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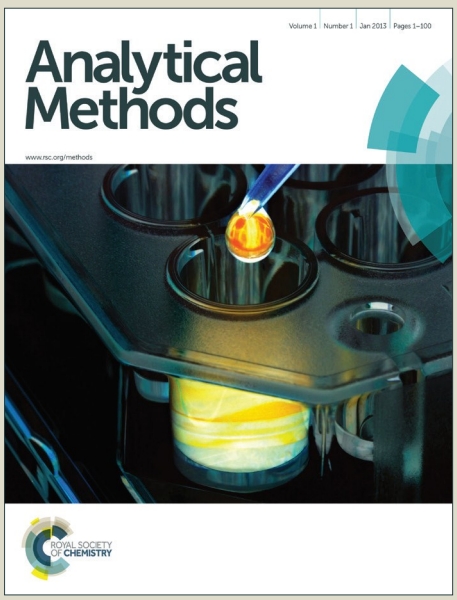

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Screening and identification strategy for 317 pesticides in fruits and vegetables by liquid chromatography – quadrupole time-of-flight high resolution mass spectrometry

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Abstract

Efficient analysis of large amounts of raw data for chemical adulterants detection and identification is always a difficult challenge in the field of food safety. The present study proposed a combined strategy for qualitative screening and identification of 317 pesticides in vegetables and fruits using the high performance liquid chromatography coupled to quadrupole-time-of-flight mass spectrometer (HPLC-Q-TOF/MS) based on a homemade accurate mass database (MS^1) and a novel MS/MS spectra library (MS^2). An accurate mass database and a collision-induced-dissociation (CID) accurate mass spectra library have been developed prior to actual application. The screening strategy need for two injections of each sample extract. Firstly, HPLC-Q-TOF/MS in full MS scan mode was conducted and all potential compounds in MS^1 database were matched against the raw data of sample for target screening. Secondly, targeted MS/MS analysis was carried out by a hybrid Q-TOF/MS and the fragment ions were identified by the MS^2 spectra library. To validate the performances of the in-house MS^1 database and the MS^2 spectra library, the cucumber and orange matrices were prepared by traditional solid phase extraction, spiked with 317 pesticides in three concentration levels, 1, 10 and 50 μg kg^{-1} for most of pesticides, and analyzed by HPLC-Q-TOF/MS. The results showed that over 83.9% of pesticides at 10 μg kg^{-1} or lower could be detected by TOF/MS combined with MS^1 database, and 76.7% of them could be identified by targeted MS/MS coupled with MS^2 library in each matrix. The total false negative rate of the proposed qualitative screening method was as low as 4.7% at 50 μg kg^{-1}. Consequently, the proposed method was applied to 328 real fresh vegetables and fruits. Finally, 57 pesticides, and 799 positive results were found. The approach to detect and to identify pesticides based on accurate mass database integrated CID accurate mass spectra library was proved to be a cost-effective and powerful strategy for routine qualitative screening of pesticides.

Key words screening; pesticide residues; HPLC-Q-TOF/MS; accurate mass database; spectra library

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1. Introduction

More than 1.74 trillion tons of fruits and vegetables have been produced in the world during 2012 according to the Food and Agriculture Organization (FAO)[1]. On the other hand, the use of the varied pesticides and related chemicals played a vital role in protecting the crops and improving their yields. There have been more than 1100 pesticides[2] possibly used in various combinations and at different stages of cultivation and postharvest storage to protect crops against a range of pests and fungi and to provide quality preservation in the world[3]. The result of using pesticides is that the chemical residues might pose a potential risk for human and animal health. For this reason, each country or region has drafted different regulations on the use of pesticides. Especially, the America, European Union and many other governments have established national chemical/pesticide residues monitoring program in food since last century[4, 5]. The organization or government agency, e.g. European Union, requires both sensitive and confirmatory methods to test pesticides in various matrices for monitoring programs and for risk assessment of consumer exposure to pesticides. Consequently, the pesticide residue analysis has increasingly attracted analytical chemist's interests all over the world.

Pesticide residues have traditionally been monitored by GC based the various multi-residue methods[6-8]. However, many new polar and ionic pesticides cannot be determined directly by this method, due to their poor thermal stability or volatility. Liquid chromatography coupled with mass spectrometry (LC-MS), especially the triple quadrupole instruments (QqQ) has been regarded as the most widely used techniques to analyze pesticide residues in various matrices, such as water, animal tissues, fruits and vegetables[9-13]. When operating in selected reaction monitoring mode (SRM), improved sensitivity and good selectivity in detection of pesticide residues can be achieved by tandem mass analyzer. However, the SRM technique could not provide specific structural information and the number of compounds that can be monitored in a single run has seriously limited the screening capability[14]. Besides, another major limitation of the routine SRM method is that it comes with the price of being a targeted-based method, which misses any compound that is not in its target list (so there is an inherent chance for many false negatives)[15]. Meanwhile, the integer-valued molecular masses may be insufficient for differentiating between molecules of many real-world compounds. These compounds illegal or misused, whose presence is not expected in the samples, will be missed by current routine monitoring techniques. Moreover, the acquisition of a large number of expensive reference standards, which are mandatory for quantification purposes, is vital to identify and confirm the suspected findings in above routine target analysis. Thus, new techniques are eagerly needed in the view of large-scale non-targeted compounds screening, especially in less-reference-consuming qualitative screening of harmful substances.

Up to now, high-resolution MS (HRMS) and QqQ MS/MS are currently the main MS-based tools for analysis of chemical contaminants in food. HRMS, such as TOF and Orbitrap mass analyzers, in combination with LC continue to gain increasingly popularity due to the significant improvements in the past several years[16, 17]. Ferrer I. et al.[18-21] have identified about 100 pesticides in food and water samples with automated molecular-feature database searching under the full-scanning liquid chromatography hyphenated time-of-flight mass spectrometer (LC-TOF/MS) method. The identification was checked either in the printout of the automated database match or by manual confirmation of the data file. Mezcua et al.[22] developed and evaluated a rapid automated screening method for determining nearly 300 pesticide residues in food using LC-TOF/MS based on the use of an accurate-mass database. Valverde et al.[23] have discussed about the forchlorfenuron residue in tomato, zucchini and watermelon using the LC-TOF/MS technology at different fragmentor voltages in the range of 120-270 V. However, the occurrence of false positives and equivocal identification due to complex matrices and isobaric interferences is

probably inevitable. In addition, those compounds without fragment ions (or fragments with low intensity) from in-source collision-induced dissociation fragmentation and/or characteristic isotope profile are hardly identified within full single mass spectra, such as TOF/MS, which is now driving TOF/MS toward new strategies and instrumental advances[24]. When coupled to a quadrupole mass filter, the best attributes of a QqQ and accurate mass TOF analyzers in a single instrument(Q-TOF/MS) allowing high confidence identification based on MS and MS/MS information. Q-TOF/MS with 10,000 or more resolving power expressed in terms of FWHM (full peak width at one-half maximum) permits MS/MS analysis and provide accurate masses (possibility to yield mass accuracy of 2 ppm with an adequate calibration range) for both precursor and product ions, which constitutes a higher order mass identification than those afforded by nominal mass measurements obtained by other types of mass analyzers[25]. Moreover, Q-TOF/MS technologies with the full scan spectra sensitivity as well as the high acquisition speed are at the forefront of a movement from traditional known contaminants detecting to extended multi-pesticide residues monitoring, especially for the non-targeted or large scale analytes screening and identification. Accurate mass measurement with Q-TOF/MS gives the elemental composition of parent and product ions, avoiding false positive findings precisely, used to identify unknown substances and a greater differentiation of isobaric species (two different compounds with the same nominal mass but different elemental composition, and thus, different exact masses)[26, 27]. Q-TOF/MS instruments have proven to be one of the most powerful approaches for screening and identifying both targeted and non-targeted compounds in complex samples[24, 28-30], metabolites [26, 31, 32], and organic pollutants in environmental fields[33-37]. Nowadays, state-of-the-art equipments have vigorous software that can incorporate databases, and/or libraries of MS/MS spectra and perform easily a quite reliable identification. To some extent, accurate mass databases and fragments spectral libraries, especially the availability of ESI mass spectra library, are still a significant bottleneck encountered in tandem mass spectra library search and rapid analysis of food samples[38, 39].

The last few studies reported the application of Q-TOF/MS for identification at trace level of pesticides in such complex matrixes as food, especially in vegetables and fruits[40-44]. To our knowledge, there is fewer works evaluating the approach to detect and identify trace level of pesticide residues based on accurate mass database and MS/MS spectra library. We recently generated a short of one novel MS database and MS/MS spectra library of about 200 pesticides[45, 46]. The database and library have been validated in different matrixes, e.g. apple, tomato and cabbage, which resulted in the true positive rate of > 99.5%. However, chemicals of interest or importance that are not detected by any particular method could be considered false negatives if they occur in the sample. Though, the scope of analysis is often the most important feature in targeted approaches, particularly in regulatory screening applications[15]. Furthermore, the idea of screening method is that data evaluation should be done in an automated, fast, and simple way with a large-scale of target compounds[47]. In this paper, a new qualitative screening strategy with lower false negative rate integrated identification and confirmation of multi-pesticide residues in vegetables and fruits was proposed. 317 toxicologically pesticides were investigated with HPLC-Q-TOF/MS before the actual sample screening to establish the accurate mass database (MS^1) and MS/MS spectra library (MS^2). The practical application of the home-made MS^1 database and MS^2 library search leading to true results was examined with spiked selected matrices. Finally, 328 real fruit and vegetable samples were investigated by the proposed technique without any reference standards and 57 relevant pesticides were distinctly confirmed based on the home-made accurate database and spectra library.

2. Experimental

2.1. Chemicals and reagents

The 317 pesticides (**Table 1**) analytical standards included in this study were purchased from Dr. Ehrenstorfer (Ausburg, Germany). Individual pesticide standard stock solutions (approximately 1 mg mL^{-1}) were prepared in pure methanol or acetonitrile, depending on the solubility of each individual compound. The different stock solutions were combined into a mixed standard solution, 240 pesticides at 1 μg mL^{-1} in acetonitrile, and the other 77 pesticides ranged from 1.4 to 15 μg mL^{-1} (see **Supplementary Table S1**). Both the stock solutions and mixed working solution were stored at 4 °C. HPLC-grade acetonitrile and methanol were obtained from Dima Technology INC (CA, USA). Formic acid was purchased from Anaqua Chemicals Supply (TX, USA). Ammonium acetate (NH_4OAc) was bought from Dima Technology INC (Richmond Hill, ON, L4B 3N6 Canada). Anhydrous sodium sulphate (Na_2SO_4, Analytical reagent) and sodium chloride (NaCl ,Analytical reagent) were obtained from Damao Chemical Factory and Fengchuan Chemical Reagent Science and Technology (Tianjin, China).

2.2. Instrument and software

A high performance liquid chromatography connected with a hybrid mass spectrometer formed by a quadrupole connected to a time-of-flight analyzer was applied to determination the pesticides in fruit and vegetable samples. The separation of the analysts was carried out using a HPLC system (Agilent 1290 series, CA, USA) consisting of vacuum degasser, auto-sampler and a binary pump, equipped with a reversed-phase Zorbax SB-C18 analytical column (100 mm×2.1 mm and 3.5 μm particle size). An Agilent quadrupole-time-of-flight mass spectrometer (Q-TOF/MS, Agilent 6530, Agilent Technologies, Santa Clara, CA, USA) with an electro-spray-ionization (ESI) interface was connected to the HPLC system for analytes determination.

Agilent MassHunter Acquisition (Agilent Technologies, Inc., Version B.05) and MassHunter Qualitative Analysis (Agilent Technologies, Inc., Version B.06) were applied for the control of the equipment, data acquisition and qualitative analysis. Microsoft Excel software (version 2007) was applied to create pesticides MS^1 database. In addition, the confirmatory MS^2 library included the exact precursor *m/z*, collision energy (CE), and the product ions spectra of each compound were created by the Personal Compound Database and Library Manager (PCDL, version B 04.00, Agilent Technologies, Inc.). Isotope Distribution Calculator (Agilent Technologies, Inc., Version 6. 0. 663. 0) was also used for accurate mass calculation of the pesticides.

A high-speed blender (Ultra-Turrax T25, Janke & Kunkel GmbH &Co., Staufen, Germany), low speed centrifuge (KDC-40, USTC Chuangxin Co.,Ltd. Zonkia branch, China), rotary evaporator (R-215, BUCHI Labortechnik AG, Switzerland), and nitrogen evaporator (Organomation Associates, EVAP 112, USA) were used for sample extraction. A Milli-Q-Plus ultra-pure water system from Millipore (Milford, MA, USA) was used throughout the study to obtain the HPLC-grade (18.2 MΩ·cm) water during the analysis. The electronic analytical balance used for sample weighing was obtained from Shimadzu (TXB622L, Shimadzu, Kyoto, Japan).

2.3. Sample preparation

The fresh vegetables and fruits (n = 328) were randomly purchased from local markets during August 6-7, 2013. The samples were chosen according to the consumption pattern of residents in the region.

The edible parts of the fresh samples were cut into small pieces without any pretreatment and were triturated with a chopper. The homogenized samples were preserved in a refrigerator at -18 °C. Before using, the samples were thawed at 5 °C overnight.

2.3.1. Extraction and clean-up

The samples were prepared according to the Chinese Official Standard Method as following[48]: a portion of 20 g sample previously homogenized was accurately weighed (precision 0.01 g) in a 80 mL Polytetrafluoroethylene (PTFE) centrifuge tube and mixed with 40 mL of acetonitrile and 5 g sodium chloride. The mixture was blended for 1 min with high-speed blender Ultra-Turrax T25 at 10, 000 rpm, and then centrifuged at 4200 rpm (equivalent to RCF 3155×g) for 5 min. The supernatants extracts (20 mL) of the extract were transferred into individual heart-shaped bottles and evaporated to 1 mL on a vacuum rotary evaporator at 40 °C.

For clean-up, the solid phase extraction (SPE) was carried out using Carbon/NH_2 cartridge (500 mg/6 cc, Waters, Milford, MA, USA). A layer of anhydrous sodium sulphate (2 cm) was added to the Carbon/NH_2 column to remove traces of water from the extract. The columns were conditioned with 4 mL acetonitrile/toluene (3:1, v: v) before adding the samples. Utmost care was taken not to allow the sorbent to dry out during the conditioning. Then loaded the extract onto the cartridge and rinsed the heart-shaped bottles with 3×2 mL acetonitrile/toluene (3:1, v: v), and decanted it to the cartridge. The retained analytes were eluted with 25 mL of acetonitrile/toluene. The entire volume of effluent was collected and concentrated to 0.5 mL at 40 °C with a rotary evaporator, then, evaporated it to dryness using a nitrogen evaporator. Finally, the residues were re-dissolved up to 1 mL with 0.1% formic acid of water -acetonitrile (1:1, v:v) thoroughly. The extract was filtered through a 0.2 μm filter into a glass vial before the HPLC-Q-TOF/MS analysis. With this treatment, 1 mL sample extract represents 10 g of sample.

2.3.2 Preparation of spiked extracts

As the main purpose of screening is to detect and identified the presence of contaminants in the sample, no quantitation is necessary, method recovery, accuracy and precision are not considered here. A qualitative validation of the screening method was performed based on European analytical guidelines[35, 49]. The aim of validation is to ensure the presence of an analyte in a sample at a certain concentration level. From this point, 5, 50 and 250 μL of the mix-pesticides standard solutions were transferred into three vials, and then evaporated the solvent in each vial to dryness using a nitrogen evaporator at room temperature. Finally, 500 μL sample extracts (equal to 5 g solid sample) were add to each vial to obtain spiked extract with concentration at 10, 100 and 500 μg L^{-1} for most pesticides, which corresponds to 1, 10 and 50 μg kg^{-1} in product(several other pesticides concentration varied from 1.4 to 750 μg kg^{-1} as listed in Table S1). A total of six fruit and vegetable extracts (three oranges and three cucumbers) were prepared at each spiked level, and the total number of spiked extract was 18.

2.4. Building MS^1 database and MS^2spectra library

The pesticides MS^1 database and targeted analytes MS^2 spectra library were established before the actual sample screening. To achieve the goal of simultaneous multi-species screening, a total of 317 pesticides, including insecticides, fungicides, plant growth regulators, herbicides, et al., were embodied in MS^1 database and MS^2 spectra library.

For MS^1 database, as listed in **Table 1**, the compound name, elemental composition, theoretical exact mass (calculated by the Isotope Distribution Calculator supplied by the instrument software), together with the t_R of each pesticide were input into an Excel sheet and saved as a *csv* format for automated searching by Agilent data analysis software. The exact t_R of each pesticide in **Table 1** was acquired using full scan mode of TOF/MS with single reference standard solution under the liquid chromatography condition depicted in Section 2.5.

The unambiguous identification of the compound was either done with standards for routine analysis or analyzed the sample at higher fragmentation voltages to obtain more accurate-mass product ions. But in this paper, each pesticide MS/MS spectra and the corresponding product ions information, such as isotope abundance and spacing, were investigated to convincingly confirm the positive results. Therefore, a second injection was implemented by the instrument. The single standard was analyzed under targeted MS/MS mode at appropriate CEs (as listed in **Table 1**) for obtaining its experimental MS/MS spectra. The whole product ions spectra and the CEs of each pesticide were then imported into the PCDL software correspondingly. The compound name, formula composition, accurate-mass and other relevant information of each compound were also input to the library within PCDL software. Then a suitable homemade pesticide MS^2 library for confirmation containing a giant of effective information was established (**Fig. 1**). As illustrated in in **Fig. 1**, four independent spectra of each pesticide were collected at four different CEs, e.g., butamifos was analyzed at CE=5, 10, 15 and 20 eV separately, and the corresponding product ion spectra were embodied in the MS^2 library. The number of major product ions (with relative abundance higher or equal to 10%, using the default 140V fragmentor voltage and the corresponding CEs) of each pesticide were also included in the **in Table 1**.

2.5 Sample analysis

The analytes were separated by an Agilent HPLC 1290 system equipped with reversed-phase ZORBAX SB-C18 column. The column temperature was maintained at 40°C. The injected sample volume was 10 μL. The injector needle was washed for 5 sec with methanol - water (80+20, v/v) at the flush port to avoid cross-contamination. The mobile phase consisted of acetonitrile (A) and water with 0.1% formic acid and 0.5 mmol L^{-1} ammonium acetate (B), respectively. The optimized chromatographic method was carried out: initial mobile phase composition 1% A, followed by a linear gradient to 30% A within 3 min; A 30%-40% from 3 to 6 min and kept for 3 min at 40%A, 40%-60%A from 9 to 15 min，60%-90%A from 15-19 min, and kept for 4 min at 90%A constant, Mobile phases A 1% from 23.01 to 27 min was adopted as the post-run time to equilibrate the column after each analysis. The flow rate used was 0.4mL min^{-1}.

The Q-TOF/MS with an ESI interface was operated under positive ionization mode to detect pesticides. Ions were generated by electrospray ionization with an Agilent Jet Stream Technology electrospray ion source (AJS ESI), which enhanced analyte desolvation by collimating the nebulizer spray and creating a dramatically "brighter signal". The sheath gas temperature and flow were controlled at 325 °C and 11 L min^{-1}. Electrospray operating parameters were the following: capillary voltage: 4000 V; nebulizer pressure: 40 psi; drying gas: 10 L min^{-1}(325 °C); skimmer voltage: 60 V; fragmentor voltage: 140 V. Ultra-pure (99.999%) nitrogen was used as collision gas. The instrument was calibrated daily using the mixture provided by the manufacturer over the *m/z* 118-2721. To assure the desired mass accuracy of recorded ions, a second orthogonal sprayer with a reference solution was used as a continuous calibration using the following reference masses purine ($C_5H_4N_4$ at *m/z* 121.0509), and HP-0921 (hexakis-(1H,1H,3H-tetrafluoropropoxy) phosphazene, $C_{18}H_{18}O_6N_3P_3F_{24}$, at *m/z* 922.009798), leading to the typical resolution of 10000 ± 500 (*m/z* 922.009798). Accurate MS and MS/MS data were collected over the *m/z* 100–1700 range in centroid mode at a rate of 4 spectra per second in the extended dynamic range mode (2 GHz resolution).

For this work, each sample extract need for two injections. The Q-TOF/MS instrument was firstly used as a TOF/MS system working in the full scan MS mode to screen the possible positive results and secondly as a Q-TOF/MS in the targeted MS/MS mode to identify the positive results. A 0.5 min delta t_R and a medium isolation width (~4*m/z*) were adopted to specify precursors in the targeted MS/MS mode.

3. Results and discussion

3.1 Data acquisition and automated screening strategy

HPLC-Q-TOF/MS was selected as the analytic instrument for the application of the database and library, because it combined the high resolution of TOF analyzer with the capability to perform TOF (MS mode) and Q-TOF experiments (MS/MS mode). Thus, it was possible to acquire full scan spectra of MS^1 and MS^2 with high resolution and accurate mass, which drastically increases the selectivity of the method due to the high amount and quality of the structural information produced. For this purpose, a proposed analysis strategy combined MS^1 screening and MS^2 identification was conducted to take advantage of mass accuracy both for precursor ions and the abundant fragments generated in the collision cell, as depicted in **Fig. 2**. For each sample extract, two injections were need. In the first chromatographic run, the single MS mode was performed and the sample was screened for possible target compounds. The resulting compounds that appeared as possibly present were confirmed in a second chromatographic run under targeted MS/MS conditions in which the resulting production ion spectra were used to search the MS^2 library for identification.

3.1.1 Screening of the pesticides

Firstly, the pretreated samples were analyzed in TOF/MS full-scan mode and the MS^1 screening for possible pesticides were implemented. The analytes separated from the LC column with the optimum elution gradient were ionized in the ESI and passed through the first quadrupole and recorded by the TOF/MS. Pesticides formed mainly $[M+H]^+$ and/or $[M+NH_4]^+$ /$[M+Na]^+$ in positive mode in the presence of ammonium acetate (5 mM) in HPLC mobile phase. The total ion chromatogram (TIC) was acquired (**Fig. 3**A) in a mass range from *m/z* 50 to 1700 by the Mass-Hunter software bundled with the instrument. The instrumental parameters were not practically optimized for each individual pesticide and consequently a generic setting was applied to all pesticides, e.g., the fragmentor voltage was set to 140 eV. Therefore, new analytes or pesticides were able to be added to the list for data acquisition without prerequisite mass spectrometric tuning as required for target analysis.

The automated screening was carried out based on the chromatograms obtained by HPLC-Q-TOF/MS analysis as following: extraction of the compounds using the "Find by formula" algorithm and searching MS^1 database based on peaks present in extracted ion chromatograms (EICs). This tool analyzed a raw data file to check if it contained any evidence for the presence of specified compounds listed in home-made MS^1 database. As a result, a compound list was obtained with a narrow-mass tolerance (±20 ppm) and a ±0.5 min time window based on the target *m/z*. An absolute area higher or equal to the abundance of 10000 counts was selected as compounds filter. The resulting potential compounds extracted from the raw data were automatically matched against that in the MS^1 database. Agreement with the database entries was assessed by use of a weighted score (see below) calculated from the mass match, the abundance match, the spacing match, and the retention time match. While the match score was $\geqslant$ 70 (**Fig. 3B**), a potential positive result was proposed. As shown in Fig. 3B, 13 pesticides were found in a celery sample TIC acquired by TOF/MS full scan mode, including propiconazole, imidacloprid, and prochloraz, etc. To decrease the rate of false positives, a confirmatory procedure of was conducted to the suspected positives.

3.1.2 Identification of the positives

False positives, as known, may have serious economic consequences and should be kept at an absolute

minimum (ideally zero) in enforcement and control while keeping the number of false negatives acceptably low (< 5%)[9]. The combined use of accurate mass and chromatographic retention time decrease the rate false positives in the automated analysis above. To further confirm the suspect positives, a second injection under the target MS/MS mode was carried out to obtain product ions of suspected pesticides. The accurate mass and the relative abundances of product ions were compared with the standard MS^2 spectra library. When the product ions are matched, according to the confirmation criteria, this compound is considered to be identified. In such case, the selected precursor ion was broken down with nitrogen as collision gas in the collision cell and much more specific product ion spectra were acquired. Normally, each precursor ion has its specific CE, and it is best to work at around the optimal CE, or just above, to maintain most control over and obtain the highest intensity of the proposed product ions[50]. Hence, the optimized CE, as an important parameter listed in **Table 1**, was included in the MS^2 library in order to achieve the greatest possible sensitivity in the QTOF/MS experiments. In this stage, the TOF portion of the instrument recorded the product ion intensity as well as all other ions (**Fig. 3C**).

For automated identification of the dubious target pesticides, new efficient tools of the MassHunter software were available. First, a tool "Find compounds by targeted MS/MS" was applied that extracted the elution profile of each precursor's production ions in the retention time range of the peak. Then, compounds identifying was conducted by matching against the MS^2 library via a qualified tool "Search accurate mass library". The reverse search, instead of the forward search, was adopted in order to reduce extraneous peaks interference from matrices. For an example, if the spectrum represents two compounds, the forward search score for either of the library spectra of either compound would be low because there were peaks in the user spectrum that were not in either of the library spectra, but reverse search score for both compounds would be high because when it was calculated, peaks in the user spectrum that were not in the library spectrum were disregarded; therefore, only user spectrum peaks belonging to one of the two compounds were considered in the calculation of the value. While the match score（as described in Section 3.2） was ≥ 70, an unequivocal positive result was confirmed (**Fig. 3D**). It was shown that only 5 hits were automatically identified as positives, and the other 5 hits were thought to be "false positives" or "negatives" (< 70) according to the match score listed in Fig. 3D. Although, the pestidcides of clothianidin, flusilazole, and bioresmethrin, were defined as possible positives in TOF/MS full scan TIC, no corresponding production ions of them were found in targeted MS/MS consequential data.

Based on a satisfactory chromatographic performance of separation[45, 46], all of the 317 pesticides in solvent were eluted from the column during a 23 - minutes gradient profile. The first pesticide eluted from the column was Mepiquat chloride at 0.84 min, and the last pesticide was pyridalyl at 20.25 min. Most pesticides (99.1%) were eluted between 2 and 19 min. Only one pesticide, pyridalyl (20.25 min), was eluted after 19 min. The t_R were reproducible under ± 0.2 min within- and between-batches for most of the pesticides in solvent.

3.2 Match score of compounds

In this paper, the compound match score, one of the key parameters to evaluate each positive finding, as aforementioned, is a weighted average of individual scores taking into account the accurate masses and the isotopic distribution[27]. The scoring of the MS^1 matching result in this proposed method is based on four factors:

Mass - How well the measured mass (or *m/z*) compared with the value predicted from the proposed formula.

Abundance - How well the abundance pattern of the measured isotope cluster compared with values predicted

from the proposed formula.

Spacing - How the *m/z* ratio spacing of isotopes detected between the lowest *m/z* ion (A) and the isotopic A+1 and/or A+2 ions compared with the values predicted from the proposed formula.

Retention time - how well the measured retention time of the compound matched an expected retention time.

For the MS^1 results, the tool of "find by formula" computes the compound overall match score as a weighted average of individual probabilities as following,

$$Score = \frac{W_{RT} \times P_{RT} + W_{mass} \times P_{mass} + W_{abundance} \times P_{abundance} + W_{spacing} \times P_{spacing}}{W_{RT} + W_{mass} + W_{abundance} + W_{spacing}}$$

Where the P for retention time (P_{RT}), mass (P_{mass}), isotope abundance ($P_{abundance}$) and isotope spacing ($P_{spacing}$) are match probabilities of each, ranged between zero (no probability) and 1.0 (certainty). The weighting factors (W) values are: retention time match (W_{RT}), 100; mass match (W_{mass}), 100; isotope abundance match ($W_{abundance}$), 60; isotope spacing match (W spacing), 50. When a target compound formula source is available as a database entry, a combined score, on a scale of 0 to 100, is calculated based on t_R, accurate mass, isotope abundance and isotope spacing. **Fig. 3B** presents the result of "find by formula", a table of detected compounds in a celery extract, including formula, overall score, mass(measured), mass (in database), *m/z*(measured), t_R by find by formula algorithm based on the homemade MS^1 database. In this paper, when the calculated score of a given compound is equal or more than 70, a possible positive result was marked. The detection of the insecticide phosphamidon ($C_{10}H_{19}ClNO_5P$) in a cucumber sample was shown in **Fig.4.** The light block (inset **Fig. 4**A) surrounding the isotopes were the predicted isotope distribution of $[M+H]^+$ at *m/z* 300.0756. All ions were matched well with theoretical values, including accurate mass, spacing and relative abundance. The measured mass of protonated molecule of phosphamidon was 300.0764, and the chlorine-37 isotope was 302.0736. Thus the difference in mass is 1.997 mass units, which is the mass defect of a chlorine 37 atom relative to the chlorine 35 atom that has been replaced. Furthermore, the intensity of the A+2 peak (302.0736) is about one third of the A peak (300.0764), which is consistent with one chlorine atom in the molecule. Finally, the weighted matching scoring of 98.16 indicated this positive result.

For the MS^2 results, the identification of compound use a very similar algorithm as the NIST library search. The scoring for matching accurate mass spectra library (MS^2) uses a dot product comparison between the mass peaks in the acquired product ion spectra and the library spectra. The reverse search was selected and a score normalized to between 0 and 100 was given as listed in compound list in **Fig. 3D** (the Score column). In most cases, compounds with scores above a defined threshold of 70 are considered to be positives. However, in the real sample detection, false-negative results occur constantly during the experiment. Mainly for MS^1 database retrieval score > 70, but spectra library retrieval score was < 70. As shown in **Fig. 3D**, where the MS^1 auto-matched score is 96.27 and 98.25 for imidacloprid and pyraclostrobin in one celery extract but their automatic retrieval score of spectra library is 64.18 and 65.01 respectively. This mainly due to a lower concentration of the pesticides, coupled with the impact of complicated matrix interference, resulting in the ineffective matching of fragment ions, and failing to meet the criteria (70). In such cases, a manual background subtraction or inspection of the spectra was performed. As shown in **Fig. 3E**, imidacloprid was confirmed after manual background subtraction, where the main ions (175, 209, 223, 265, 84, et al.) matched the spectra library fragment well. So, it was identified as a positive. Another example was the automatic identification of phosphamidon in a cucumber sample as shown in **Fig. 4B**. In the targeted MS/MS mode, up to nine fragments (relative abundance > 10% of the base peak) were confirmed to this

compound at the same t_R to TOF/MS mode (with a ±0.5 min time window), and the reverse match score against MS^2 spectra library reached 91.09.

3.3 Qualitative Validation

Validation in case of qualitative screening is focused on detectability. The limit of determination (LOD, signal-to-noise ratio of ~ 3:1), reported ordinarily by routine quantity monitoring, was inadequate in high resolution and accurate mass qualitative analysis. Because the main purpose of the qualitative screening is to identify and confirm positive samples at a given level. Most recently, SANCO documents laid down some criteria and parameters to be considered in the validation of screening qualitative methods on pesticide residue analysis[49]. The method proposed here would be considered as satisfactorily validated. The SDLs (screening detection limit) and LOIs (limit of identification) were established as the lowest spiked concentration level when the target analyte was detected and identified in all test samples (i.e. 6 out of 6), regardless of their linearity, recovery, accuracy and precision. In this paper, the screening method validation has been conducted as the similar strategy as in our previous work[46], which is in the line of Diaz et al. suggestion on validation a multiclass wide-scope qualitative screening method for organic pollutants in waters[35].

Hence, the total false negative rate of the 317 pesticides was checked as following. Six samples (three cucumbers and three oranges) were spiked at three different concentration levels (as listed in **Table S1**) with 317 pesticides and analyzed together with their respective blanks according to the procedures described above. Each of the samples needed two chromatographic runs, one in TOF/MS mode and the other in targeted MS/MS mode. Then each of data was analyzed and submitted to automatically matching against the MS^1 database and MS^2 spectra library. The supplementary material **Table S2** summarized the screening and identification result of each analyte in each selected matrix. It must be emphasized the difficulties to find realistic samples free of any target analyte. Then, those samples previously analyzed and proven to have few positive findings were selected as "blanks" to facilitate the validation process. Although several compounds were found in the "blank" samples, only one fungicide (prochloraz) was detected in 3 out of 3 samples of the same commodity (cucumber). Thus, the SDL and LOI of prochloraz could not be validated in the selected matrices. **Table S1** summarized the validation results of all pesticides spiked in the two commodities. It can be observed clearly that 48.9% of the targeted pesticides (155 compounds) could be detected at 1 μg kg^{-1} (SDL) in all spiked samples, and the SDLs obtained for 83.9% (266compounds) the studied compounds were lower than or equal to 10 μg kg^{-1}. The total false negative rate of the proposed qualitative screening method was as low as 4.7% at 50 μg kg^{-1}. As much as 98.1% (311 in 317) of the pesticides could be detected using MS^1 database at the high spiked levels (For different pesticides, the high spiked concentrations ranged from 50 to 750 μg kg^{-1} as listed in **Table S1**). Only 4 compounds (benzoylprop-ethyl, carbophenothion, metoxuron, mexacarbate) were not detected according to the proposed method. Fortunately, the four false-negative compounds have been studied and detected in other commodities, such apple and cabbage, in our previous works[45, 46]. Meanwhile, the LOIs were also listed in **Table S1** in the selected matrices using the targeted MS/MS mode and MS^2 product-ions spectra library. The reliable identification using the accurate product-ions spectra library was feasible to 77.6% of compounds (204 compounds) at LOIs ≤ 10 μg kg^{-1} over the defined identification threshold (match score ≥ 70), and 83.9% at LOIs ≤ 50 μg kg^{-1}. The method readily achieved a lower validated level of 10 μg kg^{-1} for most of the pesticides, which was fit-for-purpose in residue monitoring applications. Be noted that, only 17.3% of the compounds were identified at low concentration (1 μg kg^{-1}) due to the strongly interfered spectra and the low sensitivity of the fragments in targeted MS/MS mode.

3.4 Screening of pesticide residues in marketed samples

To verify the performance of the method, 21 fresh vegetable and fruit of samples in total(n = 328), including apple, broccoli, cabbage, cantaloupe, carrot, celery, cherry tomato , Chinese cabbage, Chinese chive, cucumber, endive, grape, lettuce, peach, pear, plum, spinach, bell pepper, tomato, watermelon, and wax gourd, were analyzed in the study. These represent different fruit/vegetable commodity categories and are also relevant with respect to consumer intake. The vegetables and fruits were pretreated and extracted according to the protocol discussed above. Each extraction was analyzed following the full scan mode of TOF/MS (MS^1) and Targeted MS/MS (MS^2). After auto processed of the raw data by the screening strategy, targeted pesticides were identified by the homemade MS^1 database and MS^2 spectra library.

At the beginning of each batch, a set of internal quality controls was carried out to check that the procedure and instrument were performing reasonably well during each sequence. They implied reagent blanks, full procedural blanks and fortified extracts at 100μg kg^{-1}. Instrument blanks were composed of acetonitrile and were analyzed at the beginning of the batch. Since analyte signals were not found in the instrumental blanks, no further actions were taken. Full procedural blanks were prepared and analyzed after instrumental blanks prior to each batch extraction analyzing to ensure that no laboratory contamination was introduced in the procedure. The fortified extracts were analyzed at the beginning and end of each batch to routinely check the instrument was performing well.

As a result, 799 residues (pesticide-commodity combinations) were identified and confirmed in 79.0% (259 in 328) of the samples, involving as much as 57 kinds of pesticide. Screening result data are shown in **Table 2**.The top-20 pesticides detected in all test samples are graphed in **Fig. 5**. Among them, fungicides, like carbendazim, dimethomorph, difenoconazole, et al. were the most frequently detected pesticides regardless of their concentration in the selected samples. Incidentally, imidacloprid, and acetamiprid were certificated as the main used insecticides in those vegetables and fruits. Besides, plant growth regulators (1,3-diphenyl urea, and paclobutrazol) were also found in several samples. Furthermore, several extremely hazardous phorate sulfoxide (metabolite of phorate) residues were confirmed in peaches, Chinese cabbages and endives, and a few of the banned, highly hazardous pesticides residues were detected, e.g. methomyl in a grape sample, omethoate in grapes and lettuce leaf, carbofuran in peaches and sweet peppers. Those should be taken more cautiously attention in the future research.

4. Conclusion

In this paper, the new qualitative screening strategy of pesticides, combined the HPLC-Q-TOF/MS technique with the use of the accurate mass database and spectra library, has been demonstrated by the development of one of the first applications reported of this technique for simultaneous determination of a large number of pesticides in complicate matrix, such as fruits and vegetables. A home-made accurate mass database and a product ion spectra library included 317 pesticides have been built and validated in selected matrix (cucumber and orange samples).the SDLs and LOCIs of this method were discussed.

The accuracy of pesticides detection has been drastically improved by the TOF/MS mode with MS^1 for target screening and the targeted MS/MS mode together with the spectra library retrieval for its identification. The established method is accurate, reliable, and especially cost-effective, can be applied to the routine monitoring of pesticides in fruit and vegetable samples. The results obtained in the analysis of real samples with the developed

method showed that most of the pesticides contained in the created database were present in the fruit and vegetable samples, and 57 pesticides out of the 328 were identified.

As well as the obvious advantage of using a TOF analyzer – allowing it to perform full-scan acquisition with efficient sensitivity and high mass accuracy (lower than 2 ppm) – it also makes the qualitative analysis easier, quicker and more accurate, because the monitoring of a specific mass of an analyte is not predefined before data acquisition. This fact is very useful in detecting the presence of an unlimited number of chemical constituents in a sample without re-analysis. Consequently, the method could be readily extended to include additional analytes.

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6. Appendix A. Supplementary data

Supplementary data associated with this article can be found online.

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Fig. 1. The screenshot of spectra library (MS^2) created by PCDL

Fig. 2. Workflow of TOF/MS and Q-TOF/MS screening strategy applied

Fig. 3. Pesticide residues screening results with the HPLC- Q-TOF/MS technology of a celery sample purchased from a local market. (A) The total ion current chromatogram (TIC) obtained in TOF/MS mode (MS^1),and (B) automatic screening results of (A) with match score ≥ 70 by Found by Formula algorithm, and (C) TIC obtained in Q-TOF/MS (MS^2) mode, pre-set CEs were applied during the black shadow part to analyze the product ions of the pre-selected precursors, and (D) the automated confirmation results by targeted MS/MS algorithm, and (E) the spectral difference of imidacloprid (*m/z*=256.0597) product ion between measured (after manual background subtraction)and library, at CE=10eV.

Fig. 4. EIC and mass spectra of phosphamidon in a cucumber sample at 10μg kg^{-1} spiked level. (A) EIC of phosphamidon at 5 mDa mass window for $[M+H]^+$ in HPLC-TOF/MS and average mass spectrum of peak at 4.87 min.(B) Q-TOF/MS EIC of precursor *m/z* 300.0756 at 4.87min (phosphamidon) at CE=10 eV(inset: the spectral difference of product ions between sample and standard was shown inner B. The matching Q-TOF/MS score against spectra library was 91.09.

Fig. 5. The top 20 pesticides according to the total findings in 328 fruit and vegetable samples

Table 1 Accurate-mass database including elemental composition, exact mass, retention time, and ionization of the studied pesticides and its MS^2 identification

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
1	1,3-Diphenyl urea	$C_{13}H_{12}N_2O$	212.0950	7.18	$[M+H]^+$	213.1061	15	3
2	1-naphthyl acetamide	$C_{12}H_{11}NO$	185.0841	4.66	$[M+H]^+$	186.0912	10	3
3	3.4.5-Trimethacarb	$C_{11}H_{15}NO_2$	193.1103	7.41	$[M+H]^+$	194.1171	5	2
4	Acetamiprid	$C_{10}H_{11}ClN_4$	222.0672	4.09	$[M+H]^+$	223.0743	15	4
5	Acetochlor	$C_{14}H_{20}ClNO_2$	269.1183	12.81	$[M+H]^+$	270.1260	10	6
6	Aldicarb	$C_7H_{14}N_2O_2S$	190.0776	4.80	$[M+Na]^+$	213.0669	15	3
7	Ametryn	$C_9H_{17}N_5S$	227.1205	6.97	$[M+H]^+$	228.1273	25	10
8	Ancymidol	$C_{15}H_{16}N_2O_2$	256.1212	5.41	$[M+H]^+$	257.1281	25	4
9	Anilofos	$C_{13}H_{19}ClNO_3PS_2$	367.0233	14.94	$[M+H]^+$	368.0299	10	5
10	Aspon	$C_{12}H_{28}O_5P_2S_2$	378.0853	19.00	$[M+H]^+$	379.0927	10	5
11	Atratone	$C_9H_{17}N_5O$	211.1433	4.56	$[M+H]^+$	212.1497	25	15
12	Atrazine	$C_8H_{14}ClN_5$	215.0938	6.58	$[M+H]^+$	216.1001	25	14
13	Atrazine-Desethyl	$C_6H_{10}ClN_5$	187.0625	3.85	$[M+H]^+$	188.0694	20	7
14	Azamethiphos	$C_9H_{10}ClN_2O_5PS$	323.9737	5.46	$[M+H]^+$	324.9808	10	5
15	Azinphos-ethyl	$C_{12}H_{16}N_3O_3PS_2$	345.0371	13.43	$[M+H]^+$	346.0439	15	12
16	Azinphos-methyl	$C_{10}H_{12}N_3O_3PS_2$	317.0058	9.68	$[M+H]^+$	318.0138	5	8
17	Azoxystrobin	$C_{22}H_{17}N_3O_5$	403.1168	11.39	$[M+H]^+$	404.1245	10	3
18	Benalaxyl	$C_{20}H_{23}NO_3$	325.1678	14.27	$[M+H]^+$	326.1753	10	9
19	Bendiocarb	$C_{11}H_{13}NO_4$	223.0845	5.93	$[M+H]^+$	224.0923	5	4
20	Benodanil	$C_{13}H_{10}INO$	322.9807	8.54	$[M+H]^+$	323.9878	20	3
21	Benoxacor	$C_{11}H_{11}Cl_2NO_2$	259.0167	10.01	$[M+H]^+$	260.0245	20	6
22	Bensulide	$C_{14}H_{24}NO_4PS_3$	397.0605	15.35	$[M+H]^+$	398.0679	5	7
23	Benzoximate	$C_{18}H_{18}ClNO_5$	363.0874	16.49	$[M+H]^+$	364.0951	5	4
24	Benzoylprop-ethyl	$C_{18}H_{17}Cl_2NO_3$	365.0586	15.37	$[M+H]^+$	366.0656	5	6
25	Bioallethrin	$C_{19}H_{26}O_3$	302.1882	17.58	$[M+H]^+$	303.1951	5	9
26	Bitertanol	$C_{20}H_{23}N_3O_2$	337.1790	13.00	$[M+H]^+$	338.1854	5	6
27	Bromacil	$C_9H_{13}BrN_2O_2$	260.0160	4.96	$[M+H]^+$	261.0232	5	4
28	Bromfenvinfos	$C_{12}H_{14}BrCl_2O_4P$	401.9190	14.28	$[M+H]^+$	402.9265	5	4
29	Brompyrazon	$C_{10}H_8BrN_3O$	264.9851	3.93	$[M+H]^+$	265.9923	35	7
30	Bromuconazole	$C_{13}H_{12}BrCl_2N_3O$	374.9541	10.77	$[M+H]^+$	375.9609	20	4
31	Bupirimate	$C_{13}H_{24}N_4O_3S$	316.1569	12.98	$[M+H]^+$	317.1635	25	11
32	Buprofezin	$C_{16}H_{23}N_3OS$	305.1562	17.56	$[M+H]^+$	306.1625	10	6
33	Butachlor	$C_{17}H_{26}ClNO_2$	311.1652	17.62	$[M+H]^+$	312.1727	10	7
34	Butafenacil	$C_{20}H_{18}ClF_3N_2O_6$	474.0806	14.36	$[M+NH_4]^+$	492.1157	10	10
35	Butamifos	$C_{13}H_{21}N_2O_4PS$	332.0960	16.63	$[M+H]^+$	333.1035	5	3
36	Butralin	$C_{14}H_{21}N_3O_4$	295.1532	18.26	$[M+H]^+$	296.1605	10	3
37	Cadusafos	$C_{10}H_{23}O_2PS_2$	270.0877	14.85	$[M+H]^+$	271.0940	10	3
38	Cafenstrole	$C_{16}H_{22}N_4O_3S$	350.1413	13.00	$[M+H]^+$	351.1491	5	1
39	Carbaryl	$C_{12}H_{11}NO_2$	201.0790	6.42	$[M+H]^+$	202.0862	5	2
40	Carbendazim	$C_9H_9N_3O_2$	191.0695	2.85	$[M+H]^+$	192.0761	15	2
41	Carbetamide	$C_{12}H_{16}N_2O_3$	236.1161	4.79	$[M+H]^+$	237.1229	5	7
42	Carbofuran	$C_{12}H_{15}NO_3$	221.1052	5.99	$[M+H]^+$	222.1117	10	4
43	Carbofuran-3-hydroxy	$C_{12}H_{15}NO_4$	237.1001	3.70	$[M+H]^+$	238.1074	5	8
44	Carbophenothion	$C_{11}H_{16}ClO_2PS_3$	341.9739	18.26	$[M+H]^+$	342.9817	5	5
45	Carboxin	$C_{12}H_{13}NO_2S$	235.0667	6.68	$[M+H]^+$	236.0729	15	2
46	Carfentrazone-ethyl	$C_{15}H_{14}Cl_2F_3N_3O_3$	411.0364	14.42	$[M+NH_4]^+$	429.0701	15	11
47	Carpropamid	$C_{15}H_{18}Cl_3NO$	333.0454	14.83	$[M+H]^+$	334.0524	5	9
48	Chlorfenvinphos	$C_{12}H_{14}Cl_3O_4P$	357.9695	13.93	$[M+H]^+$	358.9762	5	5

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
49	Chloridazon	$C_{10}H_8ClN_3O$	221.0356	3.78	$[M+H]^+$	222.0427	30	14
50	Chlorotoluron	$C_{10}H_{13}ClN_2O$	212.0716	6.29	$[M+H]^+$	213.0781	15	2
51	Chloroxuron	$C_{15}H_{15}ClN_2O_2$	290.0822	10.40	$[M+H]^+$	291.0887	15	3
52	Chlorpyrifos-ethyl	$C_9H_{11}Cl_3NO_3PS$	348.9263	17.84	$[M+H]^+$	349.9334	10	12
53	Chlorthiophos	$C_{11}H_{15}Cl_2O_3PS_2$	359.9577	18.27	$[M+H]^+$	360.9648	10	11
54	Chromafenozide	$C_{24}H_{30}N_2O_3$	394.2256	13.27	$[M+H]^+$	395.2326	5	3
55	Cinmethylin	$C_{18}H_{26}O_2$	274.1933	17.31	$[M+NH_4]^+$	292.2270	5	7
56	Clomazone	$C_{12}H_{14}ClNO_2$	239.0713	8.18	$[M+H]^+$	240.0791	15	3
57	Cloquintocet-mexyl	$C_{18}H_{22}ClNO_3$	335.1288	16.97	$[M+H]^+$	336.1352	15	5
58	Clothianidin	$C_6H_8ClN_5O_2S$	249.0087	3.64	$[M+H]^+$	250.0160	5	6
59	Crufomate	$C_{12}H_{19}ClNO_3P$	291.0791	11.09	$[M+H]^+$	292.0862	20	8
60	Cyanazine	$C_9H_{13}ClN_6$	240.0890	5.34	$[M+H]^+$	241.0960	20	7
61	Cycloate	$C_{11}H_{21}NOS$	215.1344	15.56	$[M+H]^+$	216.1418	15	8
62	Cycluron	$C_{11}H_{22}N_2O$	198.1732	6.72	$[M+H]^+$	199.1795	20	5
63	Cyflufenamid	$C_{20}H_{17}F_5N_2O_2$	412.1210	16.71	$[M+H]^+$	413.1283	10	8
64	Cyprazine	$C_9H_{14}ClN_5$	227.0938	6.60	$[M+H]^+$	228.1007	20	9
65	Cyproconazole	$C_{15}H_{18}ClN_3O$	291.1138	9.64	$[M+H]^+$	292.1206	15	3
66	Cyprodinil	$C_{14}H_{15}N_3$	225.1266	12.14	$[M+H]^+$	226.1331	40	15
67	Demeton-S	$C_8H_{19}O_3PS_2$	258.0513	7.73	$[M+H]^+$	259.0586	5	1
68	Demeton-S sulfoxide	$C_8H_{19}O_4PS_2$	274.0462	3.73	$[M+H]^+$	275.0529	10	7
69	Demeton-S-methyl	$C_6H_{15}O_3PS_2$	230.0200	5.46	$[M+Na]^+$	253.0093	10	2
70	Demeton-S-methyl sulfone	$C_6H_{15}O_5PS_2$	262.0099	3.18	$[M+H]^+$	263.0174	15	7
71	Desethyl-sebuthylazine	$C_7H_{12}ClN_5$	201.0781	4.64	$[M+H]^+$	202.0853	20	6
72	Desmedipham	$C_{16}H_{16}N_2O_4$	300.1110	9.55	$[M+NH_4]^+$	318.1449	5	5
73	Desmethyl-pirimicarb	$C_{10}H_{16}N_4O_2$	224.1273	3.35	$[M+H]^+$	225.1339	10	3
74	Diallate	$C_{10}H_{17}Cl_2NOS$	269.0408	16.84	$[M+H]^+$	270.0485	15	5
75	Diazinon	$C_{12}H_{21}N_2O_3PS$	304.1011	15.19	$[M+H]^+$	305.1089	20	8
76	Dichlofenthion	$C_{10}H_{13}Cl_2O_3PS$	313.9700	17.73	$[M+H]^+$	314.9776	15	2
77	Diclobutrazole	$C_{15}H_{19}Cl_2N_3O$	327.0905	11.97	$[M+H]^+$	328.0978	15	3
78	Dicrotophos	$C_8H_{16}NO_5P$	237.0766	3.21	$[M+H]^+$	238.0832	10	4
79	Diethatyl-ethyl	$C_{16}H_{22}ClNO_3$	311.1288	14.04	$[M+H]^+$	312.1360	10	6
80	Diethofencarb	$C_{14}H_{21}NO_4$	267.1471	9.78	$[M+H]^+$	268.1541	5	3
81	Diethyltoluamide	$C_{12}H_{17}NO$	191.1310	6.90	$[M+H]^+$	192.1373	20	2
82	Difenoconazole	$C_{19}H_{17}Cl_2N_3O_3$	405.0647	14.98	$[M+H]^+$	406.0721	15	8
83	Difenoxuron	$C_{16}H_{18}N_2O_3$	286.1317	7.27	$[M+H]^+$	287.1381	15	5
84	Dimefuron	$C_{15}H_{19}ClN_4O_3$	338.1146	8.32	$[M+H]^+$	339.1218	20	4
85	Dimepiperate	$C_{15}H_{21}NOS$	263.1344	16.19	$[M+H]^+$	264.1419	5	2
86	Dimethachlor	$C_{13}H_{18}ClNO_2$	255.1026	7.92	$[M+H]^+$	256.1101	10	5
87	Dimethametryn	$C_{11}H_{21}N_5S$	255.1518	11.32	$[M+H]^+$	256.1580	25	5
88	Dimethenamid	$C_{12}H_{18}ClNO_2S$	275.0747	9.91	$[M+H]^+$	276.0819	10	4
89	Dimethirimol	$C_{11}H_{19}N_3O$	209.1528	3.80	$[M+H]^+$	210.1597	30	6
90	Dimethoate	$C_5H_{12}NO_3PS_2$	228.9996	3.94	$[M+H]^+$	230.0066	10	5
91	Dimethomorph	$C_{21}H_{22}ClNO_4$	387.1237	9.16	$[M+H]^+$	388.1305	20	5
92	Diniconazole	$C_{15}H_{17}Cl_2N_3O$	325.0749	13.26	$[M+H]^+$	326.0821	20	3
93	Diphenamid	$C_{16}H_{17}NO$	239.1310	8.14	$[M+H]^+$	240.1374	20	3
94	Dipropetryn	$C_{11}H_{21}N_5S$	255.1518	11.87	$[M+H]^+$	256.1583	25	9
95	Disulfoton sulfone	$C_8H_{19}O_4PS_3$	306.0183	8.72	$[M+H]^+$	307.0254	10	7
96	Disulfoton sulfoxide	$C_8H_{19}O_3PS_3$	290.0234	6.57	$[M+H]^+$	291.0304	10	6
97	Dithiopyr	$C_{15}H_{16}F_5NO_2S_2$	401.0543	17.30	$[M+H]^+$	402.0618	25	34
98	Diuron	$C_9H_{10}Cl_2N_2O$	232.0170	6.86	$[M+H]^+$	233.0242	15	3
99	Dodemorph	$C_{18}H_{35}NO$	281.2719	7.94	$[M+H]^+$	282.2784	25	6

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
100	Edifenphos	$C_{14}H_{15}O_2PS_2$	310.0251	13.71	$[M+H]^+$	311.0324	15	6
101	Emamectin-benzoate	$C_{49}H_{75}NO_{13}$	885.5238	17.25	$[M+H]^+$	886.5305	30	3
102	Epoxiconazole	$C_{17}H_{13}ClFN_3O$	329.0731	11.53	$[M+H]^+$	330.0806	15	3
103	Esprocarb	$C_{15}H_{23}NOS$	265.1500	17.32	$[M+H]^+$	266.1575	10	6
104	Etaconazole	$C_{14}H_{15}Cl_2N_3O_2$	327.0541	11.40	$[M+H]^+$	328.0617	20	6
105	Ethidimuron	$C_7H_{12}N_4O_3S_2$	264.0351	3.69	$[M+H]^+$	265.0425	5	6
106	Ethiofencarb sulfone	$C_{11}H_{15}NO_4S$	257.0722	3.67	$[M+H]^+$	258.0791	5	2
107	Ethion	$C_9H_{22}O_4P_2S_4$	383.9876	18.06	$[M+H]^+$	384.9943	5	5
108	Ethiprole	$C_{13}H_9Cl_2F_3N_4OS$	395.9826	9.63	$[M+H]^+$	396.9897	20	6
109	Ethirimol	$C_{11}H_{19}N_3O$	209.1528	3.80	$[M+H]^+$	210.1592	25	9
110	Ethoprophos	$C_8H_{19}O_2PS_2$	242.0564	11.20	$[M+H]^+$	243.0641	15	7
111	Etobenzanid	$C_{16}H_{15}Cl_2NO_3$	339.0429	15.05	$[M+H]^+$	340.0512	20	5
112	Etrimfos	$C_{10}H_{17}N_2O_4PS$	292.0647	14.76	$[M+H]^+$	293.0713	20	6
113	Famphur	$C_{10}H_{16}NO_5PS_2$	325.0208	9.63	$[M+H]^+$	326.0279	15	7
114	Fenamidone	$C_{17}H_{17}N_3OS$	311.1092	11.11	$[M+H]^+$	312.1164	10	8
115	Fenamiphos	$C_{13}H_{22}NO_3PS$	303.1058	10.85	$[M+H]^+$	304.1133	15	6
116	Fenamiphos sulfone	$C_{13}H_{22}NO_5PS$	335.0956	5.79	$[M+H]^+$	336.1031	15	6
117	Fenamiphos sulfoxide	$C_{13}H_{22}NO_4PS$	319.1007	4.82	$[M+H]^+$	320.1074	15	14
118	Fenarimol	$C_{17}H_{12}Cl_2N_2O$	330.0327	10.98	$[M+H]^+$	331.0399	25	10
119	Fenazaquin	$C_{20}H_{22}N_2O$	306.1732	18.64	$[M+H]^+$	307.1798	20	3
120	Fenbuconazole	$C_{19}H_{17}ClN_4$	336.1142	12.70	$[M+H]^+$	337.1219	20	3
121	Fenfuram	$C_{12}H_{11}NO_2$	201.0790	6.87	$[M+H]^+$	202.0854	15	2
122	Fenobucarb	$C_{12}H_{17}NO_2$	207.1259	9.07	$[M+H]^+$	208.1340	5	5
123	Fenothiocarb	$C_{13}H_{19}NO_2S$	253.1137	13.08	$[M+H]^+$	254.1209	10	2
124	Fenoxanil	$C_{15}H_{18}Cl_2N_2O_2$	328.0745	14.25	$[M+H]^+$	329.0811	5	6
125	Fenpropidin	$C_{19}H_{31}N$	273.2457	9.05	$[M+H]^+$	274.2519	35	9
126	Fenpyroximate	$C_{24}H_{27}N_3O_4$	421.2002	18.32	$[M+H]^+$	422.2066	15	2
127	Fensulfothion	$C_{11}H_{17}O_4PS_2$	308.0306	7.71	$[M+H]^+$	309.0378	20	9
128	Fenthion sulfoxide	$C_{10}H_{15}O_4PS_2$	294.0149	6.24	$[M+H]^+$	295.0217	20	10
129	Fenuron	$C_9H_{12}N_2O$	164.0950	3.76	$[M+H]^+$	165.1016	10	2
130	Flamprop	$C_{16}H_{13}ClFNO_3$	321.0568	7.94	$[M+H]^+$	322.0643	5	4
131	Flamprop-methyl	$C_{17}H_{15}ClFNO_3$	335.0725	12.37	$[M+H]^+$	336.0794	5	2
132	Fluazifop-butyl	$C_{19}H_{20}F_3NO_4$	383.1344	17.76	$[M+H]^+$	384.1398	20	5
133	Flucycloxuron	$C_{25}H_{20}ClF_2N_3O_3$	483.1161	17.91	$[M+H]^+$	484.1242	5	2
134	Flufenacet	$C_{14}H_{13}F_4N_3O_2S$	363.0665	13.26	$[M+H]^+$	364.0732	10	3
135	Flufenoxuron	$C_{21}H_{11}ClF_6N_2O_3$	488.0362	17.89	$[M+H]^+$	489.0436	10	4
136	Flumiclorac-pentyl	$C_{21}H_{23}ClFNO_5$	423.1249	17.61	$[M+NH_4]^+$	441.1584	10	8
137	Fluometuron	$C_{10}H_{11}F_3N_2O$	232.0824	6.46	$[M+H]^+$	233.0894	20	2
138	Fluquinconazole	$C_{16}H_8Cl_2FN_5O$	375.0090	11.71	$[M+H]^+$	376.0162	20	9
139	Fluridone	$C_{19}H_{14}F_3NO$	329.1028	9.51	$[M+H]^+$	330.1090	40	3
140	Flurtamone	$C_{18}H_{14}F_3NO_2$	333.0977	10.20	$[M+H]^+$	334.1048	25	8
141	Flusilazole	$C_{16}H_{15}F_2N_3Si$	315.1003	12.70	$[M+H]^+$	316.1075	20	11
142	Flutolanil	$C_{17}H_{16}F_3NO_2$	323.1133	13.11	$[M+H]^+$	324.1208	10	8
143	Flutriafol	$C_{16}H_{13}F_2N_3O$	301.1027	6.61	$[M+H]^+$	302.1095	10	4
144	Fonofos	$C_{10}H_{15}OPS_2$	246.0302	15.43	$[M+H]^+$	247.0371	5	3
145	Forchlorfenuron	$C_{12}H_{10}ClN_3O$	247.0512	6.52	$[M+H]^+$	248.0585	10	5
146	Fosthiazate	$C_9H_{18}NO_3PS_2$	283.0466	6.59	$[M+H]^+$	284.0530	10	3
147	Furalaxyl	$C_{17}H_{19}NO_4$	301.1314	9.65	$[M+H]^+$	302.1382	10	4
148	Furathiocarb	$C_{18}H_{26}N_2O_5S$	382.1562	17.40	$[M+H]^+$	383.1627	10	6
149	Furmecyclox	$C_{14}H_{21}NO_3$	251.1521	13.36	$[M+H]^+$	252.1586	15	9
150	Haloxyfop-ehyoxyethyl	$C_{19}H_{19}ClF_3NO_5$	433.0904	17.20	$[M+H]^+$	434.0973	10	9

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
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151	Haloxyfop-methyl	$C_{16}H_{13}ClF_3NO_4$	375.0485	16.42	$[M+H]^+$	376.0546	15	6
152	Heptenophos	$C_9H_{12}ClO_4P$	250.0162	7.31	$[M+H]^+$	251.0232	5	5
153	Hexaconazole	$C_{14}H_{17}Cl_2N_3O$	313.0749	12.53	$[M+H]^+$	314.0825	15	3
154	Hexazinone	$C_{12}H_{20}N_4O_2$	252.1586	4.87	$[M+H]^+$	253.1656	10	2
155	Hexythiazox	$C_{17}H_{21}ClN_2O_2S$	352.1012	17.84	$[M+H]^+$	353.1079	10	8
156	Imazalil	$C_{14}H_{14}Cl_2N_2O$	296.0483	6.48	$[M+H]^+$	297.0550	25	13
157	Imazapic	$C_{14}H_{17}N_3O_3$	275.1270	3.85	$[M+H]^+$	276.1332	25	14
158	Imazethapyr	$C_{15}H_{19}N_3O_3$	289.1426	4.91	$[M+H]^+$	290.1504	25	19
159	Imidacloprid	$C_9H_{10}ClN_5O_2$	255.0523	3.82	$[M+H]^+$	256.0597	10	10
160	Indoxacarb	$C_{22}H_{17}ClF_3N_3O_7$	527.0707	16.78	$[M+H]^+$	528.0778	10	15
161	Iprobenfos	$C_{13}H_{21}O_3PS$	288.0949	12.62	$[M+H]^+$	289.1018	5	4
162	Iprovalicarb	$C_{18}H_{28}N_2O_3$	320.2100	10.80	$[M+H]^+$	321.2162	5	7
163	Isazofos	$C_9H_{17}ClN_3O_3PS$	313.0417	13.83	$[M+H]^+$	314.0477	15	10
164	Isocarbamid	$C_8H_{15}N_3O_2$	185.1164	3.72	$[M+H]^+$	186.1231	10	3
165	Isofenphos oxon	$C_{15}H_{24}NO_5P$	329.1392	10.00	$[M+H]^+$	330.1464	5	4
166	Isomethiozin	$C_{12}H_{20}N_4OS$	268.1358	13.80	$[M+H]^+$	269.1433	15	4
167	Isoprocarb	$C_{11}H_{15}NO_2$	193.1103	7.26	$[M+H]^+$	194.1167	20	2
168	Isopropalin	$C_{15}H_{23}N_3O_4$	309.1689	18.89	$[M+H]^+$	310.1756	20	25
169	Isoprothiolane	$C_{12}H_{18}O_4S_2$	290.0647	12.46	$[M+H]^+$	291.0714	5	5
170	Isoproturon	$C_{12}H_{18}N_2O$	206.1419	6.89	$[M+H]^+$	207.1491	15	3
171	Isouron	$C_{10}H_{17}N_3O_2$	211.1321	5.21	$[M+H]^+$	212.1387	15	4
172	Isoxaben	$C_{18}H_{24}N_2O_4$	332.1736	12.30	$[M+H]^+$	333.1803	10	3
173	Isoxadifen-ethyl	$C_{18}H_{17}NO_3$	295.1208	14.65	$[M+H]^+$	296.1282	10	11
174	Isoxathion	$C_{13}H_{16}NO_4PS$	313.0538	16.39	$[M+H]^+$	314.0610	10	6
175	Kadethrin	$C_{23}H_{24}O_4S$	396.1395	17.54	$[M+NH_4]^+$	414.1738	5	7
176	Karbutilate	$C_{14}H_{21}N_3O_3$	279.1583	5.74	$[M+H]^+$	280.1656	5	3
177	Kresoxim-methyl	$C_{18}H_{19}NO_4$	313.1314	14.46	$[M+H]^+$	314.1391	5	3
178	Lactofen	$C_{19}H_{15}ClF_3NO_7$	461.0489	17.66	$[M+NH_4]^+$	479.0821	5	6
179	Linuron	$C_9H_{10}Cl_2N_2O_2$	248.0119	9.38	$[M+H]^+$	249.0196	15	11
180	Malaoxon	$C_{10}H_{19}O_7PS$	314.0589	5.90	$[M+H]^+$	315.0653	5	4
181	Malathion	$C_{10}H_{19}O_6PS_2$	330.0361	12.77	$[M+H]^+$	331.0431	5	3
182	Mecarbam	$C_{10}H_{20}NO_5PS_2$	329.0521	13.92	$[M+H]^+$	330.0590	5	5
183	Mefenacet	$C_{16}H_{14}N_2O_2S$	298.0776	11.17	$[M+H]^+$	299.0840	10	5
184	Mepanipyrim	$C_{14}H_{13}N_3$	223.1110	11.77	$[M+H]^+$	224.1172	35	26
185	Mephosfolan	$C_8H_{16}NO_3PS_2$	269.0309	5.08	$[M+H]^+$	270.0374	15	6
186	Mepiquat chloride	$C_7H_{15}N$	113.1205	0.84	$[M+H]^+$	114.1278	30	5
187	Mepronil	$C_{17}H_{19}NO_2$	269.1416	12.43	$[M+H]^+$	270.1474	15	4
188	Mesosulfuron-methyl	$C_{17}H_{21}N_5O_9S_2$	503.0781	6.92	$[M+H]^+$	504.0855	15	2
189	Metalaxyl	$C_{15}H_{21}NO_4$	279.1471	6.94	$[M+H]^+$	280.1537	10	6
190	Metamitron	$C_{10}H_{10}N_4O$	202.0855	3.62	$[M+H]^+$	203.0919	25	12
191	Metazachlor	$C_{14}H_{16}ClN_3O$	277.0982	7.72	$[M+H]^+$	278.1048	5	6
192	Metconazole	$C_{17}H_{22}ClN_3O$	319.1451	12.97	$[M+H]^+$	320.1513	20	2
193	Methabenzthiazuron	$C_{10}H_{11}N_3OS$	221.0623	6.17	$[M+H]^+$	222.0687	10	3
194	Methamidophos	$C_2H_8NO_2PS$	141.0013	1.73	$[M+H]^+$	142.0082	10	3
195	Methiocarb	$C_{11}H_{15}NO_2S$	225.0824	9.07	$[M+H]^+$	226.0900	5	4
196	Methiocarb sulfoxide	$C_{11}H_{15}NO_3S$	241.0773	3.58	$[M+H]^+$	242.0837	5	3
197	Methomyl	$C_5H_{10}N_2O_2S$	162.0463	3.00	$[M+H]^+$	163.0533	5	3
198	Methoprotryne	$C_{11}H_{21}N_5OS$	271.1467	6.87	$[M+H]^+$	272.1531	25	8
199	Metobromuron	$C_9H_{11}BrN_2O_2$	258.0004	7.25	$[M+H]^+$	259.0078	15	10
200	Metolachlor	$C_{15}H_{22}ClNO_2$	283.1339	12.61	$[M+H]^+$	284.1408	10	4
201	Metoxuron	$C_{10}H_{13}ClN_2O_2$	228.0666	4.75	$[M+H]^+$	229.0732	15	2

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
202	Metribuzin	$C_8H_{14}N_4OS$	214.0888	5.45	$[M+H]^+$	215.0955	25	12
203	Mexacarbate	$C_{12}H_{18}N_2O_2$	222.1368	4.07	$[M+H]^+$	223.1439	15	4
204	Monocrotophos	$C_7H_{14}NO_5P$	223.0610	2.93	$[M+H]^+$	224.0673	5	5
205	Monuron	$C_9H_{11}ClN_2O$	198.0560	5.13	$[M+H]^+$	199.0624	15	2
206	Myclobutanil	$C_{15}H_{17}ClN_4$	288.1142	10.93	$[M+H]^+$	289.1211	15	3
207	Napropamide	$C_{17}H_{21}NO_2$	271.1572	11.93	$[M+H]^+$	272.1638	10	11
208	Neburon	$C_{12}H_{16}Cl_2N_2O$	274.0640	13.35	$[M+H]^+$	275.0711	20	4
209	Norflurazon	$C_{12}H_9ClF_3N_3O$	303.0386	7.30	$[M+H]^+$	304.0459	35	19
210	Nuarimol	$C_{17}H_{12}ClFN_2O$	314.0622	8.48	$[M+H]^+$	315.0694	25	9
211	Octhilinone	$C_{11}H_{19}NOS$	213.1187	11.57	$[M+H]^+$	214.1254	15	4
212	Ofurace	$C_{14}H_{16}ClNO_3$	281.0819	6.84	$[M+H]^+$	282.0883	10	12
213	Omethoate	$C_5H_{12}NO_4PS$	213.0225	2.22	$[M+H]^+$	214.0287	10	7
214	Orbencarb	$C_{12}H_{16}ClNOS$	257.0641	15.07	$[M+H]^+$	258.0717	10	6
215	Oxadixyl	$C_{14}H_{18}N_2O_4$	278.1267	5.18	$[M+H]^+$	279.1336	5	4
216	Oxycarboxin	$C_{12}H_{13}NO_4S$	267.0565	4.57	$[M+H]^+$	268.0638	10	2
217	Paclobutrazol	$C_{15}H_{20}ClN_3O$	293.1295	9.01	$[M+H]^+$	294.1367	15	2
218	Paraoxon-ethyl	$C_{10}H_{14}NO_6P$	275.0559	7.28	$[M+H]^+$	276.0623	10	3
219	Pebulate	$C_{10}H_{21}NOS$	203.1344	15.52	$[M+H]^+$	204.1405	10	4
220	Penconazole	$C_{13}H_{15}Cl_2N_3$	283.0643	12.79	$[M+H]^+$	284.0716	10	5
221	Pencycuron	$C_{19}H_{21}ClN_2O$	328.1342	15.89	$[M+H]^+$	329.1410	15	6
222	Pentanochlor	$C_{13}H_{18}ClNO$	239.1077	13.67	$[M+H]^+$	240.1154	20	7
223	Phenmedipham	$C_{16}H_{16}N_2O_4$	300.1110	9.52	$[M+NH_4]^+$	318.1457	5	4
224	Phenthoate	$C_{12}H_{17}O_4PS_2$	320.0306	15.16	$[M+H]^+$	321.0378	5	8
225	Phorate sulfone	$C_7H_{17}O_4PS_3$	292.0027	8.80	$[M+H]^+$	293.0097	5	6
226	Phorate sulfoxide	$C_7H_{17}O_3PS_3$	276.0077	6.54	$[M+H]^+$	277.0141	5	7
227	Phosalone	$C_{12}H_{15}ClNO_4PS_2$	366.9869	16.15	$[M+H]^+$	367.9945	5	5
228	Phosphamidon	$C_{10}H_{19}ClNO_5P$	299.0689	4.87	$[M+H]^+$	300.0756	10	9
229	Phoxim	$C_{12}H_{15}N_2O_3PS$	298.0541	16.34	$[M+H]^+$	299.0615	5	8
230	Picolinafen	$C_{19}H_{12}F_4N_2O_2$	376.0835	17.20	$[M+H]^+$	377.0906	20	4
231	Picoxystrobin	$C_{18}H_{16}F_3NO_4$	367.1031	14.87	$[M+H]^+$	368.1098	5	3
232	Piperonyl-butoxide	$C_{19}H_{30}O_5$	338.2093	17.21	$[M+NH_4]^+$	356.2423	5	2
233	Piperophos	$C_{14}H_{28}NO_3PS_2$	353.1248	16.39	$[M+H]^+$	354.1312	15	7
234	Pirimicarb-desmethyl-formamido	$C_{11}H_{16}N_4O_3$	252.1222	5.27	$[M+H]^+$	253.1290	10	2
235	Pirimiphos-ethyl	$C_{13}H_{24}N_3O_3PS$	333.1276	17.94	$[M+H]^+$	334.1335	20	4
236	Pirimiphos-methyl	$C_{11}H_{20}N_3O_3PS$	305.0963	16.09	$[M+H]^+$	306.1028	25	9
237	Pretilachlor	$C_{17}H_{26}ClNO_2$	311.1652	16.39	$[M+H]^+$	312.1726	10	4
238	Prochloraz	$C_{15}H_{16}Cl_3N_3O_2$	375.0308	13.61	$[M+H]^+$	376.0379	5	6
239	Profenofos	$C_{11}H_{15}BrClO_3PS$	371.9351	16.35	$[M+H]^+$	372.9429	10	7
240	Prometon	$C_{10}H_{19}N_5O$	225.1590	5.86	$[M+H]^+$	226.1662	25	6
241	Prometryn	$C_{10}H_{19}N_5S$	241.1361	9.14	$[M+H]^+$	242.1426	20	4
242	Pronamide	$C_{12}H_{11}Cl_2NO$	255.0218	11.26	$[M+H]^+$	256.0289	10	6
243	Propamocarb	$C_9H_{20}N_2O_2$	188.1525	2.36	$[M+H]^+$	189.1588	15	4
244	Propanil	$C_9H_9Cl_2NO$	217.0061	8.26	$[M+H]^+$	218.0136	20	6
245	Propaphos	$C_{13}H_{21}O_4PS$	304.0898	13.38	$[M+H]^+$	305.0968	5	4
246	Propaquizafop	$C_{22}H_{22}ClN_3O_5$	443.1248	17.08	$[M+H]^+$	444.1318	15	5
247	Propargite	$C_{19}H_{26}O_4S$	350.1552	18.42	$[M+NH_4]^+$	368.1886	5	5
248	Propazine	$C_9H_{16}ClN_5$	229.1094	8.40	$[M+H]^+$	230.1159	20	8
249	Propiconazole	$C_{15}H_{17}Cl_2N_3O_2$	341.0698	13.49	$[M+H]^+$	342.0768	20	5
250	Propisochlor	$C_{15}H_{22}ClNO_2$	283.1339	14.55	$[M+H]^+$	284.1411	10	9
251	Propoxur	$C_{11}H_{15}NO_3$	209.1052	5.86	$[M+H]^+$	210.1126	5	4
252	Pyraclofos	$C_{14}H_{18}ClN_2O_3PS$	360.0464	14.88	$[M+H]^+$	361.0535	20	13

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
253	Pyraclostrobin	$C_{19}H_{18}ClN_3O_4$	387.0986	15.61	$[M+H]^+$	388.1052	10	6
254	Pyraflufen-ethyl	$C_{15}H_{13}Cl_2F_3N_2O_4$	412.0205	15.18	$[M+H]^+$	413.0276	20	12
255	Pyrazophos	$C_{14}H_{20}N_3O_5PS$	373.0861	15.35	$[M+H]^+$	374.0931	20	6
256	Pyrazoxyfen	$C_{20}H_{16}Cl_2N_2O_3$	402.0538	14.13	$[M+H]^+$	403.0612	20	7
257	Pyributicarb	$C_{18}H_{22}N_2O_2S$	330.1402	17.94	$[M+H]^+$	331.1475	15	7
258	Pyridaben	$C_{19}H_{25}ClN_2OS$	364.1376	18.94	$[M+H]^+$	365.1447	5	7
259	Pyridalyl	$C_{18}H_{14}Cl_4F_3NO_3$	488.9680	20.25	$[M+H]^+$	489.9751	10	11
260	Pyridaphenthion	$C_{14}H_{17}N_2O_4PS$	340.0647	11.90	$[M+H]^+$	341.0734	15	5
261	Pyrimethanil	$C_{12}H_{13}N_3$	199.1110	7.86	$[M+H]^+$	200.1183	35	26
262	Pyrimidifen	$C_{20}H_{28}ClN_3O_2$	377.1870	16.46	$[M+H]^+$	378.1934	20	4
263	Pyriproxyfen	$C_{20}H_{19}NO_3$	321.1365	17.65	$[M+H]^+$	322.1440	10	3
264	Pyroquilon	$C_{11}H_{11}NO$	173.0841	5.10	$[M+H]^+$	174.0905	30	8
265	Quinalphos	$C_{12}H_{15}N_2O_3PS$	298.0541	14.20	$[M+H]^+$	299.0605	15	8
266	Quinoclamine	$C_{10}H_6ClNO_2$	207.0087	5.29	$[M+H]^+$	208.0160	25	12
267	Quinoxyphen	$C_{15}H_8Cl_2FNO$	306.9967	16.98	$[M+H]^+$	308.0037	35	15
268	Quizalofop-ethyl	$C_{19}H_{17}ClN_2O_4$	372.0877	16.78	$[M+H]^+$	373.0945	20	14
269	Rabenzazole	$C_{12}H_{12}N_4$	212.1062	6.64	$[M+H]^+$	213.1124	30	19
270	Rotenone	$C_{23}H_{22}O_6$	394.1416	13.43	$[M+H]^+$	395.1478	25	15
271	Sebutylazine	$C_9H_{16}ClN_5$	229.1094	8.16	$[M+H]^+$	230.1169	25	14
272	Secbumeton	$C_{10}H_{19}N_5O$	225.1590	5.60	$[M+H]^+$	226.1662	25	11
273	Simazine	$C_7H_{12}ClN_5$	201.0781	5.18	$[M+H]^+$	202.0850	25	10
274	Simeconazole	$C_{14}H_{20}FN_3OSi$	293.1360	10.69	$[M+H]^+$	294.1428	15	4
275	Simeton	$C_8H_{15}N_5O$	197.1277	3.76	$[M+H]^+$	198.1344	30	12
276	Spinosad	$C_{41}H_{65}NO_{10}$	731.4609	14.45	$[M+H]^+$	732.4670	25	3
277	Spiroxamine	$C_{18}H_{35}NO_2$	297.2668	9.23	$[M+H]^+$	298.2732	20	4
278	Sulfentrazone	$C_{11}H_{10}Cl_2F_2N_4O_3S$	385.9819	6.54	$[M+NH_4]^+$	404.0165	5	5
279	Sulfotep	$C_8H_{20}O_5P_2S_2$	322.0227	15.92	$[M+H]^+$	323.0301	10	9
280	Sulprofos	$C_{12}H_{19}O_2PS_3$	322.0285	18.12	$[M+H]^+$	323.0363	10	9
281	Tebuconazole	$C_{16}H_{22}ClN_3O$	307.1451	12.08	$[M+H]^+$	308.1527	20	3
282	Tebufenozide	$C_{22}H_{28}N_2O_2$	352.2151	14.16	$[M+H]^+$	353.2222	5	3
283	Tebupirimfos	$C_{13}H_{23}N_2O_3PS$	318.1167	17.71	$[M+H]^+$	319.1235	10	5
284	Tebutam	$C_{15}H_{23}NO$	233.1780	12.62	$[M+H]^+$	234.1845	15	2
285	Temephos	$C_{16}H_{20}O_6P_2S_3$	465.9897	17.88	$[M+NH_4]^+$	484.0224	5	4
286	Terbucarb	$C_{17}H_{27}NO_2$	277.2042	15.95	$[M+H]^+$	278.2116	5	5
287	Terbuthylazine	$C_9H_{16}ClN_5$	229.1094	9.12	$[M+H]^+$	230.1159	15	3
288	Terbutryne	$C_{10}H_{19}N_5S$	241.1361	9.57	$[M+H]^+$	242.1428	15	2
289	Tetrachlorvinphos	$C_{10}H_9Cl_4O_4P$	363.8993	12.89	$[M+H]^+$	364.9065	5	3
290	Tetraconazole	$C_{13}H_{11}Cl_2F_4N_3O$	371.0215	12.14	$[M+H]^+$	372.0290	20	5
291	Tetramethrin	$C_{19}H_{25}NO_4$	331.1784	17.38	$[M+H]^+$	332.1853	10	9
292	Thiacloprid	$C_{10}H_9ClN_4S$	252.0236	4.67	$[M+H]^+$	253.0309	15	4
293	Thiamethoxam	$C_8H_{10}ClN_5O_3S$	291.0193	3.27	$[M+H]^+$	292.0266	5	6
294	Thiazafluron	$C_6H_7F_3N_4OS$	240.0293	5.26	$[M+H]^+$	241.0366	10	2
295	Thiazopyr	$C_{16}H_{17}F_5N_2O_2S$	396.0931	15.63	$[M+H]^+$	397.0997	35	22
296	Thiobencarb	$C_{12}H_{16}ClNOS$	257.0641	15.38	$[M+H]^+$	258.0714	10	4
297	Thiofanox sulfone	$C_9H_{18}N_2O_4S$	250.0987	4.01	$[M+H]^+$	251.1060	5	2
298	Thiofanox sulfoxide	$C_9H_{18}N_2O_3S$	234.1038	3.42	$[M+H]^+$	235.1106	5	3
299	Thionazin	$C_8H_{13}N_2O_3PS$	248.0385	8.31	$[M+H]^+$	249.0456	10	9
300	Thiophanate-methyl	$C_{12}H_{14}N_4O_4S_2$	342.0457	5.62	$[M+H]^+$	343.0525	5	7
301	Tiocarbazil	$C_{16}H_{25}NOS$	279.1657	18.39	$[M+H]^+$	280.1724	15	4
302	Tolfenpyrad	$C_{21}H_{22}ClN_3O_2$	383.1401	17.09	$[M+H]^+$	384.1477	25	5
303	Tralkoxydim	$C_{20}H_{27}NO_3$	329.1991	17.75	$[M+H]^+$	330.2062	10	7

No	Pesticides	Elemental composition	Exact Mass (Da)	t_R[a] (min)	MS^1 ion	MS^2 Identification		
						Precursor	CE	No. major product ions[b]
304	Triadimefon	$C_{14}H_{16}ClN_3O_2$	293.0931	11.48	$[M+H]^+$	294.0996	15	9
305	Triadimenol	$C_{14}H_{18}ClN_3O_2$	295.1088	8.82	$[M+H]^+$	296.1158	5	2
306	Triapenthenol	$C_{15}H_{25}N_3O$	263.1998	11.71	$[M+H]^+$	264.2066	25	2
307	Triazophos	$C_{12}H_{16}N_3O_3PS$	313.0650	12.97	$[M+H]^+$	314.0723	15	2
308	Tribufos	$C_{12}H_{27}OPS_3$	314.0962	18.96	$[M+H]^+$	315.1029	15	4
309	Trichlorfon	$C_4H_8Cl_3O_4P$	255.9226	3.46	$[M+H]^+$	256.9308	10	5
310	Tricyclazole	$C_9H_7N_3S$	189.0361	4.46	$[M+H]^+$	190.0425	30	5
311	Trietazine	$C_9H_{16}ClN_5$	229.1094	11.65	$[M+H]^+$	230.1159	30	11
312	Trifloxystrobin	$C_{20}H_{19}F_3N_2O_4$	408.1297	16.85	$[M+H]^+$	409.1362	10	5
313	Triflumizole	$C_{15}H_{15}ClF_3N_3O$	345.0856	15.36	$[M+H]^+$	346.0920	5	5
314	Triflumuron	$C_{15}H_{10}ClF_3N_2O_3$	358.0332	14.68	$[M+H]^+$	359.0411	10	5
315	Triticonazole	$C_{17}H_{20}ClN_3O$	317.1295	9.73	$[M+H]^+$	318.1366	10	3
316	Vamidothion	$C_8H_{18}NO_4PS_2$	287.0415	3.54	$[M+H]^+$	288.0479	5	2
317	Zoxamide	$C_{14}H_{16}Cl_3NO_2$	335.0247	15.13	$[M+H]^+$	336.0319	15	5

[a] t_R: retention time of the analyte detected in standard solution.
[b] No. major product ions: number of product ions with relative abundance higher or equal to 10%.

Table 2 Pesticides screening results of 328 fruit and vegetable samples with the HPLC-QTOF MS technology combined MS^1 database and MS^2 library application

Sample (Number)	Total Number of findings	Pesticide (Number of Findings) [a]	TOF-MS Score	Q-TOF-MS Score
			Min-Max	Min-Max
Apple (17)	22	Carbendazim (17)	94-99	85-98
Cabbage (19)	19	1,3-Diphenyl urea (7)	80-97	75-92
		Propamocarb (5)	95-99	77-86
Cantaloupe (18)	53	Dimethomorph (7)	96-98	88-94
		Prochloraz (7)	81-100	88-90
		Propamocarb (7)	96-99	96-98
Celery (15)	80	Acetamiprid (5)	89-98	78-89
		Carbendazim (7)	73-89	75-98
		Difenoconazole (11)	92-97	81-89
		Dimethomorph (7)	92-97	84-95
		Imidacloprid (8)	84-99	72-93
		Propamocarb (5)	88-98	81-98
		Propiconazole (10)	96-99	80-87
Cherry tomato (11)	26	1,3-Diphenyl urea (5)	71-80	75-91
Chinese cabbage (13)	53	1,3-Diphenyl urea (8)	72-100	73-94
		Acetamiprid (5)	81-99	74-86
		Dimethomorph (10)	92-97	83-96
		Emamectin-benzoate (8)	74-80	78-98
Chinese chives (12)	25	Pyrimethanil (8)	81-95	79-95
Cucumber (19)	55	Acetamiprid (6)	83-98	75-85
		Metalaxyl (12)	90-98	77-96
		Oxadixyl (7)	72-92	71-93
		Propamocarb (8)	80-96	96-98
Endive (16)	47	1,3-Diphenyl urea (6)	72-84	75-93
		Carbendazim (5)	70-85	76-91
		Dimethomorph (7)	86-92	87-93
		Imidacloprid (6)	79-85	71-92
Grape (19)	99	1,3-Diphenyl urea (7)	82-98	84-94
		Azoxystrobin (7)	94-98	90-97
		Carbendazim (9)	86-90	79-97
		Difenoconazole (8)	95-98	85-89
		Dimethomorph (15)	96-99	89-94
		Omethoate (6)	99-100	78-94
		Pyrimethanil (10)	90-92	83-93
		Tebuconazole (5)	84-98	80-86
Lettuce (12)	31	Dimethomorph (5)	90-94	86-92
		Imidacloprid (6)	89-99	72-93
		Paclobutrazol (7)	82-93	84-94
Peach (17)	96	Acetamiprid (5)	92-97	72-86
		Carbendazim (14)	72-91	76-98
		Chlorpyrifos-ethyl (10)	93-97	70-82
		Difenoconazole (13)	90-99	82-94
		Imidacloprid (6)	72-77	72-87
		Paclobutrazol (7)	90-98	79-94
		Pyridaben (9)	93-96	86-92
Pear (18)	36	1,3-Diphenyl urea (5)	82-98	86-94

Sample (Number)	Total Number of findings	Pesticide (Number of Findings) [a]	TOF-MS Score	Q-TOF-MS Score
			Min-Max	Min-Max
		Azoxystrobin (11)	94-97	94-97
		Carbendazim (11)	79-89	73-95
Plum (15)	28	Carbendazim (7)	74-85	75-95
Spinach (11)	15	Dimethomorph (6)	94-97	82-95
Sweet pepper (19)	45	Difenoconazole (5)	95-100	77-83
		Dimethomorph (8)	95-96	87-94
		Imidacloprid (7)	93-99	73-91
Tomato (19)	28	1,3-Diphenyl urea (5)	78-97	72-90
Wax gourd (16)	10	Acetamiprid (5)	98-100	72-86
Broccoli (15)[b]	3			
Carrot (18) [b]	3			
Watermelon (9) [b]	25			

[a]. The result of finding numbers less than 5 are not included in the table.

[b]. Broccoli, Carrot, and Watermelon samples were also analyzed applied to the HPLC-QTOF-MS screening technology, however, no given targeted pesticide residue were found more than 5 times.

Fig. 1

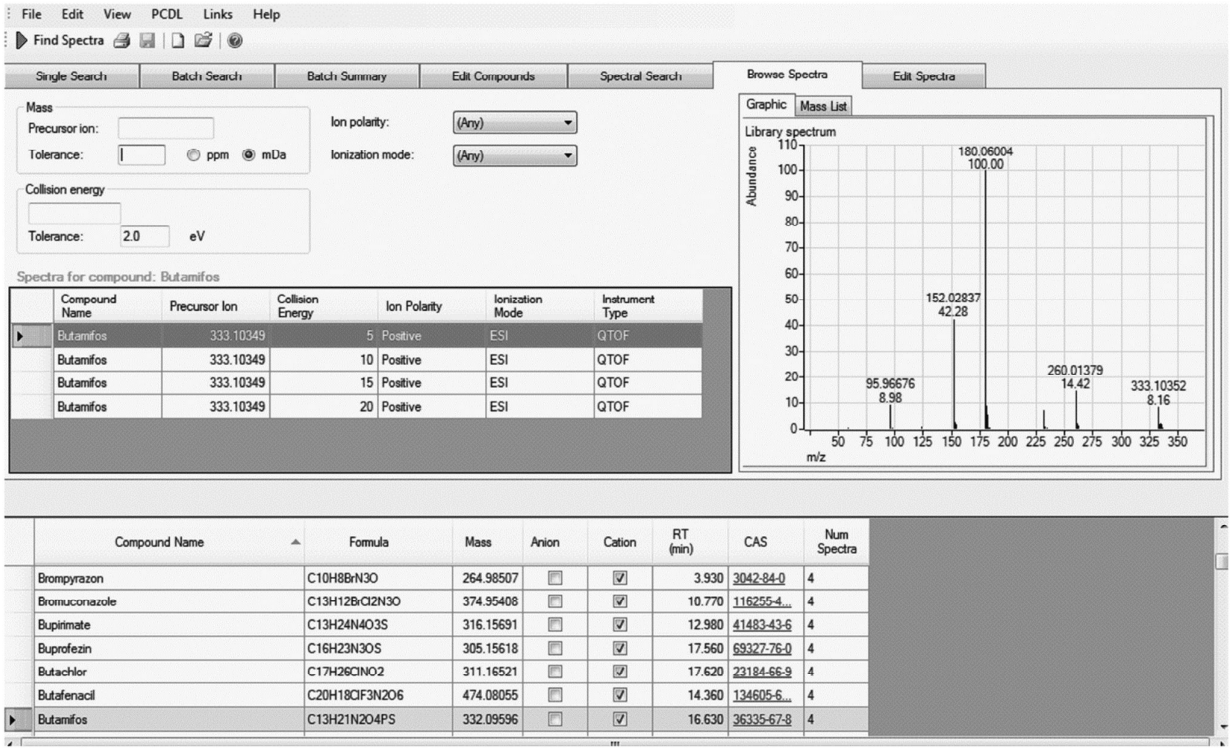


Fig. 2

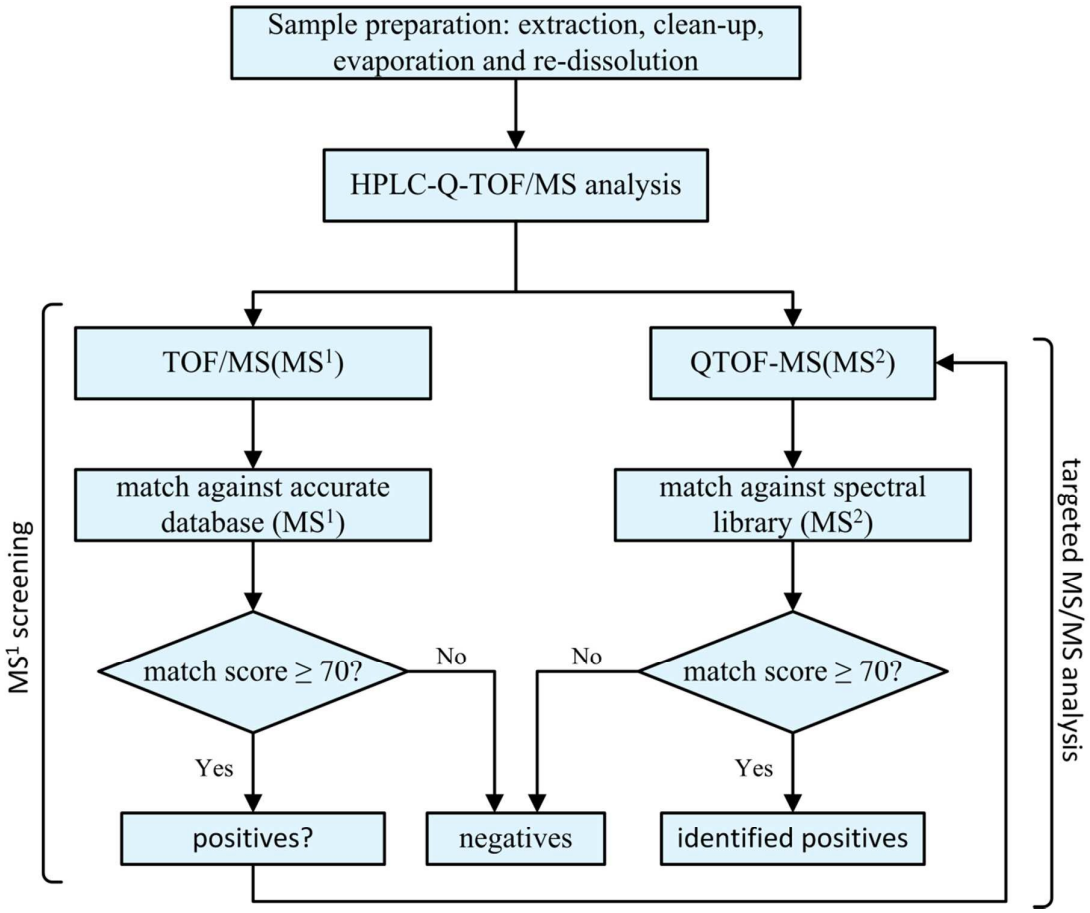


Fig. 3

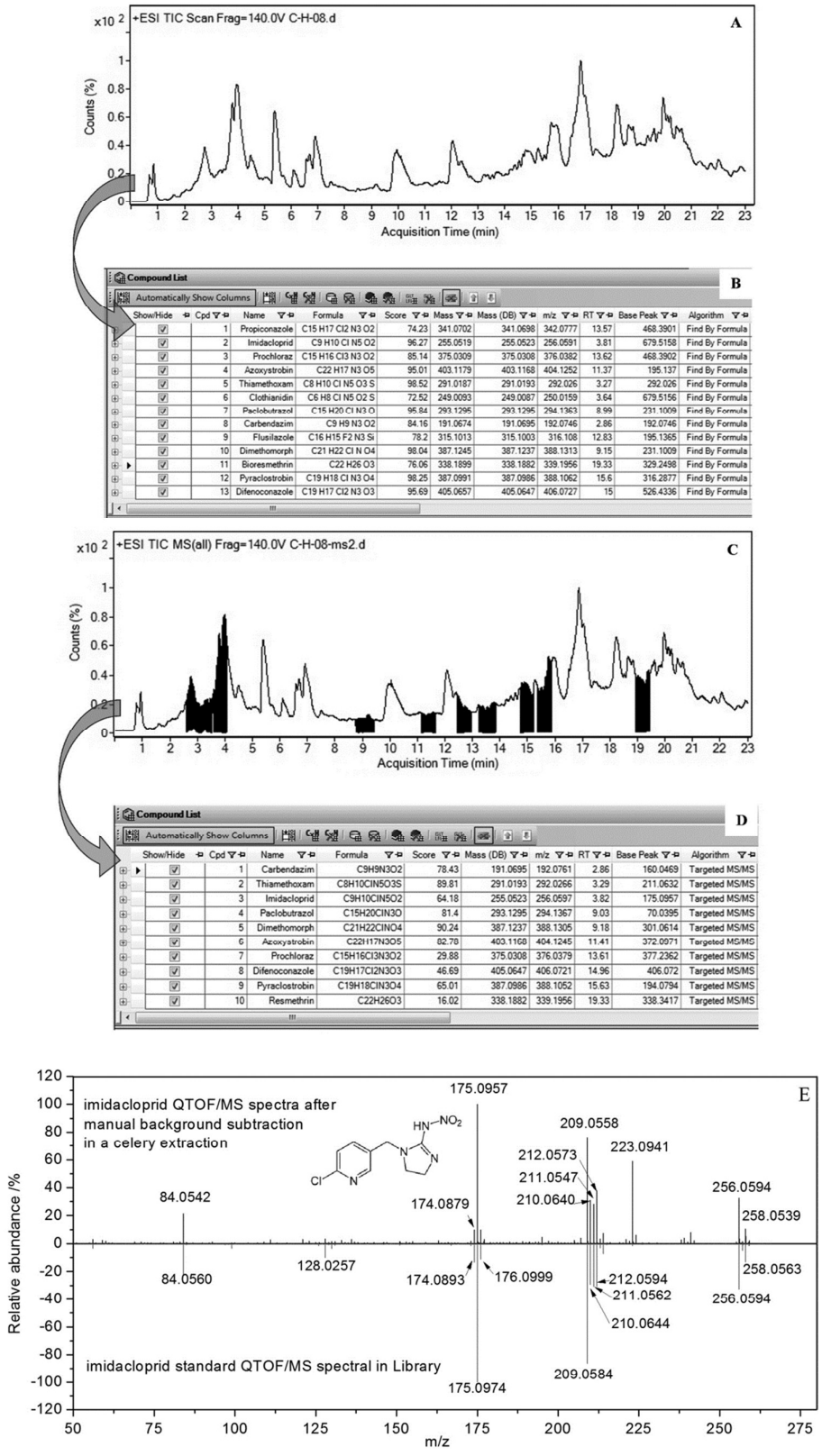


Fig. 4

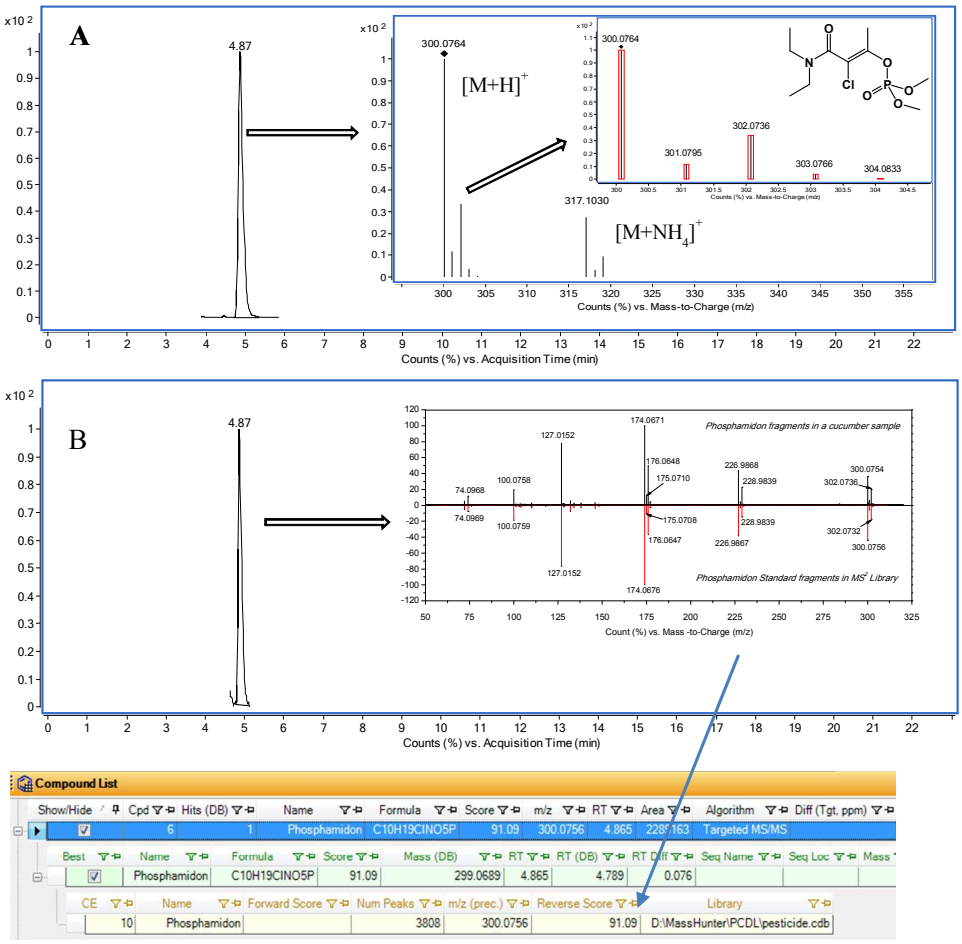
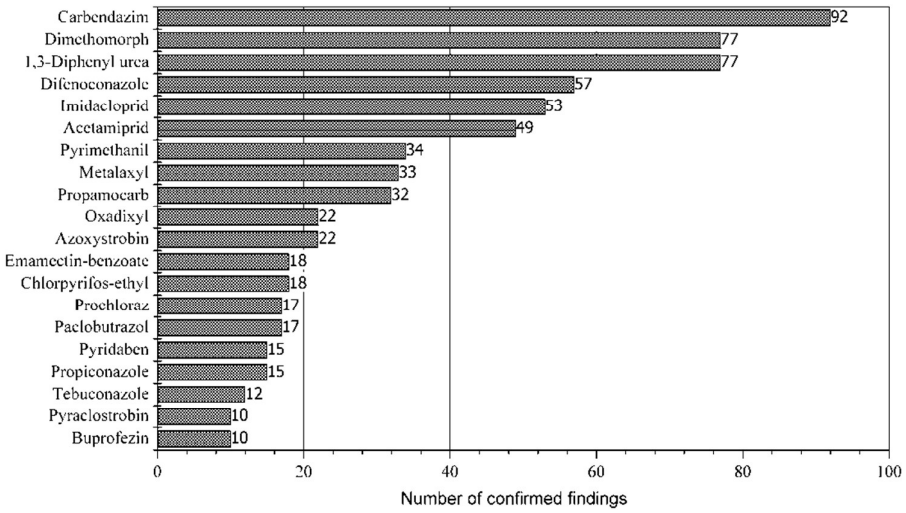


Fig. 5



Graphical Abstract

A screening and identification method was set up for routine qualitative detection of multi-pesticide residues in fruits and vegetables based on the home-made accurate database and spectra library.