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# Suspected-target pesticide screening using gas chromatography–quadrupole time-of-flight mass spectrometry with high resolution deconvolution and retention index/mass spectrum library

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ABSTRACT

A strategy for suspected-target screening of pesticide residues in complicated matrices was exploited using gas chromatography in combination with hybrid quadrupole time-of-flight mass spectrometry (GC–QTOF MS). The screening workflow followed three key steps of, initial detection, preliminary identification, and final confirmation. The initial detection of components in a matrix was done by a high resolution mass spectrum deconvolution; the preliminary identification of suspected pesticides was based on a special retention index/mass spectrum (RI/MS) library that contained both the first-stage mass spectra ($MS^1$ spectra) and retention indices; and the final confirmation was accomplished by accurate mass measurements of representative ions with their response ratios from the $MS^1$ spectra or representative product ions from the second-stage mass spectra ($MS^2$ spectra). To evaluate the applicability of the workflow in real samples, three matrices of apple, spinach, and scallion, each spiked with 165 test pesticides in a set of concentrations, were selected as the models. The results showed that the use of high-resolution TOF enabled effective extractions of spectra from noisy chromatograms, which was based on a narrow mass window (5 mDa) and suspected-target compounds identified by the similarity match of deconvoluted full mass spectra and filtering of linear RIs. On average, over 74% of pesticides at 50 ng/mL could be identified using deconvolution and the RI/MS library. Over 80% of pesticides at 5 ng/mL or lower concentrations could be confirmed in each matrix using at least two representative ions with their response ratios from the $MS^1$ spectra. In addition, the application of product ion spectra was capable of confirming suspected pesticides with specificity for some pesticides in complicated matrices. In conclusion, GC–QTOF MS combined with the RI/MS library seems to be one of the most efficient tools for the analysis of suspected-target pesticide residues in complicated matrices.


## 1. Introduction

With increasing concern over food safety, pesticide residues and their significant adverse effects on human health have been noted. Pesticide residues have been reported to cause diseases [1–4], birth defects [5,6], and even death from poisoning [7,8]. Detecting pesticide residues in our food system accurately and rapidly is in great demand. Many approaches have been developed for the screening of pesticide residues using gas chromatography–mass spectrometry [9–13], but most of them are focusing on target pesticides. However, in addition to some known pesticides, many samples may contain residues of suspected-target pesticides that may be the degradation and conversion products, metabolites, reaction products, and other impurities of the target pesticides [14]. These unknown residues can be rather persistent and equally hazardous [15–18]. Therefore, it is necessary to also screen and identify suspected-target pesticide residues. Unfortunately the detection of these residues is not included in the routine monitoring protocols.

In target analysis, pesticides can be detected only if there is a priori included in the method. Using single- or triple-quadrupole MS in the selected-ion monitoring (SIM) or multiple reaction monitoring (MRM), respectively, or ion trap MS in the tandem mass scan mode (MS/MS), the selection of pesticides must be

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completed before the acquisition. The essential information such as retention time (RT), representative ion, and MS/MS transition is collected in advance and included in the method set-up for subsequent detection. In suspected- or non-target analysis, the analytes of interest are uncertain. This uncertainty makes the priori information fuzzy. Although it is possible to confirm the suspected pesticides using their standards, screening methods must be performed prior to these procedures. Hence, the instruments operating in full-scan modes are given exclusive priority to perform suspected-target analysis. Because of this priority, the poor sensitivity of quadrupole MS and the low selectivity of ion-trap MS in full-scan modes limit their application for the pesticide residues present only in trace amounts of complicated matrices. As an alternative, quadrupole time-of-flight mass spectrometry (QTOF MS) owning MS and MS/MS scan modes is recommended for its strong analytical power in solving complex analytical problems. First, QTOF MS can provide high resolution, full-scan spectra for MS (TOF scan mode) and MS/MS (QTOF scan mode). The abundant accurate mass ions acquired can also support the structural elucidation and improve the structural confirmation level for analyte. Second, the elevated mass resolution of TOF allows the extraction of ion chromatograms with narrow mass windows. This obviously results in the decrease of background noise in chromatograms thereby the increase of the sensitivity and selectivity. Third, QTOF MS owns a high scan rate. As fast as 50 Hz, QTOF MS can perform effective MS/MS dissociations of multiple precursor ions in one measurement cycle. Considering these highlighted features in improving sensitivity, selectivity, and accuracy, GC–QTOF MS would have a great application potential in the screening of suspected- or non-target multi-pesticide residues in complicated matrix.

Gas chromatography–mass spectrometry is a common and conventional method in identifying volatile and semi-volatile compounds in complex mixtures. This method, however, can fail when acquired spectra are “contaminated” with extraneous mass spectral peaks, as commonly arise from co-eluting compounds, column bleed and ion-chamber contaminants. The extraneous peaks pose a serious problem for compound identification. To resolve the respective problem, a mathematic algorithm, deconvolution supported by automated software, is exploited [19–21]. In short, the core concept of deconvolution includes four steps as: (1) an extracted ion chromatogram (EIC) for each mass found in the sample is created; (2) each EIC is integrated using the agile integrator to create a set of “EIC peaks”; (3) the “EIC peaks” are grouped into sets based on a common RT through the determination of the exact apex of each EIC peak; and (4) the relative area (or height) of the EIC peaks and the mass of the EIC are used to create a purified spectra. When a chromatographic peak is satisfied to user-defined parameters, the software will display its deconvoluted mass spectrum, which is a “pure” component spectrum from complex chromatograms.

A typical attempt to identify a given component from a MS profile is by finding a match of mass spectrum to a compound from a reference library. However, given the variety of homologs and isomers of pesticides in different complicated matrices, the traditional mass spectral comparison often fails to find an exact match. Other than the stand-alone mass spectrometry, hyphenated techniques, as in GC–MS, provide the potential to separate conformational isomers prior to mass detection [22]. Thus, two characteristic substance properties provided by GC–MS, retention index (RI), and mass spectrum are exploited. RI is a concept used in gas chromatography where it is converted from the RT [23]. It is also the natural property that a compound is dependent on the stationary phase used. Additionally, RI is system-independent and allows comparison of values measured by different analytical laboratories under varying conditions (e.g. with regards to column length, film thickness, diameter, carrier gas velocity and pressure, and void time). With the aim to group and annotate unknown compounds from multiple matrices, it appears that utilization of RI is highly efficient in presenting the chromatographic property of component from a GC–MS profile.

Novel software development seems to be promising for automated calculation of RI and deconvolution of mass spectra from GC–MS chromatograms. The combination of both technologies has been applied for qualitative analysis of GC–MS based metabolic profiles [22,24]. In the area of pesticide screening, several studies have roughly reported the potential of deconvolution in the analysis of organic compounds in waste water, urine or other matrices [25–29]. In contrast, the usability and effectiveness of deconvolution for analyte identification under heavy matrix interference has not been evaluated systematically. Furthermore, the capacity of GC–QTOF MS in the suspected-target screening is still need to be further investigated thoroughly, although its application in the pesticide residue analysis was introduced previously [30]. In this work, a strategy for the suspected-target screening of pesticide residues in complicated matrices with high resolution mass spectrum deconvolution and RI/MS library was exploited using GC–QTOF MS. High resolution mass spectrum deconvolution supported by powerful software was applied for the detection of components in the sample. A special user library containing both the theoretical mass spectrum and RI was also utilized for the identification of pesticides. Finally, structural confirmation was performed using two scan modes of QTOF MS. In the TOF scan mode, at least two representative ions from $MS^1$ spectrum were measured for their accurate masses and response ratios. While in the QTOF scan mode, a MS/MS transition ion with accurate mass was measured. Each step under these modes was evaluated with the spiked matrixes for its practical application.

## 2. Experimental

### 2.1. Chemicals and reagents

The solvents and chemicals were purchased as follows: 165 references of pesticides from J&K Scientific Ltd. (Beijing, China), n-hexane (HPLC grade) from Fisher Scientific (Santa Clara, USA), Bond Elut Carbon/$NH_2$ cartridges (500 mg/500 mg, 6 mL) from Agilent Technologies (Santa Clara, USA). Other solvents and reagents used for sample preparations were obtained from Shanghai Reagent Company (Shanghai, PR China) in analytical grade purity.

### 2.2. Instrument and software

A 7200 accurate-mass GC–QTOF MS instrument (Agilent Technologies, Santa Clara, USA) operated in electron impact ionization (EI) mode at 70 eV and controlled by MassHunter Acquisition B.06 was used for the determination of pesticide residues. The GC separation was performed using a fused silica DB-35 MS 30 m × 0.25 mm i.d, 0.25 μm film thickness capillary column. The GC oven temperature was programmed starting at 80 °C (1 min held), and followed by increases of 25 °C/min to 170 °C, then 6 °C/min to final 300 °C (10 min held). Splitless injections of 1 μL sample were carried out at 250 °C and ultrapure grade helium was used as the carrier gas at 1.2 mL/min flow. The interface and ion source temperatures were set to 300 °C and 250 °C. A solvent delay of 4 min was used to prevent damage in the ion source filament. QTOF MS was operated at 5 spectra/s in the mass range *m/z* 50–600 and the resolution was about 12,500 (full width half maximum, FWHM) at *m/z* 272. Mass spectrometric grade PFTBA (Perfluorotri-n-butylamine) was used for the daily mass

calibration. The MS/MS experiments were fixed for each compound with a quadrupole for isolation of precursor ion at a medium MS resolution (1.2 *m/z* FWHM) and a linear hexapole collision cell with nitrogen at 1.5 mL/min as the collision gas. MassHunter Quantitative Analysis B.05 and Unknown Analysis B.05 were applied for the treatment of data. Agilent RTL Pesticide Library was used and updated with the retention indices for the creation of retention index/mass spectrum library.

### 2.3. Sample source

The fresh organic apple, scallion and spinach were purchased from a local market in Shanghai, China.

### 2.4. Sample preparation

The fresh matrices of apple, scallion and spinach were chopped separately into small pieces. Each 20 g of chopped matrix was weighed, transferred into an 80-mL centrifugal tube and added with 40 mL acetonitrile. The mixture was blended at 15,000 rpm for 1 min with 5 g of sodium chloride added during the blending. Then, the homogenate was centrifuged at 4200 rpm for 5 min. 20 mL of the acetonitrile layer was transferred into a 100-mL rotary evaporator flask and concentrated to 1 mL at 40 °C.

The clean-up process was carried out by using a Bond Elut Carbon/$NH_2$ cartridge (500 mg/500 mg, 6 mL). The cartridge was added with 2 cm anhydrous sodium sulfate and activated by 4 mL of acetonitrile/toluene (3:1). Then each 1 mL of the solution from the extraction was added to the cartridge and eluted with 25 mL of acetonitrile/toluene (3:1). The entire volume of effluent was collected, concentrated to 0.5 mL by rotary evaporation at 40 °C, and added n-hexane to make a 10 mL blank extract solution.

To fortify the spiked samples, a standard mixture solution of 165 pesticides was prepared at a concentration of 5 μg/mL in n-hexane. Matrices spiked pesticides with seven concentrations at 1, 2, 5, 10, 20, 50 and 100 ng/mL, were prepared by an appropriate dilution of the standard mixture (5 μg/L) in blank extracts of the matrix.

## 3. Results and discussion

### 3.1. Strategy for screening of suspected-target multi-pesticide residues

The analytical strategy for suspected-target screening here comprises three steps as component detection, identification, and structural confirmation. The approach involves the combination of deconvolution, library matching, and accurate mass measurements (Fig. 1). At the beginning of the suspected-target analysis, mass spectrum of each peak from the total ion chromatogram (TIC) should be carefully scrutinized to find the potential compounds. With the performance of deconvolution, suspected-target components in the sample along with their RTs and purified spectra can be found as much as possible. This step then prepares the sample for submission for further identification.

In the library matching, in addition to mass spectrum, RI was also used. First, the RI of an unknown component was experimentally obtained. Then it was compared with the RI of known compounds. The experimental RI is calculated by the following equation (temperature programmed chromatography) [31]:

$$\mathrm{RI} = 100 \times \left[ Z + \frac{T_{R(\mathrm{unknown})} - T_{R(Z)}}{T_{R(Z+1)} - T_{R(Z)}} \right]$$

Where $T_{R(\mathrm{unknown})}$ represents the RT of the unknown component. $T_{R(Z)}$ and $T_{R(z+1)}$ represent the RTs for two n-alkanes eluted prior to and after the unknown component. $Z$ represents the carbon number of the n-alkane of retention $t_{R(Z)}$.

According to the equation, it is necessary to analyze a homologous series of n-alkanes as RT markers under the same experimental conditions as the sample. This facilitates the bracketing of unknown components and ensures accuracy of updated RTs with changing chromatographic conditions.

Once a match was signaled, further structural confirmation would be performed as the target analysis. Conversely, if no match was found, the compound would remain unknown and subjected to multi-studies. Focusing on the positive matching results, two approaches differing in scan modes and meeting four identification points for the structural confirmation are developed [32]. In the TOF scan mode, no additional GC–MS acquisition is needed but calculation is required. Based on the initial sample measurement, the ratio of the most abundant ion (Q) and one of the other measured ions ($q_i$) is calculated and compared with that of standards or reliable references. In the MS/MS mode, an additional GC–MS/MS acquisition of the sample is necessary to achieve a high resolution MS/MS spectrum of the selected precursor ion. Theoretically, the precursor ion calculated from its formula is separated in the quadrupole and submitted to collision-induced dissociation (CID) for MS/MS spectrum. The accurate mass of the most abundant product ion is then compared with the standards or reliable references.

### 3.2. Application of suspected-target screening in spiked samples

To evaluate the developed strategy of suspected-target screening, three organic vegetable matrices including apple, scallion, and spinach were pretreated first according to the Chinese Official Standard Method, and then prepared by a proven extraction and clean-up method for the volatile and semi-volatile pesticides [33,34]. In this method, solid phase extraction was applied for the clean-up, which has been universally adopted for modern residue analysis of non-fatty samples. No signals were found from the analyses of the blank reagent and blank matrices, indicated that these materials were free of the 165 test pesticides.

#### 3.2.1. Component detection by deconvolution

Deconvolution supported by software was performed to automatically extract possible components in a sample. As illustrated in Fig. 2, TIC of a scallion sample spiked with 165 pesticides at 100 ng/mL was deconvoluted (Fig. 2a). This process resulted in 1997 possible components that were auto-identified by computer. The possible components included the test pesticides and the co-eluting compounds from matrix extract, column bleed, and ion-chamber contaminants. Fig. 2b showed 136 out of 1997 possible components that matched known compounds in the library. Each component was accompanied by a deconvoluted spectrum and EICs of its extracted ions owning to the similar GC property. For example, dichlorvos, one of test pesticides, was detected at 5.05 min. Ions like *m/z* 109.0060, 184.9774 and 78.9847 etc. having similar peak shapes at 5.05 min were grouped to re-construct a deconvoluted spectrum (Fig. 2c). The power of deconvolution was evident when comparing the deconvoluted spectrum with the average spectrum extracted by conventional manual background subtraction (Fig. 2d). Not only the representative ions of dichlorvos were kept in the deconvoluted spectrum, but also extraneous mass spectral peaks like *m/z* 63.9440, 79.9754, 93.9912, 157.9359, etc. were subtracted to make the spectrum much “cleaner”.

*3.2.1.1. Deconvolution optimization.* The high mass resolution of TOF MS allows deconvolution to perform with a narrow extracted mass window (EMW). This means that more ions will

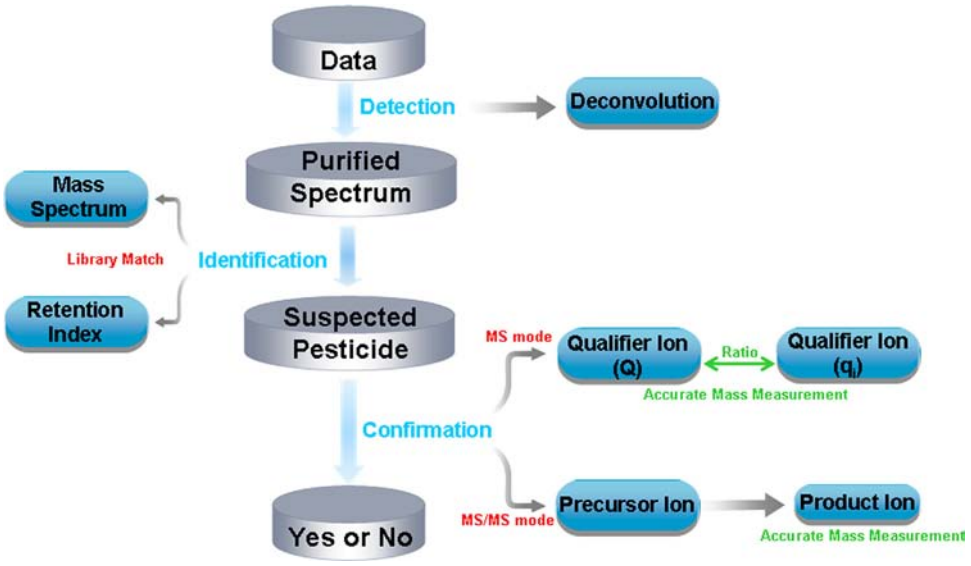


**Fig. 1.** The workflow of strategy for suspected-target screening using GC–QTOF MS.

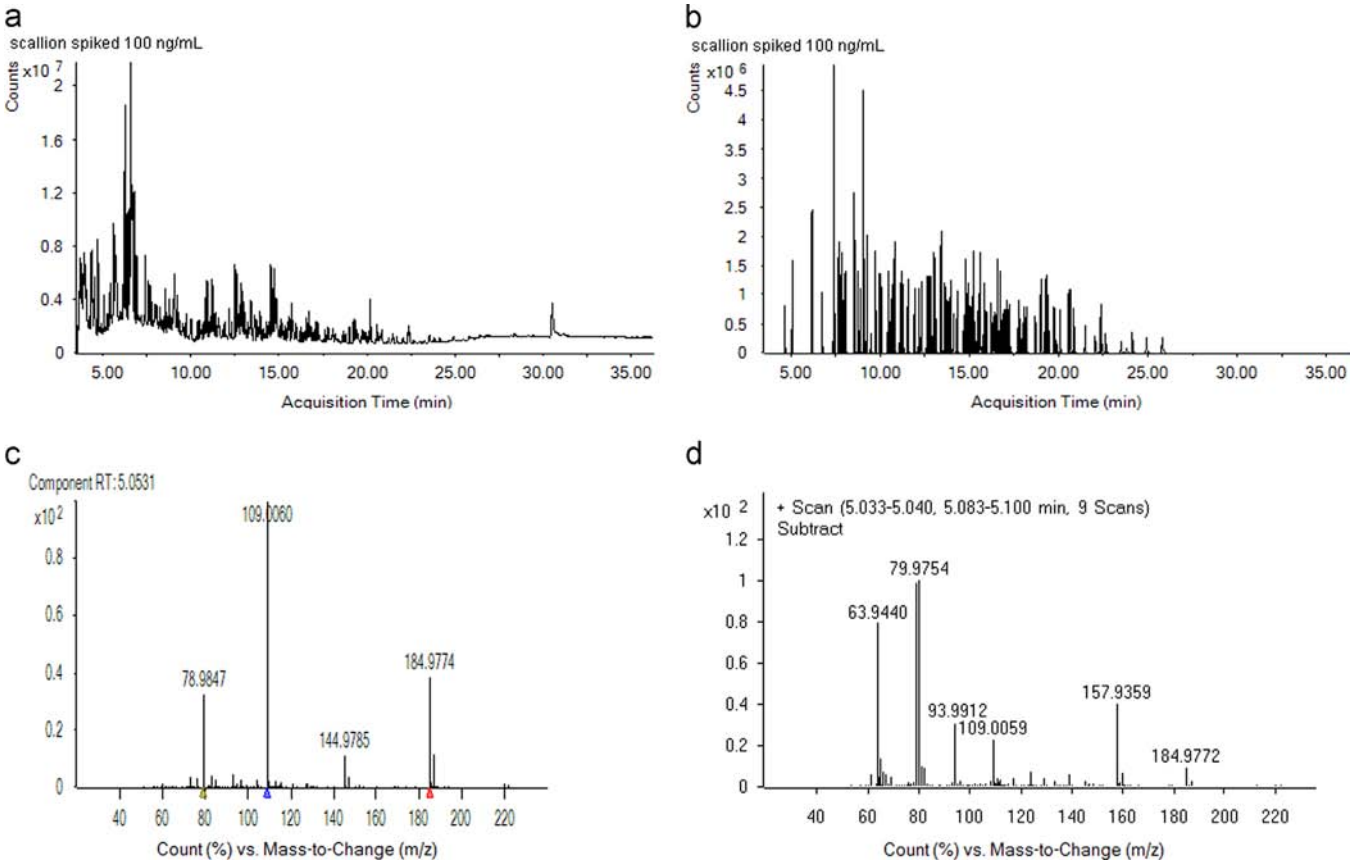


**Fig. 2.** Component detection in a scallion sample spiked with pesticides at 100 ng/mL by deconvolution. (a): Raw TIC; (b): 136 components found by deconvolution and subsequent library match; (c): the deconvoluted spectrum of dichlorvos at 5.05 min and (d): the average spectrum of dichlorvos extracted by conventional manual background subtraction.

be extracted in the deconvolution process to gain significant selectivity. Fig. 3a compared the numbers of pesticides identified under different EMWs. Four matrices spiked with pesticides at 100 ng/mL were deconvoluted. With the EMW narrowed from 500 mDa to 5 mDa, the increasing numbers of pesticides were identified, for example, from 128 to 142 in apple, 123 to 136 in scallion, 127 to 140 in spinach, and 132 to 141 in n-hexane. These results illustrated the ability of high resolution in promoting deconvolution.

As peak maximization was used as the only means for perceiving components in deconvolution, some problems arose unavoidably. Taking chlorpyrifos methyl at 12.61 min as an example, due to its broad peak top and several local maxima, it was deconvoluted as four components at 12.59, 12.61, 12.63, and 12.63 min

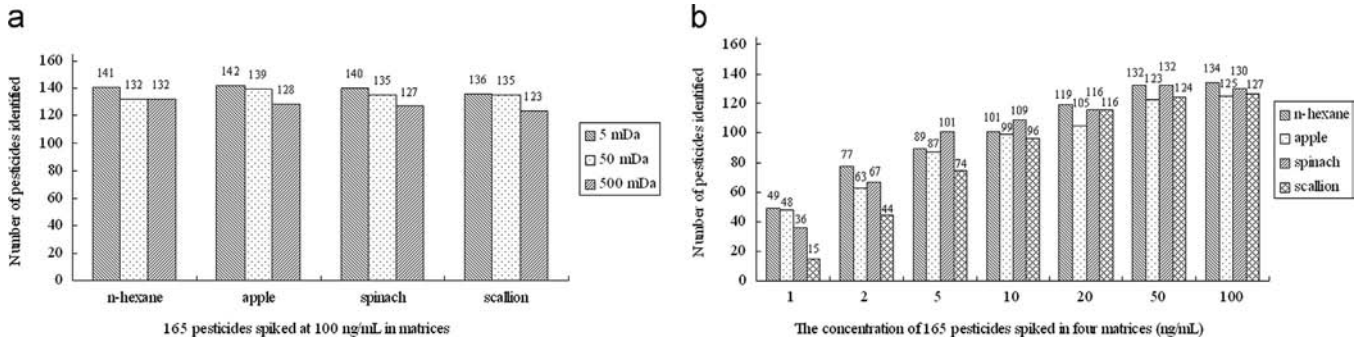


**Fig. 3.** (a): The number of pesticides identified in n-hexane, apple, spinach, and scallion matrices spiked with pesticides at 100 ng/mL, as a result of deconvolution under the EMWs of 5, 50, and 500 mDa respectively and (b): comparison of pesticide numbers detected by deconvolution in four matrices spiked with pesticides (two replicates).

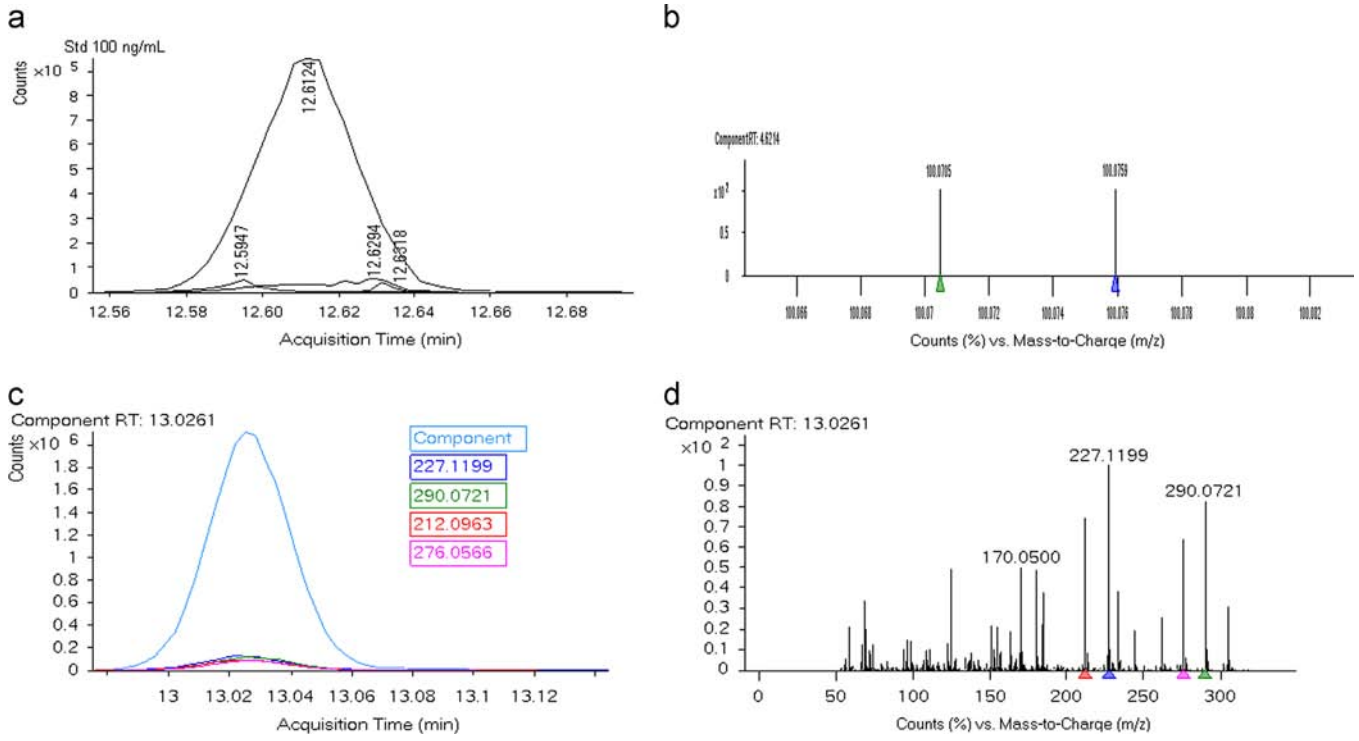


**Fig. 4.** Component detection in n-hexane solutions of pesticides at 100 ng/mL. (a): 4 components detected by deconvolution between 12.56 and 12.66 min; (b): the split peaks of *m*/*z* 100 from the deconvoluted spectrum of ethiolate measured at resolution of 10531 FWHM; (c): the component detected at 13.03 min and (d): the deconvoluted spectrum from the component at 13.03 min.

(Fig. 4a). Each deconvoluted spectrum contained the same fragment ions of chlorpyrifos methyl. This phenomenon appeared more frequently when the EMW became narrowed, but did not increase the false negative risk. Another problem was the split of a mass peak caused by a combined limitation of the deconvolution algorithm and the mass resolution of TOF instrument. In the case of one fragment of ethiolate, the raw profile of a peak at *m*/*z* 100 was shown to have a width of 20 mDa with two local maxima at *m*/*z* 100.071 and 100.076. Had the ion extraction occurred between the two local maxima, it would have been recognized as two individual ions from the same component and constructed in the deconvoluted spectrum (Fig. 4b). Additionally, the difference between the two split masses was close to the EWM used.

In order to reduce the above problems, in addition to EMW, other parameters including RT size window factor and peak shape was set to control the peaks extracted by deconvolution. In this study, they were finally optimized at 100% and 25% under EMW set to 5 mDa, which resulted in the detection of 148 out of 165 test pesticides in an n-hexane solution spiked at 1 μg/mL. The remaining 17 pesticides were not deconvoluted because of co-eluent with other pesticides. One example was that ametryn and pirimiphos-methyl co-eluted precisely at 13.03 min and had identical peak shapes. Because of this, the deconvolution misdeemed them as one component (Fig. 4c) and created a deconvoluted spectrum (Fig. 4d). In this deconvoluted spectrum, the *m*/*z* 227.1199 and 212.0963 from ametryn overlapped in retention time the *m*/*z* 290.0721 and 276.0566 from pirimiphos-methyl. This problem may be reduced via reverse matching logic (ignoring mass spectral peaks not in the library spectrum), but this would increase false positive risk significantly.

*3.2.1.2. Capacity of deconvolution in matrix.* The capacity of deconvolution was evaluated by the number of pesticides detected out of the total 165 test pesticides. The minimum match factor was set to 30 and the RT window was limited to the normal $\pm$ 0.25 mins to qualify the hits in the RI/MS library matching. Fig. 3b showed the effect of component concentration and matrix on the capability of deconvolution. On average, over 74% of pesticides at 50 ng/mL could be identified using

deconvolution and the RI/MS library. For the n-hexane group, only 49 out of 165 pesticides were detected at 1 ng/mL, but increased to 101 at 10 ng/mL, and finally reached 134 at 100 ng/mL. Because a pure solvent was used as a matrix in this group, the increased pesticide number mainly contributed to the levels of concentration. Compared to the n-hexane group, the other three complicated matrices including apple, spinach, and scallion caused the signals of pesticides to be either suppressed or enhanced [35–38]. Among them, scallion was the most "dirty" matrix showing the greatest variation, whereas spinach and apple were the "cleaner" matrices with little variation. The negative effect of matrices was remarkably weakened with the increasing pesticide concentrations. The decrease in coefficient of variation (CV) of the number of pesticides detected among the four groups from 43.7% at 1 ng/mL to 3.0% at 100 ng/mL illustrated the concentration effect. The absolute intensity of MS signal was a major constraint to the efficiency of deconvolution in removing extraneous signals from closely overlapping components.

An additional consideration was the scan rate in the MS measurement. According to its specifications, QTOF MS could realize a scan rate between 1 and 50 Hz (1–50 spectra/s). Faster mass spectrometric acquisition, theoretically, better captures the information contained in the narrower peaks, which in turn facilitates deconvolution of peaks with smaller retention time differences. However, with the scan rate up to 10 Hz or more, significant losses in signal, sensitivity, and spectral fidelity were observed in our study. Higher scan rates, thus, could weaken the ability of deconvolution in the practical application, especially for some pyrethroids with low sensitivity. After a comprehensive consideration, the scan rate operated at 5 spectra/s was found to be appropriate and meet the requirement of sensitivity in our previous investigation [39].

### 3.2.2. Identification through RI/MS library matching

Choosing or building a wider theoretical computer-generated reference library is necessary for suspected-target identification. Fortunately, commercial or standardized spectral libraries such as NIST and other special electron ionization (EI) MS libraries are available for GC–MS, due to its normalized EI interface. These libraries collect a large number of compounds with structural information and allow automatic search for the information within various GC–MS systems. Taking advantage of these broad databases makes the identification of suspected-target compound more available and convenient. In this work, a commercial library named "RTL library", focusing on pesticides and related compounds, was used and updated with the retention indices of the test pesticides (see Supplementary material).

Many pesticides possess homologs or isomers, like four benzenehexachloride (BHC) isomers (Figure S1 in Supplementary material). As such, they often fail to be distinguished from each other due to their highly similar mass spectra. Facing this problem, introducing RI value as a filter significantly increased the reliability of peak identifications by providing a second, independent parameter for library matching (Table S2 in Supplementary material). A traditional MS library process produced four BHC candidates with a match factor (MF) of $\geq$85% for all four peaks. When the experimental RIs were taken to filter, referring to the references in the library, all but one peak matched.

Considering the variation caused by the interference of matrix, instruments, and different GC conditions, the precision of retention time and the repeatability of RI were investigated in this study. Using two GC–QTOF MS systems with the same kind of columns (DB-35MS) and different GC conditions (column length, gas velocity and pressure, temperature program), the experimental RIs of 165 test pesticides in scallion matrix were measured. The results showed that the average standard deviation (SD) of retention time was 0.02 min and the maximal CV of RI was less than 0.2%. It not only proved RI's system-independency, but also indicated the reliability of RI as a criterion in the screening of pesticide in complicated matrices.

### 3.2.3. Structural confirmation

Based on the deconvoluted MS spectra, a special retention index/mass spectrum (RI/MS) library was used for the structural identifications. Once positive results from the library matching found the suspected pesticides or other interesting compounds, further structural confirmation would be performed as the target analysis.

*3.2.3.1. In TOF mode.* The potential of GC–TOF MS has been proved in structural confirmation following the established criterion. At least two representative ions were presented at the expected retention time and measured at their accurate masses. These ions attained their $Q/q_i$ response ratios in specified tolerances ($Q/q_i$: $<2$, deviation $\pm$10%; 2–5, $\pm$15%; 5–10, $\pm$20%; $\geq$10, $\pm$50%) [25,40,41]. Here, QTOF MS in TOF scan mode was also evaluated for its confirmatory capacity in the same way (the representative ions of the pesticides shown in supplementary material). An overview of the results was given in Fig. 5. Over

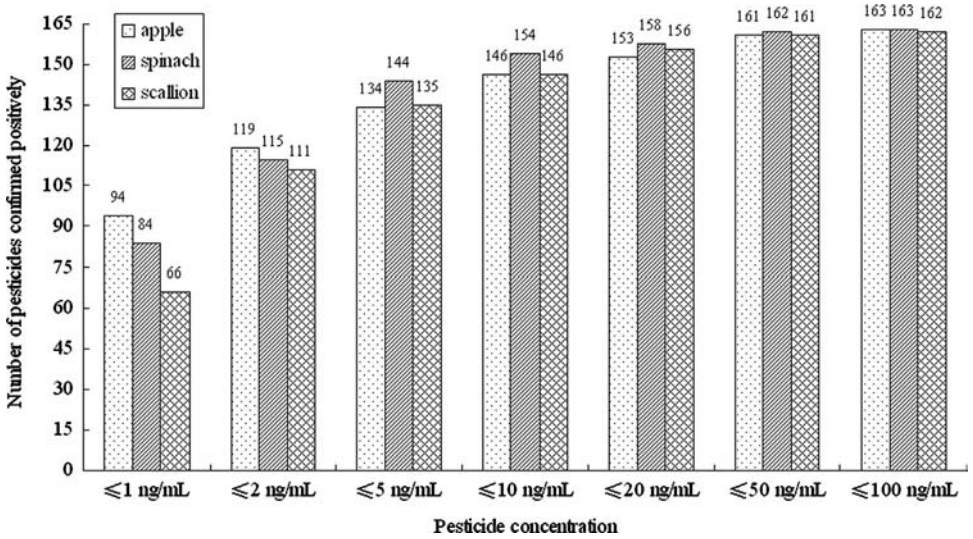


**Fig. 5.** The confirmation capability of QTOF MS in the TOF mode.

**Table 1**
Mass errors of the accurate mass measurements for nicotine in scallion matrix.

| Scan mode | Ion | Absolute of mass error (ppm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | 1 ng/mL | 2 ng/mL | 5 ng/mL | 10 ng/mL | 20 ng/mL | 50 ng/mL | 100 ng/mL | Average |
| TOF mode | $m/z$ 84.0808 | 130 | 125 | 117 | 78 | 27 | 17 | 40 | 76 |
| QTOF mode | $m/z$ 162→84.0808 | 23 | 11 | 4 | 5 | 2 | 5 | 4 | 8 |

**Table 2**
Comparison of confirmation for omethoate in scallion matrix by two scan modes.

| Concentration (ng/mL) | TOF scan mode Percent of standard $Q_{m/z\ 110.0127}/q_{m/z\ 156.0005}$ (1.57) (%) | QTOF scan mode Mass error of $m/z$ 110→78.9943 (ABS ppm) |
|---|---|---|
| 10 | 126.4 | 0.6 |
| 20 | 128.4 | 18.4 |
| 50 | 98.1 | 3.8 |
| 100 | 106.3 | 2.5 |

80% of 165 test pesticides could be positively confirmed at 5 ng/mL regardless of the matrix type. At 100 ng/mL, two pesticides, dimethomorph I and azoxystrobin, were not confirmed due to their poor sensitivity under GC–MS detection in any of the three matrices. The signal of propamocarb was lost from the scallion matrix, possibly due to its structural instability. The results showed QTOF MS in the TOF scan mode could be viewed as an efficient approach for structural confirmation of pesticides. This is not always predictable. In some cases (see Section 3.2.3.2), the matrix effect could go either way of suppressing or enhancing the ion response thus result in failures in confirming the structure effectively [35–38].

*3.2.3.2. In QTOF mode.* Although the TOF MS had been well calculated for high resolution and mass accuracy before measurements, some factors known as dead time of detector and abundance of ions, could affect measurement accuracy and even cause mass error [42]. These factors imposed more severe effect on the low $m/z$ ratios because of matrix and co-eluting substances. In contrast to the TOF scan mode, QTOF scan mode has its advantage. The product ion is much less disturbed resulting in the improvement of mass accuracy, ion selectivity, and confirmation capability. As an illustrative example, Table 1 compared the results of accurate mass measurements for nicotine in the scallion matrix from 1 ng/mL to 100 ng/mL. The average of absolute mass error for $m/z$ 162→84.0808 (the most abundant ion) achieved in the QTOF mode was 8 ppm, much lower than 76 ppm for $m/z$ 84.0808 (the most abundant ion) achieved in the TOF mode. Another example was presented for omethoate in the scallion matrix with the comparison of two confirmation approaches (Table 2). In the TOF mode, when the concentration was as low as 20 ng/mL and 10 ng/mL, the Q/q of $m/z$ 110.0127 (Q) and 156.0005 (q) exceeded the maximum tolerance ($\pm$10%). This limited the confirmation of omethoate that requires a higher concentration at 50 ng/mL. While in the QTOF mode, from 10 to 100 ng/mL, the mass errors of the accurate mass measurements of the product ion $m/z$ 110→78.9943 were all less than 20 ppm, which showed an improved confirmation capability. Both cases indicated that QTOF scan mode is effective in structural confirmation for pesticides.

Unlike the soft ionization sources, EI source generated intense fragment ion peaks and much less intense molecular ion peak. In most cases, choosing molecular ion as precursor for EI-MS/MS measurement is obviously unsuitable or even impossible. Thus, the optimization of MS/MS method may be particularly important for the structure confirmation using QTOF MS. The optimization included full scan under TOF and QTOF modes to determine suitable precursor and product ions, respectively. Then, the optimum collision energies were determined for each precursor–product ion pair. The most abundant ion from the $MS^1$ full scan spectrum was selected preferentially as the precursor ion in order to achieve the best sensitivity. Other measured ions that could generate the most abundant product ion would also be considered. Following this principle, the sensitivities of 50 test pesticides have been evaluated in our previous work and a satisfactory result was achieved [39]. It demonstrated that the application of QTOF MS in QTOF mode was required when screening for pesticides in complicated matrices.

## 4. Conclusions

GC–QTOF MS demonstrated a strong potential in pesticide residue analysis and proved to be a powerful tool for the structure elucidation of unknown compounds in complicated matrices. On the one hand, GC provided an efficient separation to minimize the co-elution of components, while on the other RIs optimized the quality and reliability of library hits in compound identification. The full scan mass spectra and the accurate mass measurements for representative ions provided by QTOF MS also facilitated confident identification of suspected-target compounds. The use of hybrid QTOF, instead of single TOF, was feasible in accessing the MS/MS acquisition mode, providing valuable fragmentation information and high-mass accuracy of product ions for use in the elucidation and confirmation of the unknowns.

In the current work, we illustrated the application of GC–QTOF MS in suspected-target screening of pesticides in complicated matrices, which enabled high resolution mass spectrum deconvolution, the identification of suspected pesticides based on special user library containing both the $MS^1$ spectra and RIs. Under the strategy of powerful deconvolution and automated calculation of RI, ion-counting noise was explicitly treated and a number of characteristic features of GC–MS data were considered. Test results validated the ability of this system to rapidly and comprehensively screen suspected-target compounds comparable to that of conventional analysis.

GC–QTOF MS is predicted to become one of the most efficient tools for the analysis of pesticide residues in various matrices. To facilitate the method, homemade libraries with a large number of pesticides are needed. In addition, exact masses from MS together with RIs need to be included in future library construction.

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## Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.talanta.2014.04.068.

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