In recent years, safety of TCMs has gained more attention in China, owing to their therapeutic effects and edible safety. Similar to other food products, TCMs are exposed to contaminants external contaminations such as pesticides, which are used in the course of growth, harvesting, storage and processing. The high demand for TCM has increased their scale of artificial cultivation. In addition, pesticides are

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inevitably used to increase their production both in the wild and in artificial systems, and pesticide residues may affect the safety of such TCMs.

The World Health Organization [6] has established guidelines and criteria to ensure TCM quality. However, currently, China has only defined a few limits for pesticide residues in TCMs; which has led to inconsistencies in standards between exporting and importing countries, which, in turn, affects the global trade in TCMs. In China, Maximum Residue Levels (MRL) for approximately 600 pesticides have been defined for food. However, limits for only 5 organochlorine pesticides have been defined for only 5 TCM materials such as ginseng [1]. The European Pharmacopoeia and the United States Pharmacopoeia have set much more limits for pesticide residues in TCMs. The European Pharmacopoeia (EP8.0) [7] and the United States Pharmacopoeia (USP38) [8] have established MRLs for a total of 105 pesticides including organophosphorus, organochlorine and pyrethroid pesticides. However, the standards do not specifically target the TCMs studied in this article; therefore, to take into account the Limits of Quantitation (LOQ) of the instrument and the pesticide residues in the real samples, the limits will be compared with those in GB 2763-2019 [9]. We conducted field investigations in Sichuan Province and observed that paclobutrazol, a growth retardant used in large-scale, was applied in the cultivation of *O. japonicas* to increase production. However, some studies have shown that the application of paclobutrazol could affect active substances, for example, by inhibiting saponin accumulation in *O. japonicas*, in turn, affecting its quality [10,11]. Therefore, the development of a convenient, accurate, quantitative, and sensitive methods for the analysis of pesticide residues in TCMs is essential for the appropriate application of different types of pesticides during TCM cultivation.

The Quick Easy Cheap Effective Rugged and Safe multiresidue (QuEChERS) method is a novel sample preparation methodology for pesticide multiresidue analysis which was first reported in 2003 [12]. The main reason why QuEChERS is widely used is that it can achieve rapid and effective extraction. Some researchers have modified the method and made it applicable in some complex matrix like TCM [13–16]. Due to complex components of TCMs and trace amounts of pesticides in herbs, it is difficult and challenging to detect pesticides in TCMs. Various analytical methods have been developed for the detection of pesticide residues in TCMs, in addition to some novel detection technologies and rapid inspection technologies like dual-readout immunochromatographic assay [17], sweeping-micellar electrokinetic chromatography [18], and enzyme inhibition method [19], some common methods such as gas chromatography or liquid chromatography coupled with different detectors including flame photometric detector (FPD) [20,21], electron capture detector (ECD) [22,23], nitrogen phosphorus detector (NPD) [24] are often used. However, the most common methods are gas chromatography-mass spectrometry (GC–MS) [13,25], gas chromatography-tandem mass spectrometry (GC–MS/MS) [26–29], and liquid chromatography-tandem mass spectrometry (LC-MS/MS) [30–34]. Since most pesticides decompose at high temperatures, derivatization may be required while using GC, which makes the method complicated and time consuming [34]; thus, LC-MS/MS is the most commonly used detection method. Ultra High Performance Liquid Chromatography coupled to Tandem Mass Spectrometry (UHPLC-MS/MS) can provide qualitative and quantitative information for a wide range of analytes [35]. Its dynamic multiple reaction monitoring (dMRM) mode not only has the advantages of MRM mode, such as reduced interference and improved instrument analysis accuracy [36], but can also scan in positive and negative ion modes simultaneously. This saves analysis time and improves efficiency considerably. Owing to these features, the popularity of the technology is increasing gradually.

The aim of this study was to develop a robust and high-throughput method for the simultaneous determination of 108 pesticides (including insecticide, fungicides, herbicides and plant growth regulators) in TCMs. This approach is based on the rapid and sensitive UHPLC-MS/MS method coupled with a modified QuEChERS method, which uses a dispersive-solid phase extraction (d-SPE) clean-up procedure. The detection was optimized for the qualification and quantitation of each analyte within 21 min per sample. We investigated the optimal volume of the water and the extraction solvent, acid concentrations, ultrasonic extraction time, type and amount of the sorbent, because these are the major factors which affect the extraction and clean-up efficiency. To assess the efficacy of the method, it was used to analyze 108 pesticides in several batches of *O. japonicus*, *P. odoratum* and Cortex Moutan.

2. Materials and methods

2.1. Chemicals and reagents

A total of 108 pesticides with purity exceeding 98.0% were purchased from Dr. Ehrenstorfer (LGC Standards; Augsburg, Germany). Acetonitrile, methanol, formic acid, and ammonium acetate were HPLC-grade and were purchased from Thermo Fisher Scientific (Fisher, NJ, USA). Sodium chloride (NaCl) and anhydrous magnesium sulfate ($MgSO_4$) were purchased from Beijing Chemical and Reagent (Beijing, China). Primary secondary amine (PSA), octadecylsilyl (C18), graphitized carbon (GCB), TPH (500 mg/6 mL) and TPT (500 mg/6 mL) SPE cartridges were obtained from Agela technologies Co., Ltd (Tianjin, China). Nanomaterials including different sizes of multi-walled carbon nanotube (MWCNT) (< 8nm, 10–20 nm, 20–30 nm) and Al_2O_3 (10–20 nm) were purchased from Macklin Biochemical Co., Ltd (Shanghai, China). Multi-plug filtration clean-up (m-PFC) was obtained from Lumiere Tech Ltd (Beijing, China). Ultra-pure water was obtained using a Milli-Q water purification system (Millipore, Bedford, MA, USA). *O. japonicus*, *P. odoratum* and Cortex Moutan used in method optimization and validation processes were obtained from the test field, where it could be verified that no target pesticides had been applied. The real samples of the three TCMs were purchased online from Tmall.com. A total of 12 samples of *O. japonicus* were purchased, and 11 samples originated from Sichuan and the other sample originated from Zhejiang; 14 samples of *P. odoratum* were purchased, and 13 samples originated from Hunan and the other sample originated from Anhui; 13 samples of Cortex Moutan were purchased, and 12 samples originated from Anhui and the other sample originated from Yunnan. All the TCM samples were ground into fine powder using a high-speed pulverizer and passed through a 0.25 mm sieve and then stored at −20 °C prior to analyses.

2.2. Chromatography and mass spectrometry conditions

Chromatographic separation was carried out on a 1290 Infinity UHPLC system coupled to a 6495A Triple Quadrupole mass spectrometer (Agilent Technologies, Wilmington, DE, USA) equipped with a degasser, a binary pump, and an electrospray ionization source (AJS ESI), with dynamic multi reaction monitoring for detection to obtain the highest response and best sensitivity. All target pesticides were separated in an alternative column, Agilent Poroshell 120 EC C18 column of 100 mm × 3.0 mm, 2.7 μm (Agilent Zorbax Eclipse), at 40 °C. This column enables a good peak shape and separation for these target analytes and moderately reduced the coeluting interference from the matrices. In addition, the composition of the mobile phase could considerably influence the separation of the analytes and the performance of the ionization process. The mobile phases were water containing 0.05% formic acid and 2.5 mmol/L ammonium acetate (phase A), and pure methanol (phase B). Furthermore, gradient elution was carried out as the follows: 0–0.5 min, 10% B; 0.5–5 min, 10–50% B; 5–20 min, 50–100% B; 20–21 min, 100% B; 21–21.1 min, 100–10% B; finally, the mobile phase was maintained for 2 min under the initial conditions to rebalance the system before the subsequent injection with a flow rate of 0.4 mL/min. Under such gradient elution conditions, the

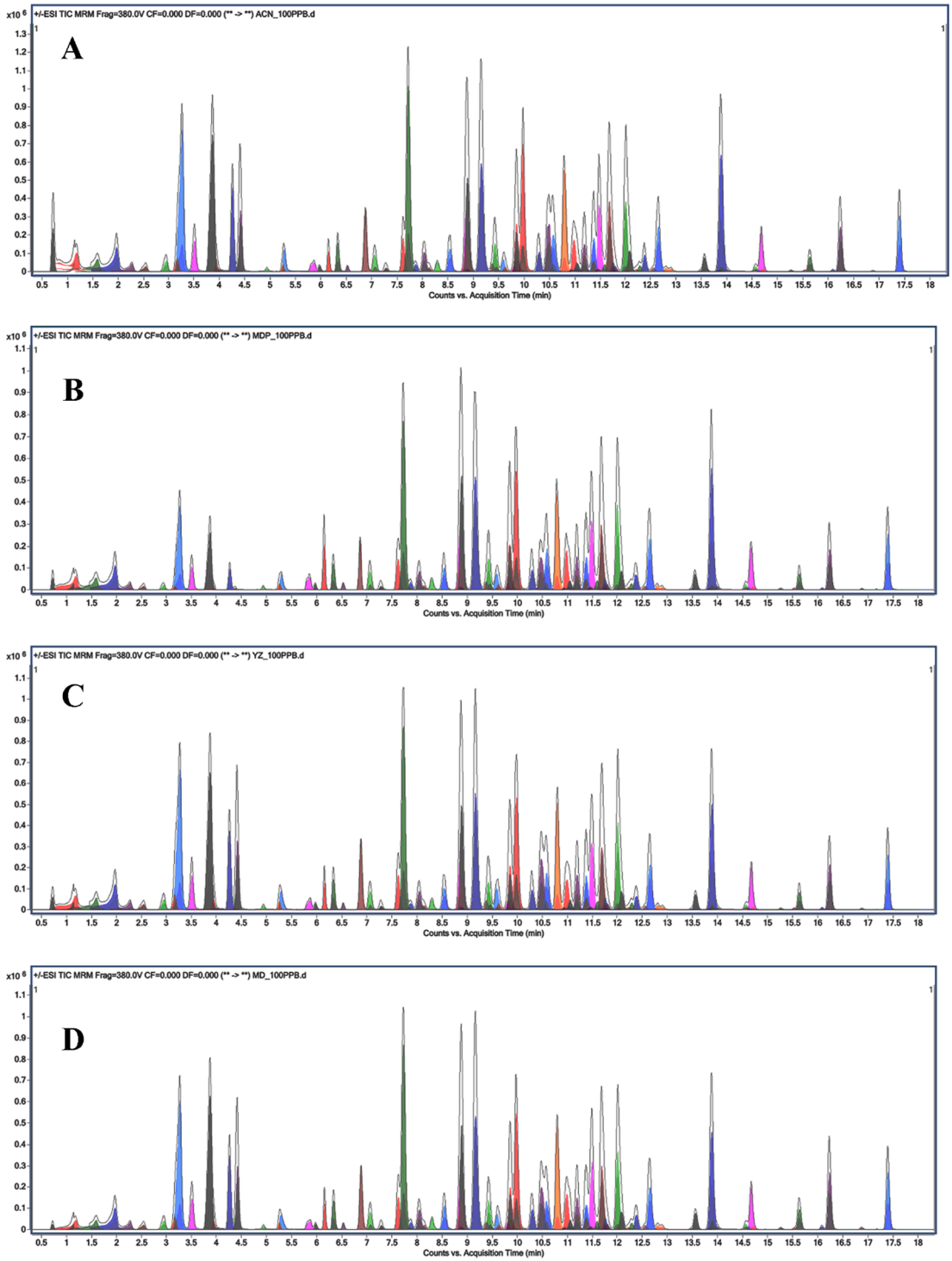

Fig. 1. MRM stacked chromatogram of 108 pesticides in mixture standards (A) and different matrix extracts- *O. japonicus* (B), *P. odoratum* (C) and Cortex Moutan (D).

detection can be completed within 21 min; with every pesticide well separated and good peak shapes. Afterwards, 2 μL of the sample or standard solution was injected into the column. The target pesticides were determined using dMRM, where both positive ion and negative ion mode exist simultaneously. For the mass spectrometry analysis, nitrogen was supplied as the nebulizer and the collision gas. The ion source parameters were set as follows: a capillary voltage of 3.5 kV for the positive mode and 3 kV for the negative mode; a source temperature of 150 °C; a desolvation temperature of 325 °C; a sheath gas (argon) flow rate of 15 L/h; and a drying gas (nitrogen) flow rate of 11 L/h. The retention time, parent ion, daughter ion, mode, and collision energy were optimized individually for each of the analytes and are listed in Table S1. The UHPLC-MS/MS dMRM chromatograms of the 108 pesticide standards and TCM samples have been illustrated in Fig. 1.

2.3. Standard solution preparation

The stock solutions of each of the pesticides were prepared at a concentration of 1000 mg/L in acetonitrile or methanol. Prior to the analysis, a stock of multi-standard solution containing 10 mg/L of each pesticide was prepared in acetonitrile, and stored at −20 °C. To avoid the degradation of the analytes, various concentrations of standard

working solutions need to be prepared daily by appropriately diluting the stock multi-standard solutions in blank matrix extracts or acetonitrile. All solutions need to be filtered through a 0.22 μm membrane prior to analysis.

2.4. Sample preparation

2.4.1. Extraction method optimization

Extraction method optimization involved the optimized volume of the water, the extraction solvent, acid concentrations, and ultrasonic extraction time. We designed 25 sets of experiments, listed in Table S2. Homogenized samples (2.00 g) were placed into 50 mL centrifuge tubes and certain amounts of 10 mg/kg pesticide mixed standard solutions added to achieve a final concentration of 100 μg/kg, and then mixed with A mL water. In addition, C mL acetonitrile containing B% acetic acid was added to the mixture, and then extracted ultrasonically for D min at room temperature. The sample was centrifuged at 8195 *g* for 5 min. Finally, the supernatant was filtered through a 0.22 μm nylon organic membrane and transferred to the injection vial prior to the UHPLC-MS/MS analysis. The proportion of pesticides with a recovery rate between 70% and 120% among 108 pesticides under different extraction conditions was calculated. In addition, the average recovery rates and their Relative Standard Deviations (RSDs) were determined during analyses. The preferred recovery rate is one close to 100% with an RSD $<$ 20%.

2.4.2. Clean up method optimization

This procedure consisted mainly of sorbent type and amount optimization. First, the pesticide recoveries of the sorbent used alone were investigated, and then the effect of the combined application of different sorbent dosages was examined (16 sets of experiments, listed in Table S3). Finally, the results of the optimal combinations were compared with those of commercially available products. The exact procedure was as follows: after extraction, 1.0 mL of the upper organic layer was introduced into a new Teflon centrifuge tube containing different dosages of sorbent. They were mixed and then vortexed for 1 min, then centrifuged at 16,725 *g* for 5 min. Finally, the supernatant was filtered through a 0.22 μm nylon organic membrane and transferred into an injection vial prior to the UHPLC-MS/MS analysis. The proportions of pesticides with recovery rates in the 70–120% range among 108 pesticides under different clean up conditions, average recovery rates and RSD, were determined.

2.4.3. Optimized sample preparation

Homogenized samples (2.00 g) were placed into 50 mL centrifuge tubes and mixed with 10 mL water. In addition, 6 mL acetonitrile containing 0.75% acetic acid was added to the mixture, and ultrasonically extracted for 15 min at room temperature. The sample was centrifuged at 8195 *g* for 5 min. Thereafter, 1.0 mL of the upper organic layer was introduced into a new Teflon centrifuge tube containing 150 mg anhydrous $MgSO_4$ and 25 mg C18. Mixed them and vortexed for 1 min, then centrifuged at 16,725 *g* for 5 min. Finally, the supernatant was filtered through a 0.22 μm nylon organic membrane and transferred to the injection vial prior to the UHPLC-MS/MS analyses.

2.5. Method validation

The method was validated with regard to linearity, sensitivity, precision (intra- and inter-day variability) and accuracy. The calibration curves are linear equations of peak area in relation to solution concentration. Each calibration curve was plotted with at least five appropriate concentrations (generally 0.05–0.2 mg/L, for pesticides with LOQ $>$ 0.05 mg/L, the concentration levels are LOQ-0.2 mg/L) in triplicates. The limits of determination (LODs) and the LOQs for each target pesticides were determined at the minimum detection levels with signal-to-noise ratios (S/N) of approximately 3 and 10, respectively. Precision was assessed by replicating the analyses (n = 6) of standard samples within a day (intra-day variation) and in three consecutive days (inter-day variation). The accuracy of the method was determined by adding the target pesticides at four different concentrations (10 μg/L, 50 μg/L 100 μg/L, and 200 μg/L) to the sample that were previously analyzed. The repeatability of the method was determined by analyzing the six independently prepared solutions of sample that spiked the same concentration of standard solvent. Stability was evaluated by repeat analyses of the same spiked sample solutions at 0 h, 3 h, 6 h, 12 h, 18 h and 24 h at room temperature. The formula for calculating the average recovery rates was: recovery (%) = (amount detected/amount added) × 100%.

2.6. Matrix effect

To assess the matrix effect (ME), serial concentrations (5 ng/mL, 20 ng/mL, 50 ng/mL, 100 ng/mL, and 200 ng/mL) of standards which were prepared in three types of blank matrix extract (*O. japonicus*, *P. ordoratum* and Cortex Moutan) and in solvent, respectively. The ME was calculated using the following equation: ME (%) = $k_{matrix}/k_{solvent} \times 100$, k_{matrix} is the slope of the matrix-matched calibration curve and $k_{solvent}$ is the solvent-only calibration curve. In general, if the ME (%) is between 80% and 120%, we can ignore the ME, a value greater than 120% is considered a signal enhancement, while a value $<$ 80% is considered signal suppression. Data processing was performed using Excel (Microsoft Corp., Redmond, WA, USA) (2016) and Origin v8.5 (OriginLab Corp., Northampton, MA, USA).

3. Results and discussion

3.1. Extraction method optimization

Previously, the QuEChERS method was used to extract pesticides in fruits and vegetables [12]. Now, QuEChERS method is used widely because it can achieve a quick and effective extraction, this method enables introduction of various modifications at almost each step of analysis [37].

To detect pesticide residues in TCMs, improved extraction methods are required for superior analysis results for the target analytes. Most commercial TCMs have a moisture content $<$ 10%. The QuEChERS method requires the sample to have a certain level of moisture; therefore, it cannot be applied directly, and some water has to be added to a sample to make pores in the sample accessible during extraction [30,38]. We investigated the effects of adding different volumes of water (0 mL, 5 mL, and 10 mL) on extraction efficiency. We did not use methanol as the extraction solvent considering its high polarity, which may inhibit the complete extraction of non-polar or mid polar pesticides. In addition, extraction with methanol would extract high amounts of sugars and make the extraction solution dark and sticky [39]. Hence, in this study we selected acetonitrile as the extraction solvent. In the multi-residue analyses, the use of acid may influence the efficiency of the extraction and the stability of some pesticides; it can improve the extraction efficiency of pesticides, especially plant growth regulators [40]. Therefore, this study investigated the volume of acetic acid (0%, 0.75%, 1.5%) added to acetonitrile while investigating the addition volume of acetonitrile (2 mL, 6 mL, 10 mL). For the ultrasonication process, the most important factor is extraction time; therefore, the effect of ultrasonication time on the analyte extraction between 5 and 15 min was investigated. The results have been presented in Fig. 2. Under the experimental conditions of groups 3, 16, 17, 20 and 23, approximately 96% of the pesticide recovery rate was 70–120%; however, under the group 23 condition, the recovery rate was closer to 100% and the RSD was lower than those of the others. Consequently, we selected 10 mL water and 6 mL acetonitrile (containing 0.75% formic acid) with 15 min ultrasonic treatment as the extraction procedure. Approximately 96% of the pesticide recoveries

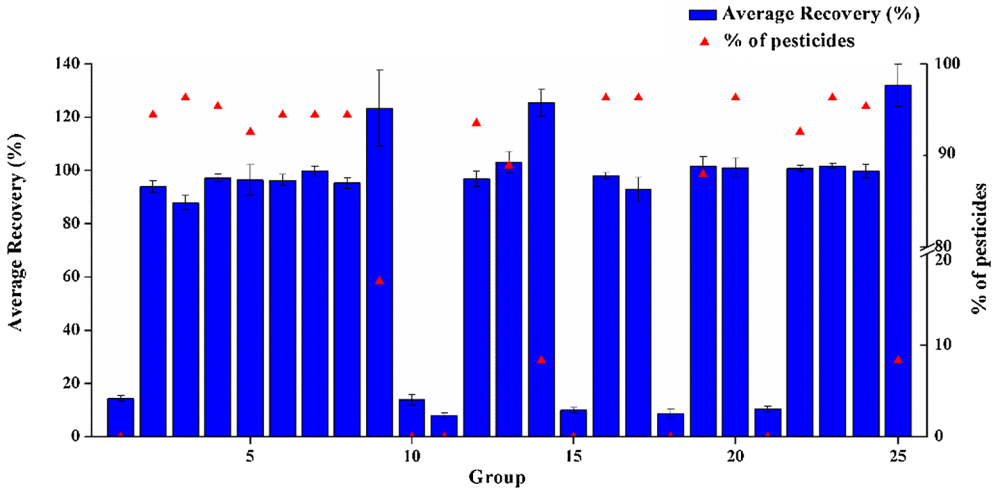

Fig. 2. Effect of different extraction conditions on the recoveries and proportions of qualified pesticides of target compounds.

were in the 70–120% range, with RSD < 20%, and the average recovery rates under such a condition was 101.59%, RSD was 0.9%.

3.2. Clean up method optimization

Owing to the presence of high concentrations of numerous natural molecules and redox-active secondary metabolites or antioxidants (ascorbic acid, carotenoids, flavonoids, polyphenols, glutathione, tocopherols, tocotrienols and enzymes) and also a polar molecules of essential oils such as monoterpenes and sesquiterpenes [41], the extractions and analyses could be hindered, leading to low pesticide recoveries due to either interference or ion suppression. The d-SPE, a key clean-up step, is often used to eliminate the matrix interference.

GCB has a good adsorption effect on color impurities which makes it a frequently used carbon material [15,20]. However, according to the results in Fig. 3A, only 68% and 71% of the pesticides were qualified (average recovery was 86.01% with an RSD of 1.56%, average recovery of 83.22% with an RSD of 3.62%, respectively) after using 25 mg and 50 mg GCB purification. The proportion of the qualified pesticides was much lower than those under the use of other purification sorbents, which could be because the GCB provides a six-membered ring plane. Therefore, using considerable amounts of GCB could retain some targeted planar compounds such as ametryn and abamectin [42]; when using 25 mg and 50 mg GCB, the recoveries of these two pesticides were 68.40% and 46.88%, 27.38% and 23.36%, respectively. However, when using other purifiers, the recovery rates could satisfy the requirements. From Fig. 3A, we can infer if Al_2O_3 is used, although the overall recovery is good, the recovery of the most commonly applied

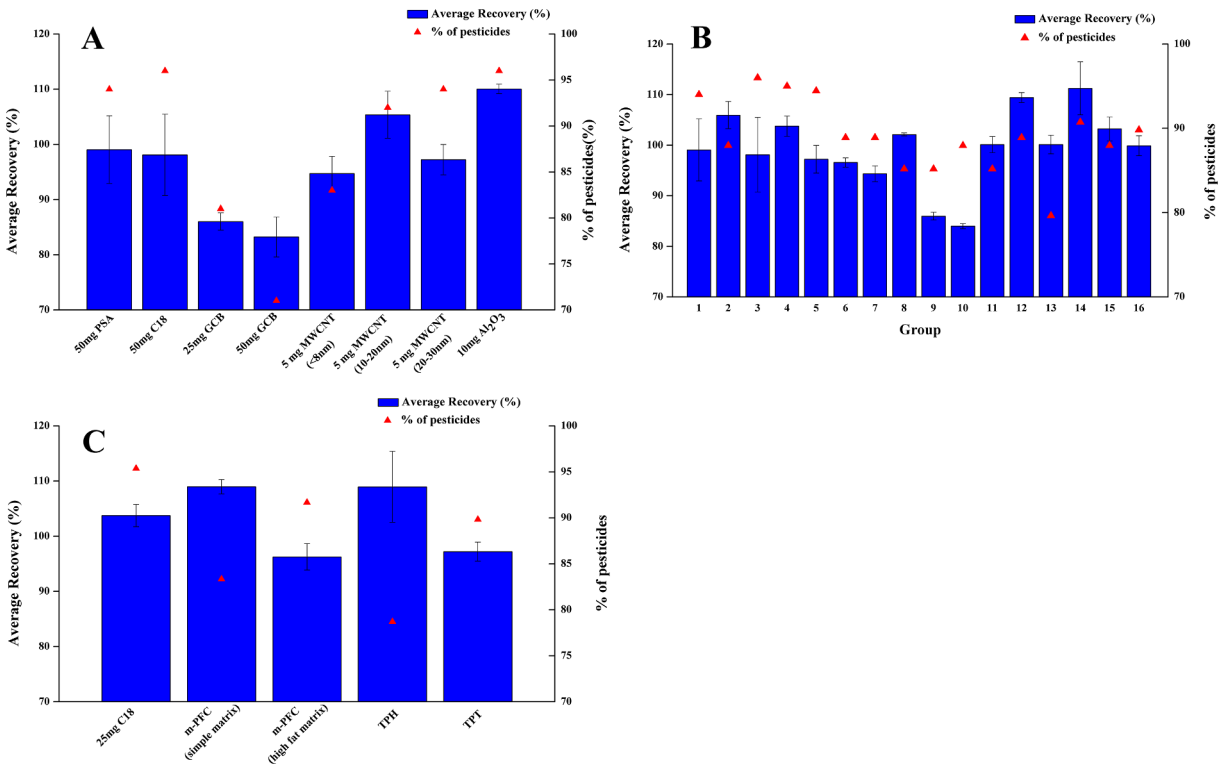

Fig. 3. Proportions of qualified pesticides and average recovery after using different sorbents to purify (A), different combinations of sorbents to purify (B), and comparison with commercially available purifiers (C).

pesticides in *O. japonicus*, such as paclobutrazol, is too high (about 125%) and could not satisfy the requirements. Therefore, in the subsequent optimization process, these two sorbents were not considered. MWCNT is a novel nanomaterial, with a large surface area and high adsorption capacity, and could be used to eliminate the interferences associated with pigments in fruits and vegetables [43,44], and in other complex matrices such as tea [45]. In addition, it has been reported that MWCNT could enrich pesticides [46]. So this study investigated MWCNTs with three different particle sizes (< 8 nm, 10–20 nm and 20–30 nm), and observed that the purification effect increased with an increase in particle size, with the proportions of qualified pesticides being 83%, 93%, and 94%, respectively, which suggest that small-sized nano-materials can adsorb target pesticides more easily. Although the proportions obtained using 10–20 nm and 20–30 nm MWCNT were similar, the average recovery of the latter (97.23%) was closer to 100% than the former (106%); therefore, we selected 20–30 nm MWCNT. When MWCNT is used as a sorbent, it influences the recovery rate of carbendazim, chlorbenzuron, epoxiconazole, methamidophos, and thiabendazole, and their recoveries were 68%, 59%, 139%, 66%, and 26%, respectively, based on 20–30 nm MWCNT. In addition, PSA and C18 had good results, with about 95% and 96% of the pesticides in a good recovery, respectively. Therefore, we focused on PSA, C18 and MWCNT with a particle size of 20–30 μm. Using these three purifiers, both the proportions of the qualified pesticides and the average recovery were good.

We observed that the recovery after the combination of the purifiers was significantly lower than when they were used individually (Fig. 3B). The highest proportion of qualified pesticides was observed when using C18 (96% for using 25 mg and 50 mg C18), followed by MWCNT (94%) and PSA (94%). PSA is a weak anion exchanger, and it is reported to have significant retaining activity for organic acids, fatty acids, sugars, and pigments; however, its pair acidity has an adsorption effect on some acidic substances [21]. Therefore, poor recoveries of plant growth regulators such as 2,4-D (12.12%), gibberellin (25.98%), indole acetic acid (56.91%) were obtained. Comparing the recovery of different amounts of C18, we find that the recoveries of the whole pesticides were not considerably different (both were 96%); however, when 50 mg C18 was used, the recovery of paclobutrazol (71.37%) met the requirements but was much lower than that obtained following the use of 25 mg C18 (100.15%). Therefore, we finally opted to use a combination of 25 mg C18 and 150 mg anhydrous $MgSO_4$.

Because there are already many purifying agents for TCMs and some complex matrices, this study compared the average recoveries of the commercially available purifiers with the sorbents selected in the present study (Fig. 3C) and observed that the proportions of qualified pesticides of 150 mg anhydrous $MgSO_4$ combined with 25 mg C18 (96%) was superior to those of other purifying agents (83% for m-PFC of simple matrix; 92% for m-PFC of high fat matrix; 79% for TPH; 90% for TPT).

3.3. Matrix effect

When using LC-MS/MS as the detection instrument, the potential for the ME to occur should be assessed, because the co-eluted substances could be protonated easily in competition with analytes in the ESI source. They may cause some quantitation challenges owing to signal enhancement or suppression, which would be a major drawback for LC-ESI-MS/MS. In this paper, the ME may cause inhibition or enhancement of ionization, which could lead to quantification errors. Therefore, The MEs for all the target pesticides in the three TCMs are illustrated in Fig. 4, where the MEs of most of the target pesticides were in the 80–120% range, and it is noticeable that 13 and 21 pesticides showed different degrees of signal enhancement or signal suppression in *P. odoratum* and *O. japonicus*, respectively. In Cortex Moutan, the matrix effect was more evident, which could be because of the presence of high concentrations of numerous natural molecules such as paeonol and paeoniflorin which may cause interferences or ion suppression [47]. Approximately 42 pesticides (39%) exhibited different degrees of signal enhancement or suppression, which means that during the HPLC-MS/MS analysis, some specific ingredients in the TCMs could have caused the ME. In addition, for pesticides with a strong ME, the scatter graph showed that pesticides with shorter RTs are more likely to cause signal suppression, while pesticides with longer RTs are more likely to lead to matrix enhancement effects.

To obtain accurate quantitative results, the most effective way of correcting errors caused by ME is calibration using the standard addition method, which is referred to as matrix-matched calibration. In this study, we used this method to compensate for the ME and, in turn, achieve accurate quantification of pesticide residues. Subsequent method validation results also showed that UHPLC-MS/MS could be used to analyze pesticide residues in TCM samples prepared using the QuEChERS method.

3.4. Method validation

The LODs and LOQs are listed in Tables 1, S7 and S8. The method proposed above exhibited high sensitivity, with the LOQs ranging from 0.01 to 20 ng/mL in Cortex Moutan and 0.01–50 ng/mL range in the other TCMS, which is lower than the MRL value for agricultural products specified in the national standard. In all three TCMs, r^2s of the calibration curves for all analytes were higher than 0.9901 which showed good linearity. The measurement of intra- and inter-day variability was used to determine the precision of the developed method. In *O. japonicus*, the precisions (based on RSD values) were in 1.08–11.91% (intra-day) and 1.32–16.16% (inter-day) ranges with 0.53–15.05% (intra-day) and 0.15–26.56% (inter-day) for *P. odoratum* and 0.46–19.07% (intra-day) and 0.25–18.86% (inter-day) for Cortex Moutan, indicating that the proposed method is highly sensitive and meets the regulatory requirements. The repeatability of the method for *O. japonicus*, *P. odoratum* and Cortex Moutan for the 108 pesticides was not more than 11% and the stabilities were in the 1.99–16.95%, 1.36–25.09% and 1.99–16.95% ranges, respectively. In *O. japonicus*, except for cyromazine, tetramethirn, phorate sulfoxide, methiocarb, chlorbenzuron, diflubenzuron, fenamiphos, hexaflumuron, IBA, phorate sulfone, sulfotep and epoxiconazole, the recoveries of the other pesticides (89%) were in the 70.30–119.96% range, with RSD < 19%. In *P. odoratum*, excluding cyromazine, GA3, IAA, IBA and malathion, the recoveries of the other pesticides (96%) were in the 63.89–119.70% range, with RSD < 18%. In Cortex Moutan, excluding cyromazine, thiabendazole, phorate sulfoxide, methiocarb, diflubenzuron, IBA, chlorpyrifos methamidophos, phorate, pendimethalin, triazophos, bitertanol, 6-BA and diazinon, the recoveries of the other pesticides (87%) were in the 71.48–119.08% range with RSD < 19%. The results confirmed that the method was accurate.

3.5. Application to real samples

The modified method was applied for the analysis of 39 samples including *O. japonicus* (n = 12), *P. odoratum* (n = 14) and Cortex Moutan (n = 13) collected from different regions in China. In different samples, Tables S4–S6 show that pesticides are widely applied in TCM cultivation activities to increase yield. In this study, totally 26 pesticides were detected in the three TCMs, and only 7.69% samples did not detect any pesticides, while more than four pesticides were detected in 1/3rd of the samples (Fig. 5A).

The detection of some pesticides was not necessarily due to the application of pesticides. TCM contamination could be caused by the pesticide residues in the soil or the migration of pesticides sprayed on other crops. Among the 26 detected pesticides, more than a half of the pesticides were insecticides and the proportion of fungicides was also large (34.62%) (Fig. 5B). The three pesticides with relatively high detection rates (Fig. 5C) were Tebuconazol (69.23%), Triadimefon

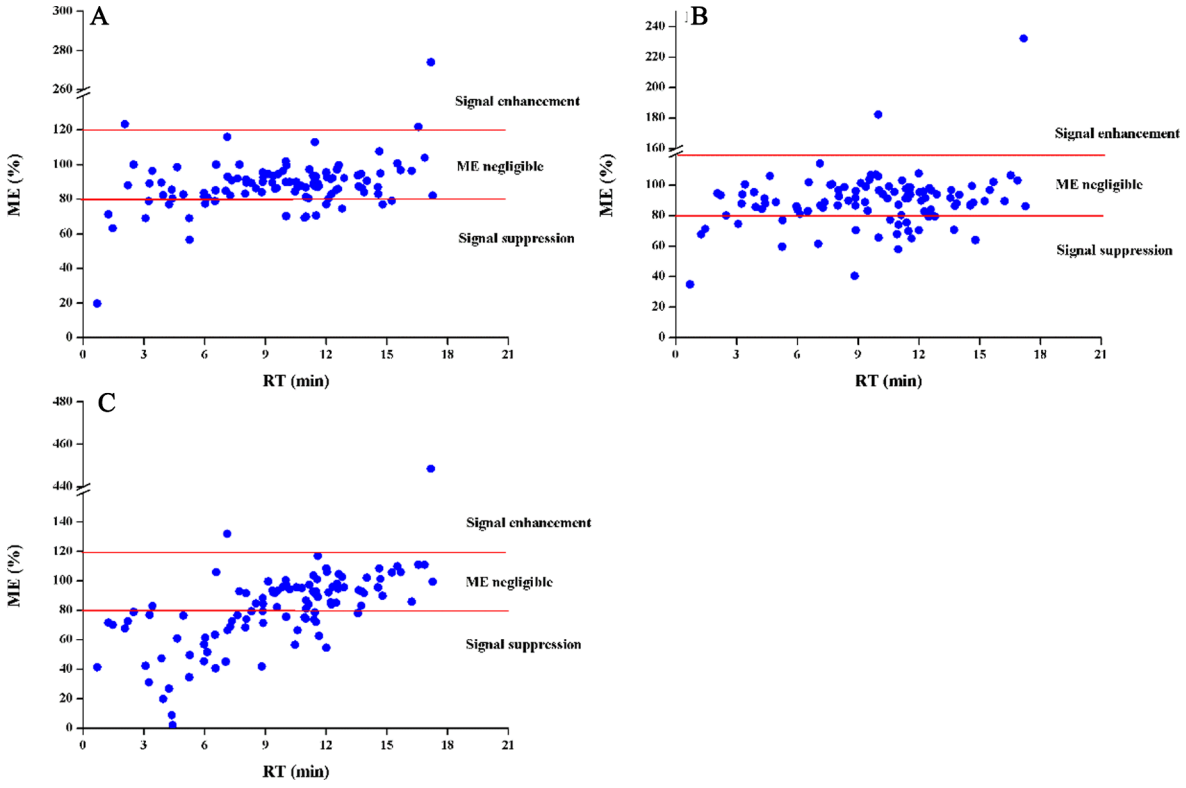

Fig. 4. Scatter plot of retention time and matrix effects of 108 pesticides in *O. japonicus* (A), *P. odoratum* (B) and Cortex Moutan (C).

(33.33%) and Paclobutrazol (30.77%). Tebuconazol had a high detection rate in all three TCMs while Triadimefon and Paclobutrazol were only detected in Cortex Moutan and *O. japonicus*, respectively. Although they had high detection rates, their residual amounts were very low and other detected pesticides had low concentrations, excluding Paclobutrazol (Fig. 5D). Paclobutrazol was detected in all *O. japonicus* samples at concentrations ranging from 4.18 μg/kg to 783.73 μg/kg. According to the GB 2763-2019 national standard [9], the paclobutrazol concentrations in most samples exceeded the MRLs set for vegetables (0.05 mg/kg). However, the MRLs of the pesticides in TCMs are not specified in the national standard. The results mentioned above are consistent with the findings of our previous field survey and monitoring data reported by Zhao et al. [48], which indicate that paclobutrazol is a plant growth retardant commonly used in *O. japonicus* production. Besides that, a high frequency Pyraclostrobin detection (10 of the 13 samples in *O. japonicus*) was observed and the concentrations in one sample (21.24 μg/kg) exceeded the MRLs set for vegetables (0.02 mg/kg) according to the GB 2763-2019 standards [9].

Residual concentrations caused by the unsustainable application of pesticides will not only adversely affect the safety of TCMs, but also pollute the environment and affect the growth of subsequent crops planted. Therefore, the establishment of application standards and MRLs for TCMs should be considered in future studies.

4. Conclusion

In this study, a rapid, simple, robust and high throughput method was applied for the determination of 108 pesticide residues in three widely used TCMs, *O. japonicus*, *P. odoratum* and Cortex Moutan. This modified QuEChERS method coupled with UHPLC-MS/MS was applicable to all the three selected TCMs and resulted in excellent selectivity, precision (intra-day and inter-day variability) and repeatability. The method worked in the dMRM mode coupled with an ESI source facilitated the simultaneous quantification of 108 pesticides from the different TCMs with complex compositions within 21 min. After method optimization, we concluded that extraction conducted in acetonitrile containing 0.75% (v/v) acetic acid with ultrasonication for 15 min and d-SPE clean-up with 150 mg anhydrous $MgSO_4$ in combination with 25 mg C18 achieved satisfactory recoveries. A comprehensive verification of the method was carried out to demonstrate its high sensitivity, specificity and accuracy. The detection frequencies of paclobutrazol, tebuconazole, etc., which pose very serious environmental risks, were high, which indicated that they need to be managed, for example, through the reassessment of their use and the definition of their MRLs in China. Considering the advantages of simple pretreatment requirements and high-throughput, the modified method developed in the present study may be applied in the detection of pesticide residues or other contaminants in similar TCMs.

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CRediT authorship contribution statement

Rui-Xing Li: Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Min-Min Li:** Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization. **Tao Wang:** Methodology, Validation, Investigation, Resources, Visualization. **Tie-Lin Wang:** Software, Formal analysis, Data curation. **Jie-Yin Chen:** Software, Formal analysis, Resources. **Frédéric Francis:** Methodology, Validation, Writing - review & editing. **Bei Fan:** Conceptualization, Formal analysis, Resources, Writing - review & editing, Project administration, Funding acquisition. **Zhi-Qiang Kong:** Conceptualization, Software, Validation, Resources, Writing - review &

Table 1
Linear ranges, calibration curves, correlation coefficients (r^2), limits of quantification (LOQs), matrix effects and recoveries of 108 target pesticides in *Ophiopogon japonicas*.

No.	Pesticide	LOQ (μg kg^{-1})	LOD (μg kg^{-1})	ME (%)	Recoveries (%) (RSDs) (n = 6)				Precision (%) (RSDs)	
					0.01 (mg kg^{-1})	0.05 (mg kg^{-1})	0.1 (mg kg^{-1})	0.2 (mg kg^{-1})	Intra-day	Inter-day
1	2,4-D	5	2	115.82	99.57 (8.14)	102.13 (5.04)	101.68 (3.88)	93.73 (3.71)	5.05	5.09
2	3-Hydroxycarbofuran	0.05	0.02	85.49	101.33 (7.46)	111.88 (3.38)	105.09 (1.75)	110.47 (2.66)	3.05	3.67
3	6-BA	0.25	0.1	56.60	85.00 (6.49)	89.08 (5.38)	85.64 (3.17)	86.85 (2.02)	2.58	2.27
4	Abamectin	1	0.3	274.05	106.40 (8.27)	103.61 (5.58)	114.36 (1.92)	109.49 (4.09)	11.91	8.90
5	Acephate	10	3	71.29	78.90 (7.70)	92.09 (3.97)	85.53 (1.51)	85.74 (2.75)	1.14	2.90
6	Acetamiprid	0.01	0.005	80.41	114.38 (5.43)	115.49 (2.13)	115.45 (3.02)	120.82 (1.80)	2.46	2.86
7	Aldicarb	5	2	69.03	95.17 (9.89)	102.92 (4.40)	98.94 (3.13)	105.39 (2.12)	1.86	2.24
8	Aldicarb sulfone	0.5	0.15	88.08	103.85 (7.25)	108.87 (4.57)	101.81 (2.25)	108.32 (1.23)	2.15	2.70
9	Aldicarb sulfoxide	0.5	0.15	100.02	90.22 (9.52)	103.90 (3.52)	96.53 (1.89)	100.00 (2.37)	1.96	2.08
10	Ametryn	0.05	0.02	100.07	102.70 (6.05)	109.16 (3.66)	99.73 (2.47)	97.77 (2.62)	3.16	4.09
11	Azoxystrobin	0.25	0.1	92.70	102.63 (6.30)	109.44 (3.75)	108.06 (3.82)	114.36 (2.66)	5.92	5.95
12	Benalaxyl	1	0.3	70.59	98.41 (10.72)	114.64 (4.18)	110.81 (4.90)	117.52 (2.74)	6.46	8.29
13	Benoxacor	0.5	0.15	89.50	102.60 (6.05)	108.50 (3.34)	99.09 (1.52)	106.53 (1.30)	2.88	2.53
14	Bitertanol	5	2	82.94	115.27 (13.17)	108.65 (3.42)	102.84 (6.96)	101.89 (10.85)	4.73	5.76
15	Buprofezin	0.01	0.005	84.11	101.90 (4.86)	102.24 (3.48)	96.67 (1.26)	103.63 (2.01)	5.80	5.60
16	Cadusafos	0.05	0.02	86.05	100.64 (8.38)	107.30 (3.64)	101.50 (4.78)	104.75 (2.17)	2.96	2.22
17	Carbaryl	0.25	0.1	78.94	102.28 (5.75)	113.35 (3.30)	102.00 (2.12)	114.23 (1.03)	2.56	2.21
18	Carbendazim	5	2	89.07	111.05 (8.64)	102.56 (3.52)	100.64 (1.97)	97.87 (0.88)	2.44	2.94
19	Carbofuran	0.01	0.005	80.92	103.28 (6.01)	110.62 (3.68)	100.88 (2.09)	106.47 (0.93)	3.44	3.75
20	Chlorbenzuron	5	2	112.93	101.04 (7.78)	120.36 (5.03)	115.86 (7.35)	128.80 (4.15)	8.92	6.59
21	Chlordimeform	5	2	96.49	99.56 (6.86)	102.08 (3.76)	97.14 (0.95)	104.29 (1.35)	2.43	3.22
22	Chlorfluazuron	0.25	0.1	121.67	109.08 (18.33)	104.08 (3.51)	99.75 (2.84)	114.26 (4.64)	7.08	5.03
23	Chlorpyrifos	10	3	86.92	117.08 (8.56)	115.53 (4.07)	99.82 (2.04)	105.54 (2.26)	4.29	3.60
24	Chlorpyrifos-methyl	20	6	99.64	–	113.78 (8.43)	103.82 (4.92)	106.92 (10.58)	5.29	4.92
25	Coumaphos	0.5	0.15	87.59	100.16 (6.08)	119.50 (4.70)	117.81 (4.72)	121.72 (2.98)	4.96	4.98
26	Cyprodinil	0.25	0.1	90.09	99.33 (4.10)	102.56 (3.23)	102.87 (1.57)	102.55 (3.27)	2.73	2.66
27	Cyromazine	5	2	19.63	31.96 (17.60)	24.47 (5.73)	27.68 (9.09)	28.81 (5.46)	1.08	14.64
28	Diazinon	0.05	0.02	87.36	96.03 (9.93)	112.00 (3.59)	94.54 (4.44)	106.21 (5.75)	3.43	4.22
29	Dichlorvos	5	2	81.35	101.08 (6.39)	103.11 (2.84)	98.02 (1.76)	104.82 (1.83)	1.75	1.60
30	Diclofop-methyl	5	2	90.78	102.54 (9.20)	109.15 (3.24)	101.61 (1.24)	104.02 (3.32)	6.01	4.86
31	Difenoconazole	1	0.3	74.49	110.41 (7.33)	100.82 (20.62)	101.65 (3.80)	106.72 (2.67)	5.44	4.56
32	Diflubenzuron	0.25	0.1	86.77	110.41 (7.33)	149.03 (4.84)	110.71 (4.70)	126.40 (3.43)	4.80	4.00
33	Dimethenamid	0.25	0.1	95.47	97.81 (5.79)	111.39 (3.55)	105.44 (2.69)	110.81 (1.43)	2.99	3.73
34	Dimethoate	0.05	0.02	77.07	99.91 (4.61)	109.22 (4.24)	98.72 (3.31)	108.47 (0.61)	2.32	1.93
35	Dimethomorph	0.25	0.1	86.56	98.05 (4.83)	113.54 (4.63)	102.58 (3.02)	103.39 (2.59)	6.01	5.51
36	Diniconazol	10	3	97.21	103.72 (7.20)	108.92 (2.91)	103.23 (2.20)	101.36 (5.07)	3.91	3.66
37	Diphenylamine	50	15	90.31	–	104.56 (3.35)	101.37 (3.15)	117.79 (2.88)	3.53	4.01
38	Emamectin-benzoate	0.05	0.02	94.86	98.02 (6.77)	102.26 (2.50)	91.35 (3.14)	102.88 (1.24)	7.67	7.29
39	Epoxiconazole	1	0.3	86.92	125.03 (4.13)	167.11 (5.59)	121.13 (4.85)	125.42 (1.93)	6.39	6.54
40	Ethoprophos	0.1	0.03	90.12	97.96 (7.67)	106.56 (6.50)	94.13 (3.16)	104.64 (4.48)	2.68	3.10
41	Etofenprox	0.25	0.1	81.99	98.95 (2.50)	104.68 (4.16)	99.31 (1.74)	106.33 (1.85)	8.63	4.99
42	Fenamiphos	0.05	0.02	69.92	106.82 (2.26)	171.73 (3.37)	105.21 (5.46)	115.04 (1.55)	5.24	3.74
43	Fenarimol	5	2	101.96	113.29 (11.30)	112.49 (2.36)	103.52 (2.02)	114.49 (2.41)	5.69	6.72
44	Fenbuconazole	5	2	69.25	112.72 (4.25)	117.05 (6.16)	99.54 (3.58)	105.80 (9.52)	9.17	8.37
45	Fenitrothion	5	2	90.07	99.90 (6.41)	109.86 (4.17)	106.78 (1.98)	112.35 (2.28)	2.31	2.24
46	Fenobucarb	0.01	0.005	86.37	100.43 (6.73)	112.74 (5.33)	101.34 (1.14)	105.37 (2.25)	3.06	2.98
47	Fenpropathrin	5	2	83.02	105.44 (4.12)	119.59 (4.98)	96.02 (2.05)	100.56 (2.80)	4.25	3.20
48	Fenpyroximate	0.1	0.03	96.87	102.71 (7.79)	105.44 (4.12)	105.21 (3.47)	104.67 (2.19)	6.70	4.95
49	Fenthion	5	2	88.41	95.35 (10.72)	103.71 (6.37)	90.59 (3.69)	106.94 (3.23)	2.14	4.49
50	Fipronil	0.1	0.03	97.35	95.94 (3.03)	115.63 (3.56)	103.36 (2.96)	119.96 (2.95)	3.53	4.81
51	Fipronil sulfide	0.1	0.03	93.07	103.01 (6.43)	115.26 (3.79)	103.75 (2.34)	107.74 (6.08)	4.83	6.73
52	Fipronil-desulnyl	0.1	0.03	87.53	104.30 (7.02)	106.54 (5.36)	96.61 (3.41)	98.86 (1.82)	5.18	7.49
53	Fipronil-sulfone	0.01	0.005	95.47	95.33 (8.03)	113.45 (3.41)	112.63 (2.67)	109.60 (2.51)	5.19	6.89
54	Flufenoxuron	1	0.3	100.57	116.17 (10.70)	103.56 (4.91)	85.54 (2.04)	99.54 (5.55)	7.27	5.99
55	Fluometuron	0.1	0.03	85.13	98.64 (7.83)	106.17 (2.81)	105.24 (2.10)	107.59 (2.47)	3.52	3.55
56	Flusilazole	1	0.3	81.26	106.39 (9.70)	132.71 (4.92)	101.16 (2.70)	107.40 (2.35)	5.66	5.45
57	GA3	10	3	98.50	94.12 (17.47)	105.18 (8.26)	105.55 (5.99)	95.47 (3.39)	6.62	8.51
58	Hexaconazole	0.5	0.15	92.59	101.55 (8.38)	113.69 (6.13)	98.32 (2.23)	114.90 (2.46)	4.90	5.97
59	Hexaflumuron	10	3	93.74	126.23 (18.77)	132.11 (11.39)	112.97 (3.05)	108.08 (9.44)	3.75	15.28
60	Hexythiazox	0.25	0.1	76.92	104.77 (5.92)	105.77 (5.40)	102.08 (4.15)	108.10 (2.40)	6.91	4.82
61	IAA	5	2	82.70	119.02 (4.90)	114.76 (3.35)	107.73 (1.62)	107.14 (2.30)	3.22	3.37
62	IBA	10	3	100.00	113.44 (21.41)	109.44 (31.41)	107.65 (9.31)	111.99 (11.93)	4.46	5.06
63	Imidacloprid	0.1	0.03	82.33	108.92 (6.73)	115.93 (3.47)	103.18 (1.77)	116.09 (1.76)	2.52	2.22
64	Isazophos	0.05	0.02	90.12	105.51 (6.97)	111.52 (2.15)	90.86 (3.53)	111.17 (4.60)	7.43	8.50
65	Isofenphos	0.1	0.03	92.26	105.54 (5.11)	112.73 (6.50)	109.63 (3.76)	108.93 (5.16)	3.12	2.22
66	Iso-malathion	0.05	0.02	92.97	102.88 (5.62)	112.88 (3.55)	104.52 (3.56)	116.77 (2.41)	4.19	2.81
67	Isoprocarb	0.01	0.005	82.13	106.55 (6.44)	110.55 (3.73)	103.96 (2.92)	109.34 (1.34)	3.31	3.98
68	Isoprothiolane	0.25	0.1	85.85	104.28 (5.89)	107.47 (3,45)	102.69 (2.53)	115.28 (2.82)	2.89	3.54
69	Malaoxon	0.05	0.02	77.51	105.65 (6.55)	113.52 (3.80)	98.55 (1.79)	111.79 (2.58)	5.18	5.85
70	Malathion	0.01	0.005	89.66	107.57 (5.71)	110.80 (5.04)	117.56 (5.11)	114.13 (3.15)	7.77	16.16
71	Metalaxyl	0.01	0.005	92.09	103.21 (5.90)	113.10 (5.30)	102.58 (2.97)	106.62 (2.91)	2.54	2.69

(*continued on next page*)

Table 1 (*continued*)

No.	Pesticide	LOQ (μg kg^{-1})	LOD (μg kg^{-1})	ME (%)	Recoveries (%) (RSDs) (n = 6)				Precision (%) (RSDs)	
					0.01 (mg kg^{-1})	0.05 (mg kg^{-1})	0.1 (mg kg^{-1})	0.2 (mg kg^{-1})	Intra-day	Inter-day
72	Methamidophos	1	0.3	63.27	71.64 (10.51)	71.64 (5.06)	70.30 (2.50)	75.66 (5.29)	2.79	2.07
73	Methidathion	0.5	0.15	83.16	99.16 (4.98)	112.63 (3.26)	101.13 (3.31)	123.24 (5.81)	1.91	2.23
74	Methiocarb	0.25	0.1	84.10	105.49 (6.27)	115.56 (4.67)	114.47 (1.62)	130.61 (1.95)	2.14	1.61
75	Methomyl	0.25	0.1	69.07	97.47 (6.93)	106.90 (4.21)	96.23 (1.36)	103.86 (1.26)	3.18	3.76
76	Metolachlor	0.01	0.003	84.44	110.07 (5.94)	110.21 (4.32)	99.55 (3.78)	99.94 (3.56)	2.70	1.94
77	Myclobutanil	5	2	96.53	101.64 (5.88)	109.02 (3.49)	109.79 (3.48)	104.20 (2.16)	5.99	5.70
78	Omethoate	0.25	0.1	123.31	81.01 (6.21)	88.80 (4.22)	88.77 (1.11)	91.79 (3.16)	1.42	3.18
79	Paclobutrazol	5	2	93.41	113.15 (7.14)	106.77 (3.78)	108.28 (2.98)	115.24 (2.62)	5.15	5.99
80	Penconazole	0.25	0.1	88.83	94.45 (6.54)	106.31 (3.30)	113.99 (4.05)	104.82 (2.85)	2.28	2.44
81	pendimethalin	5	2	107.61	101.64 (4.04)	107.90 (3.82)	98.23 (2.31)	113.87 (1.90)	5.30	4.14
82	phenthoate	0.1	0.03	93.54	101.30 (6.03)	117.64 (5.46)	91.48 (5.30)	113.19 (4.86)	4.78	3.87
83	Phorate	10	3	77.01	90.16 (9.06)	85.32 (6.49)	92.74 (4.85)	101.55 (6.72)	2.52	2.97
84	Phorate sulfone	0.01	0.005	91.00	128.90 (4.01)	128.90 (3.01)	113.55 (2.23)	117.12 (2.85)	4.75	5.55
85	Phorate sulfoxide	0.01	0.005	84.86	123.20 (4.03)	123.20 (4.33)	126.46 (3.83)	116.88 (3.04)	1.14	1.32
86	Phosalone	0.5	0.15	85.33	104.23 (6.60)	114.23 (4.06)	102.88 (4.07)	112.45 (4.22)	4.25	3.66
87	Phosmet	0.25	0.1	89.30	103.42 (6.08)	106.76 (4.53)	104.75 (1.93)	105.84 (1.53)	4.76	4.64
88	Phoxim	0.01	0.005	80.27	99.77 (7.16)	105.52 (7.80)	103.69 (5.77)	108.95 (3.01)	3.71	6.55
89	Pirimicarb	0.05	0.02	83.65	101.70 (6.26)	107.37 (3.95)	98.39 (2.95)	103.21 (2.53)	2.55	2.51
90	Prochloraz	5	2	91.55	106.58 (9.68)	102.93 (3.70)	99.39 (2.93)	107.39 (2.70)	5.78	5.02
91	Profenofos	0.01	0.005	87.27	108.04 (11.35)	105.87 (4.99)	98.78 (2.85)	108.18 (2.97)	5.06	3.98
92	Prometryne	0.01	0.003	94.77	99.02 (7.34)	103.45 (5.20)	101.90 (3.57)	105.20 (3.04)	2.18	2.07
93	Propargite	0.5	0.15	79.08	101.39 (8.24)	108.39 (3.66)	90.34 (1.40)	105.51 (2.18)	8.03	5.56
94	Pyraclostrobin	0.25	0.1	92.19	102.98 (7.76)	114.98 (6.62)	93.15 (4.47)	115.02 (3.98)	6.41	5.54
95	Pyridaben	0.05	0.02	96.32	98.79 (6.53)	107.21 (3.48)	98.49 (2.31)	106.51 (2.5)	7.98	5.06
96	Pyrimethanil	0.05	0.02	91.36	102.08 (5.11)	106.29 (2.38)	98.98 (2.10)	105.33 (1.97)	3.02	2.82
97	Quinalphos	0.5	0.15	80.53	104.70 (8.65)	134.70 (3.31)	105.13 (5.64)	111.99 (5.62)	4.17	3.79
98	Sulfotep	0.1	0.03	88.24	99.12 (6.84)	103.06 (6.99)	128.47 (9.91)	108.08 (4.06)	3.81	4.18
99	Tau fluvalinate	0.5	0.15	104.00	105.48 (6.65)	110.39 (4.35)	98.87 (3.40)	106.30 (3.10)	7.52	5.27
100	Tebuconazol	1	0.3	86.93	96.28 (6.87)	109.39 (5.45)	100.27 (4.46)	111.40 (4.35)	5.25	5.39
101	Terbufos	5	2	86.47	109.07 (13.75)	108.33 (3.91)	91.59 (2.40)	105.70 (2.62)	3.83	2.77
102	Tetramethirn	0.5	0.15	94.71	106.93 (12.86)	118.93 (3.73)	122.10 (3.63)	121.63 (2.88)	3.63	3.01
103	Thiabendazole	1	0.3	89.64	90.56 (5.66)	96.83 (3.88)	89.23 (1.33)	96.84 (2.41)	3.48	4.66
104	Thiamethoxam	0.01	0.005	79.06	102.68 (6.87)	109.07 (3.05)	102.84 (1.42)	110.93 (2.56)	3.26	3.70
105	Triadimefon	5	2	94.40	108.30 (8.22)	110.24 (6.09)	100.38 (3.99)	113.73 (2.02)	6.15	6.28
106	Triadimenol	5	2	99.51	102.93 (9.38)	109.97 (4.10)	113.71 (2.70)	109.52 (3.03)	7.64	8.65
107	Triazophos	0.25	0.1	70.00	103.33 (8.58)	108.53 (3.61)	99.64 (4.48)	102.74 (3.81)	4.45	4.23
108	Zoxamide	0.25	0.1	89.70	107.04 (5.26)	113.37 (3.62)	105.73 (3.79)	119.29 (2.98)	4.09	4.23

editing, Project administration, Funding acquisition. **Xiao-Feng Dai:** Conceptualization, Validation, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing 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.

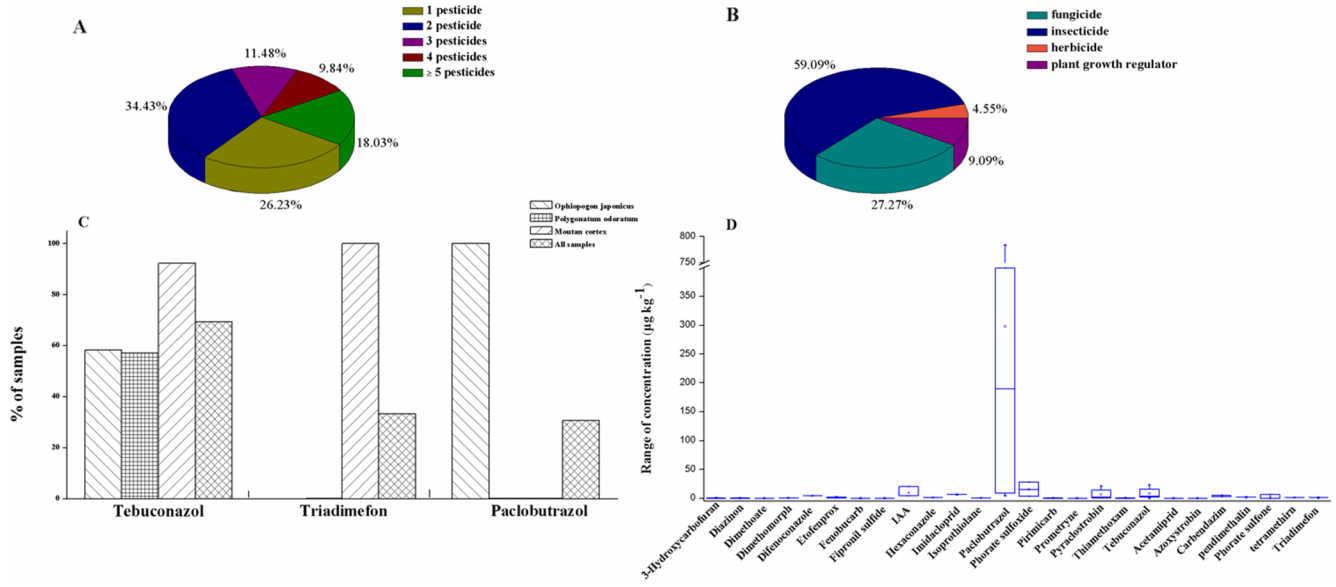

Fig. 5. Proportions of pesticide residues in real samples (A), proportions of detected pesticide types (B), three pesticides with relatively high detection rates in three TCMs (C), and box plots of the measured concentrations (μg kg^{-1}) of 26 detected pesticides (D).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jchromb.2020.122224.

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