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Journal of Chromatography A, 754 (1996) 411–422

JOURNAL OF CHROMATOGRAPHY A

Pesticide residue analysis in fresh produce by gas chromatography–tandem mass spectrometry

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Abstract

GC–MS–MS was used to analyze for multiple pesticide residues in fresh fruits and vegetables. Nineteen pesticides, including fungicides, herbicides, organophosphorus insecticides and chlorinated insecticides were spiked into seven different fruit and vegetable matrices and analyzed. The specificity of GC–MS–MS provided for low detection limits (ranging from 1–5 ppb) and unambiguous spectral confirmation for the target compounds in these complex matrices. Good precision was obtained (RSD values ranged from 1 to 9%), even at the 10 ppb level, without extensive sample clean-up steps.

Keywords: Detection, GC; Fruits; Vegetables; Food analysis; Pesticides

1. Introduction

The analysis of pesticides in food is an important problem because of the large number and large amounts applied to crops worldwide. In addition, there is no international standard for pesticide residue levels in agricultural products. This means that the country producing the products may allow pesticides that are severely regulated in the country importing the products. Interferences in the testing methods come from the food matrix which may cause the signal from the pesticide to be obscured. This analysis is made even more difficult by the large concentration difference between the food component and the pesticide. Analytical procedures that provide unambiguous results are therefore necessary.

Gas chromatography has been used with class-selective detectors such as the electron-capture, flame photometric and nitrogen–phosphorus detectors. None of these detectors is confirmatory and all are subject to interferences from the food matrix. To lessen false results, extensive clean-up and extraction procedures are used [1,2]. GC–MS has been used in both the full scan and selected ion monitoring modes. The latter is used for target analysis usually to confirm results from other GC detectors. Durand et al. [3] compared GC–MS, GC-high resolution MS and GC–MS–MS and they concluded that only GC–MS–MS provides the confirmation of pesticides in soil with a high degree of certainty. MS–MS without chromatography has seen some use in detecting trace pesticides in biological matrices, but these procedures are limited by potential overlap of multiple pesticides and, without sample clean-up steps, require frequent cleaning of the ion source [4].

GC coupled to MS–MS has seen limited application to routine pesticide residue analysis [3], primarily because of instrument cost and the requirement of specially trained personnel. Bench-top ion traps offer routine GC–MS–MS capability without the high cost or added complexity of multi-sector instruments [5,6].

The process of product ion MS–MS involves two

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0021-9673/96/$15.00
PII S0021-9673(96)00492-X

additional steps between the formation and detection of ions. These steps are isolation of a single parent ion from the other ions present and dissociation of the parent ion into characteristic product ions before mass analysis of the product ions. This process is accomplished in an ion trap by applying the appropriate wave forms first to isolate a particular ion or range of ions. The isolated ion(s) are then exposed to additional wave forms to increase their translational kinetic energy. These energetic ions may then dissociate as the collisions with the background gas cause some of the kinetic energy to be converted to sufficient internal energy to cause fragmentation. Following this fragmentation, the product ions are mass analyzed using the typical mass-selective instability method [7].

In the dissociation process energy is usually imparted to ions by applying an external voltage to alter their trajectories inside the ion trap. Because the frequency of the trajectory is fixed by the trapping field and the mass to charge ratio of the ion, increasing the amplitude of the motion of the ion requires that it move farther in the same time and, therefore, faster. If the applied voltage is a sine wave whose frequency matches the secular frequency of the ion, it is a resonant process and only those ions of a particular m/z will acquire energy [8]. Alternatively, the RF trapping field can be changed rapidly by the application of a step function. This is called nonresonant excitation where the kinetic energy of all ions remaining in the trap after the isolation step will be instantaneously increased [9]. In addition to removing the frequency dependence from the excitation voltage, nonresonant excitation can excite an entire cluster of ions. This is useful for compounds containing several chorine atoms —the product ions will also demonstrate the isotopic pattern according to the number of chlorines remaining in each ion.

Product ion GC–MS–MS is necessarily a target compound technique with each compound requiring its own conditions for isolating the parent ion and for dissociating it into product ions. The determination of optimum conditions for dissociation of each parent ion can be a time-consuming task, since the amplitude of the excitation voltage and the excitation storage level need to be determined for each ion. If the applied voltage is too high for the excitation storage level selected, all of the parent ions will be ejected from the ion trap, while a voltage which is too low for the excitation storage level will cause little, if any, dissociation. AUTOMATED METHODS DEVELOPMENT is a software program that facilitates the process of finding the optimum excitation voltage and excitation storage level. The applied voltage is increased on a scan-by-scan basis throughout the eluting GC peak. After the chromatogram is complete, each spectrum is examined to determine which voltage produces the optimum product ion spectrum. With rapid scan rates (5–10 scans/s) the optimum excitation voltage can be determined for many compounds by injecting a standard mix only a few times. This work demonstrates the applicability of GC–MS–MS to the analysis of several pesticides in fruit and vegetable extracts.

2. Experimental

2.1. Instrumental

A Saturn 4D ion trap GC–MS system (Varian, Walnut Creek, CA, USA) was used for all work. The electrodes were SilChrom coated to reduce chromatographic activity. The Ion Trap MS–MS Toolkit editor was used to create AUTOMATED METHODS DEVELOPMENT (AMD) methods for the optimization of the excitation conditions for each compound and to create multiple reaction monitoring (MRM) methods for the analysis of coeluting or closely eluting peaks. The IPM (ion preparation method) editor was used to create MS–MS methods for those singly eluting compounds. For all of the compounds selected for this work, nonresonant excitation was chosen. Table 1 lists the pesticides and the MS–MS conditions used. The mass spectrometer scan time was 1 s/scan for single compound chromatographic segments and was adjusted for multiple compound segments so that the net scan time after merging the file would be 1 s/scan.

Capillary column: Rtx-5MS (Restek, Bellefonte, PA, USA), 30 m×0.25 mm I.D., 0.25 μm film thickness. Column program: hold at 60°C for 2 min, ramp to 150°C at 20°C/min, then ramp to 230°C at 4°C/min, then ramp to 300°C at 15°C/min. This program provided good separation for the pesticides

Table 1
MS–MS conditions

	Compound	Parent ion (*m/z*)	Excitation storage level (*m/z*)	Nonresonant excitation voltage (V)	Product ions used for quantitation (*m/z*)
1	Dichlobenil	171–173	60	63	75+100
2	[$^2H_{10}$]Acenaphthene (IS)	162–164	75	90	156
3	Trifluralin	306	75	45	206+264
4	DCNA	206–208	80	62	176+178
5	Simazine	201	90	60	138+172+186
6	Atrazine	215	143	100	200
7	Lindane	181–183	75	65	146+148
8	Terbufos	231	125	75	203+175
9	Alachlor	188	48	37	132+146+160
10	Prometryn	241	119	90	166+184+226
11	Aldrin	261–265	90	92	191+193
12	Chlorpyrifos	314–316	172	90	258+260+286
13	Heptachlor epoxide	351–355	75	47	261+263+265
14	Thiabendazole	201	71	60	174
15	α-Chlordane	371–377	100	67	264+266+301
16	γ-Chlordane	371–377	100	67	264+266+301
17	*trans*-Nonachlor	235–239	88	100	119+141+143
18	Endrin	279–283	75	60	209+243+245
19	Ethion	231	75	45	175+203
20	[$^2H_{12}$]Chrysene (IS)	240	85	85	228+236
21	Azinphos-methyl	132	65	69	104

Excitation time 20 ms.
Ion trap temperature 250°C.

selected for this study. Injector: 1078 Universal Capillary Injector (Varian) with 0.5 mm I.D. insert. Injector program: temperature-programmed splitless injection, hold injector at 50°C (split mode 50:1) for 0.3 min, switch to splitless mode and ramp to 290°C at 180°C/min. After an additional 0.4 min switch back to split mode. Hold for 7 min. Helium was used as the carrier gas at a flow-rate of approximately 1.2 ml/min, measured at 200°C. The transfer line was held at 280°C and the ion trap manifold was set to 250°C. A Varian 8200 AutoSampler was used to perform 5 μl injections using the solvent flush method.

2.2. MS–MS methods development

Dissociation conditions were selected for each pesticide using methods built with the automated methods development editor. In general, the parent ion was selected as the highest-molecular-mass ion with the highest intensity. For some compounds this was the molecular ion in the EI spectrum, but for others the most intense ion was chosen. For a few compounds, an ion was chosen which was neither the molecular ion nor the most intense ion in order to provide more immunity to chemical interference. (High mass ions are less likely to have a coeluting interference.) For some compounds, a cluster of ions was isolated rather than a single ion in order to provide more information (and more signal) from the distribution of chlorine atoms in each fragment.

To optimize the dissociation conditions, the excitation storage level was selected first as the minimum value which would allow the parent ion to be dissociated. A higher excitation storage level holds the ions in the trapping field more strongly and allows a higher excitation voltage to be applied which may produce more product ions. However, if the excitation storage level gets too high, the lower weight product ions will not be trapped and will not be observed in the spectrum. The dissociation conditions, therefore, must specify both the excitation

storage level and the excitation voltage in addition to the trap operating temperature.

The excitation voltage was chosen to maximize the intensity of product ions. Preference was given to maximizing a single product ion or cluster over generating multiple ions or clusters. Because the presence of the parent ion is implicit in the method, excitation voltages were chosen which would produce the most intense product ions, which generally occurred at the voltage where the height of the remaining parent ion was no more than 5% of the most intense product ion. Product ions chosen for quantitation were the 1–3 most intense ions in each product ion spectrum. When chosen, multiple ions were summed to increase the signal from the analytes.

2.3. Chemicals

The pesticides listed in Table 1 (PolyScience, Niles, IL, USA or ChemService, West Chester, PA, USA) were dissolved in hexane (J.T. Baker, Phillipsburg, NJ, USA) to prepare standard mixtures over the concentration range of 10–500 pg/μl. The target compounds were chosen to be representative of major classes of pesticides: fungicides, herbicides, organophosphorus insecticides and chlorinated insecticides. [$^2H_{10}$]Acenaphthene and [$^2H_{12}$]chrysene (Supelco, Bellefonte, PA, USA) were included as internal standards at the 100 pg/μl level and were added when the final extracts were spiked with the target pesticides.

2.4. Sample preparation

The sample preparation method was chosen to create a test matrix containing as many extractable food components as possible in order to test GC–MS–MS under worst case conditions. While the extraction was performed over a fairly long time, it is not a labor-intensive procedure. A 50 g sample of each whole fruit or vegetable was weighed and then chopped before soaking overnight in 125 ml of methylene chloride. The extracts were filtered to remove the undissolved material. Water was removed by adding anhydrous sodium sulfate and then filtering the entire extract again. The methylene chloride phase was decanted and evaporated to near dryness. The remaining residue was dissolved in hexane to give a final volume of 25 ml. 1 μl of this solution was equivalent to 2 mg of the original fruit or vegetable. These final extracts were then spiked at the 20 pg/μl level to determine precision and accuracy of the measurement process. This corresponds to 10 ppb (10 μg/kg) in the crop based on the original sample weight and the final extract volume. Internal standards were included at the 100 pg/μl level for quantitative accuracy and were added to the final extract. Each spiked extract was injected ten times to determine the reproducibility of the instrumental technique.

2.5. System calibration

Five point calibration curves were prepared for all analytes at levels of 10 pg/μl, 20 pg/μl, 50 pg/μl, 100 pg/μl and 500 pg/μl. All compounds showed a linear response in this calibration range. After showing linearity for each of the compounds, a standard at the 40 pg/μl level was injected between each series of 10 extract injections. The response factors from all of these standard runs were averaged for each pesticide and used as a one-point calibration to quantitate each run from the extracts.

3. Results and discussion

3.1. Optimization of MS–MS conditions

To determine MS–MS conditions, each pesticide or internal standard was injected at least four times: For the first injection the ion trap was used in the EI mode to determine the retention time and to verify the identity of the compound using the library search. On the second injection the parent ion was isolated (either a single ion or an isotopic cluster) to show that the parent ion could be successfully isolated and to provide a benchmark for the MS–MS sensitivity. This step is necessary because some ions are unstable enough that they acquire sufficient energy in the isolation step and undergo collision induced dissociation (CID) even without the application of an excitation voltage. Because this CID occurs during the isolation step, the product ions formed may or may not be detected. On the third

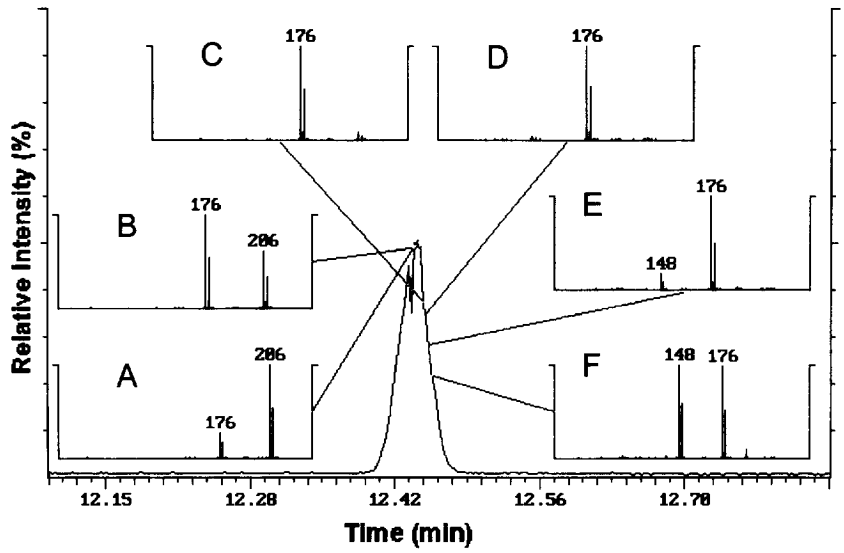

Fig. 1. CID product ion spectra across DCNA standard peak showing different excitation voltage applied on each scan using AMD method. Inset spectra are relative intensity versus m/z and are normalized to 100%. Excitation storage level=80 m/z; nonresonant excitation voltage applied for 20 ms: (A) 50 V (B) 55 V (C) 60 V (D) 65 V (E) 70 V (F) 75 V. The spectra are normalized.

injection, the excitation voltage was stepped through a range by 5 or 10 V steps using the AMD method. Fig. 1 shows the CID product ion spectra across the chromatographic peak for the DCNA (2,6-dichloro-4-nitroaniline) standard. As more energy is supplied by a higher excitation voltage, smaller m/z fragments can be obtained, but often at the expense of ion intensity. Because these spectra are normalized, the absolute ion intensities must be examined to determine the voltage which produces the most intense product ions. One way to do this is to plot the ion intensities as a function of excitation voltage to construct a breakdown curve as in Fig. 2. For DCNA, the highest intensity of product ions occurs at an excitation voltage of ~60 V. After examining the results from the third injection, the excitation voltage was selected for each compound. If the maximum intensity of the product ions was not at least 50% of the intensity of the isolated parent ion, the excitation storage level was increased and the compound reinjected while stepping the excitation voltage by 5 or 10 V using an AMD method. The fourth injection was used to verify that the MS–MS conditions chosen were appropriate and to obtain the product ion spectrum for each compound to select the ions to be used for quantitation.

3.2. Linearity

MS–MS calibration curves were prepared after injection of the standard mixtures and were based on the peak area using 1–3 of the most intense product ion(s) for each compound. The ions used are listed in Table 1. The calibration curves for 5 concentrations (2 injections for each) were linear over the entire range from 10 pg/μl to 500 pg/μl with correlation coefficients between 0.995 and 1.00. The response factor, based on internal standards, and the slope and intercept of the calibration curve for each of the pesticides studied is listed in Table 2. The response factors depend on a number of factors in MS–MS which causes their value to differ widely between analytes. Higher response factors are observed when the original EI mass spectrum shows little fragmentation and the product ion spectrum also contains only a single ion. Thiabendazole is an example of this case: the original EI mass spectrum consists of only two ions. The product ion spectrum produces only one ion with a high MS–MS efficiency and the response factor is high. Endrin, on the other hand, has an EI mass spectrum with many ions —there are 10 mass peaks having intensities of at least 40% of the base peak in the spectrum. Coupled with a

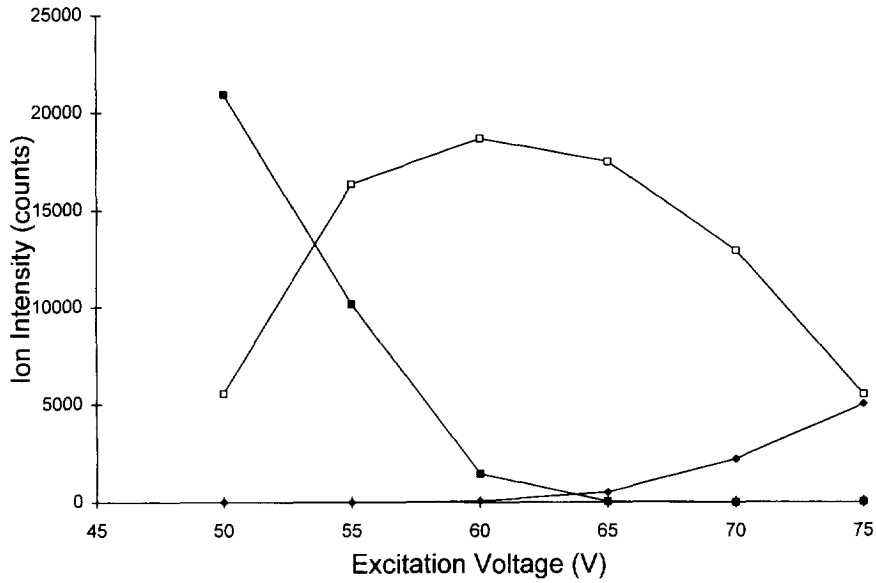

Fig. 2. Breakdown curve for DCNA. The ion intensities from Fig. 1 are plotted. The optimum excitation voltage for producing the maximum number of product ions is 60 V. ■=m/z 206; □=m/z 176; ◆=m/z 148.

product ion spectrum containing 5 mass peaks having intensities of at least 40% of the base peak in the spectrum, the response factor is lower. Therefore, for the same weight of sample, fewer product ions will be formed for those compounds having lower response factors. While the ultimate detection limit

Table 2
Response factors and linearity of calibration curves for pesticide standards over the concentration range of 10–500 pg/μl

Compound	Response factor	Correlation coefficient	Slope $\times 10^{-3}$ (area counts/pg)	Intercept $\times 10^{-2}$ (area counts
Dichlobenil	0.18	0.998	1.6	1.8
Trifuralin	0.095	1.00	1.3	−1.4
DCNA	0.065	1.00	0.74	−5.2
Simazine	0.046	0.999	0.47	1.3
Atrazine	0.28	1.00	2.6	1.5
Lindane	0.091	0.999	1.2	−1.3
Terbufos	0.059	1.00	0.78	−8.5
Alachlor	0.077	0.998	0.92	−1.1
Prometryn	0.032	1.00	0.30	0.01
Aldrin	0.065	1.00	0.73	−0.29
Chlorpyrifos	0.075	0.999	0.88	−0.88
Heptachlor epoxide	0.029	0.998	0.37	−0.48
Thiabendazole	0.20	0.997	2.4	−0.55
α-Chlordane	0.035	0.996	0.44	−0.71
γ-Chlordane	0.033	0.998	0.41	−0.53
trans-Nonachlor	0.006	0.998	0.08	−0.11
Endrin	0.006	0.995	0.10	−0.22
Ethion	0.016	0.999	0.17	0.00
Azinphos-methyl	0.015	0.999	0.19	−0.26

for compounds will be dependent on their degree of fragmentation, the selectivity of MS–MS will enhance the signal relative to the background interferences for all compounds.

3.3. Accuracy

The spiked sample extracts were analyzed to determine the accuracy of this analytical methodology. The results for ten replicate injections of each extract are listed in Table 3. Blank injections were made for each extract, spiked with the internal standards only. Values were excluded from the table where the blank had a value larger than 1 ppb for the target pesticide. The calculated recoveries indicate that a range of recoveries between 50 and 180% can be expected for the different pesticides in the crops tested. The RSD values for the entire data set range from 1 to 9% and average 4%. The result for DCNA in celery was also excluded from the table because of an interference from the celery matrix which interfered with the quantitation of the pesticide. The largest matrix peak from the celery eluted exactly as the DCNA eluted and contributed sufficient ions to the signal to prevent accurate quantitation of the DCNA. The retention time of DCNA shifted by 15 s in the celery extract, while all other compounds were unaffected, indicating that the concentration of the interference was sufficiently large to overload the capillary column. It is not expected that this situation would arise very often and, when it does, could be alleviated by changing either the extraction process or the GC column oven program.

3.4. Minimum detectable quantity

The minimum detectable quantity (MDQ) for the GC–MS–MS technique was determined by calculating the standard deviation for a series of injections of a typical sample at a spike level corresponding to 5–10 times the expected MDQ. The MDQ was calculated by multiplying the standard deviation in ppb by the Student's t factor for the number of injections made. For ten injections this factor was 2.821. Table 4 contains the calculated MDQ values for the different pesticides in the produce tested.

Table 3
Average recovery for spiked extracts, (ppb)

	Apple	Carrot	Green Bean	Celery	Lemon	Pear	Cantaloupe
Dichlobenil	9	9	9	9	6	9	9
Trifluralin	7	[b]	10	10	10	9	10
DCNA	7	11	8	[a]	9	7	8
Simazine	5	8	7	7	7	6	7
Atrazine	6	8	7	7	7	6	7
Lindane	6	10	8	7	8	7	8
Terbufos	7	11	9	9	10	8	9
Alachlor	6	10	8	8	9	7	8
Prometryn	6	8	8	7	8	6	7
Aldrin	6	9	7	8	8	7	7
Chlorpyrifos	6	10	9	8	9	7	8
Heptachlor epoxide	6	9	7	7	8	7	7
Thiabendazole	[b]	6	10	[b]	[b]	[b]	[b]
α-Chlordane	10	11	11	10	10	10	10
γ-Chlordane	9	10	11	10	10	10	10
trans-Nonachlor	7	10	10	9	9	9	10
Endrin	10	11	11	10	11	11	11
Ethion	11	12	13	12	13	12	12
Azinphos-methyl	[b]	8	17	17	18	[b]	17

Spike level 10 ppb.
Average of 10 injections.
[a] Interference present.
[b] Present in original sample at >1 ppb.

Table 4
Minimum detectable quantity for spiked extracts

	Apple	Carrot	Green Bean	Celery	Lemon	Pear	Cantaloupe
Dichlobenil	3	1	1	2	1	1	2
Trifluralin	4	[b]	3	2	2	1	2
DCNA	2	3	2	[a]	2	2	2
Simazine	1	2	2	3	2	2	2
Atrazine	1	1	2	2	1	2	2
Lindane	2	2	2	1	1	2	1
Terbufos	2	2	2	2	2	2	1
Alachlor	3	2	2	2	2	2	2
Prometryn	1	2	2	2	2	1	1
Aldrin	1	2	2	2	1	2	2
Chlorpyrifos	3	2	2	2	1	2	1
Heptachlor epoxide	1	2	3	2	1	1	1
Thiabendazole	[b]	2	3	[b]	[b]	[b]	[b]
α-Chlordane	2	2	2	1	2	1	2
γ-Chlordane	1	1	2	1	2	1	2
trans-Nonachlor	2	2	2	1	1	2	3
Endrin	1	2	2	1	1	1	2
Ethion	3	2	2	2	2	1	2
Azinphos-methyl	[b]	1	5	3	5	[b]	3

Spike level 10 ppb, average of 10 injections, MDQ=standard deviation (in ppb)×2.821
[a] Interference present.
[b] Present in original sample at >1 ppb.

These range from 1 to 5 ppb, with a median value of 2 ppb.

3.5. Method selectivity

The GC–MS–MS analysis allows for more accurate analysis than GC–MS primarily due to the removal of matrix interference. The typical food matrix contains many compounds that are soluble in the extraction solvent. This matrix is thousands of times more concentrated than the pesticide residue levels in the extract. Even relatively small ion intensities from a coeluting matrix compound can cause a significant positive interference. In addition, the background can be so intense that spectral confirmation is impossible for certain pesticides in certain crops. Fig. 3 shows a typical GC–MS–MS chromatogram for the standards at a level of 40 pg/μl. The peak numbers correspond to the compound numbers in Table 1. The peak marked with an * in Figs. 3–5 is an internal standard which was present in the internal standard mix used, but was not used in the quantitation. In Fig. 4 the effect of the chemical matrix in the GC–MS full scan EI mode can be seen. Notice that even the internal standards that are clearly present in Fig. 3 are not easily discerned in Fig. 4, but are mixed in with the matrix components from the carrot which were extracted by methylene chloride. The target compounds present at a much lower level are not observed at all in the total ion current trace. This illustrates the typical problem where the intense background overshadows the analytes and internal standards. In Fig. 5 we see the same sample used in Fig. 4, now used in the GC–MS–MS mode. Notice how similar this looks to the standard in Fig. 3. There are a few extra peaks caused by the background matrix, but most of the pesticides are easily observed. The selectivity of GC–MS–MS is so great that low ppb levels can easily be measured. The spectra observed are interference-free also, which allows the desired result of unambiguous identification. Figs. 6 and 7 show the MS–MS spectrum of ethion in the standard and the carrot extract respectively. The match is undeniable. Fig. 8 shows the full scan EI spectrum of ethion in the carrot extract for the 10 ppb spike. Although this is a background-subtracted spectrum, it does not resemble the NIST library spectrum for this com-

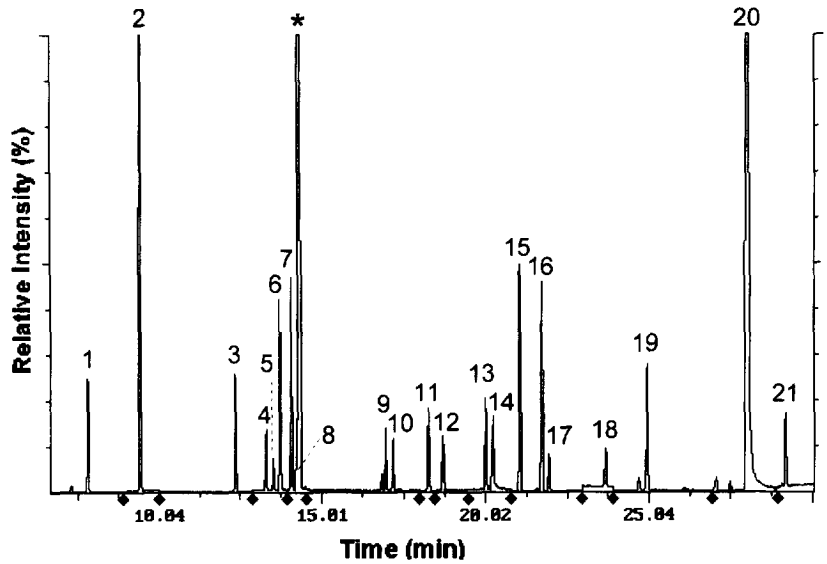

Fig. 3. GC–MS–MS product ion chromatogram of standards at 40 pg/μl. The peak numbers are listed in Table 1.

pound due to the heavy matrix present. If GC–MS alone was used for confirmation purposes, the results of this sample would not be conclusive. Only GC–MS–MS can give the desired information.

4. Conclusions

GC–MS–MS offers a sensitive target compound method for analyzing for trace levels of pesticides in

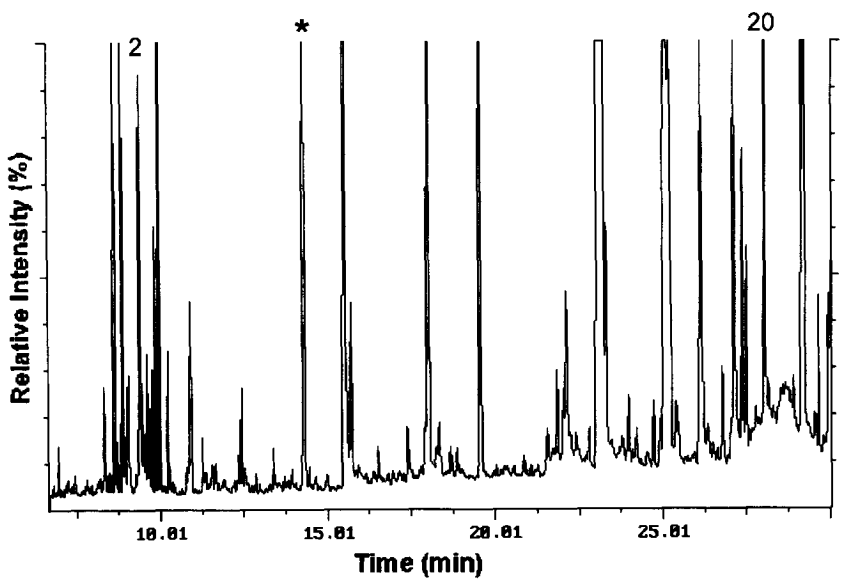

Fig. 4. Full scan EI chromatogram of spiked carrot extract. Internal standards are present at 100 pg/μl. Pesticides are present at 10 ppb (10 μg/kg). Only the internal standards are visible in the total ion current trace.

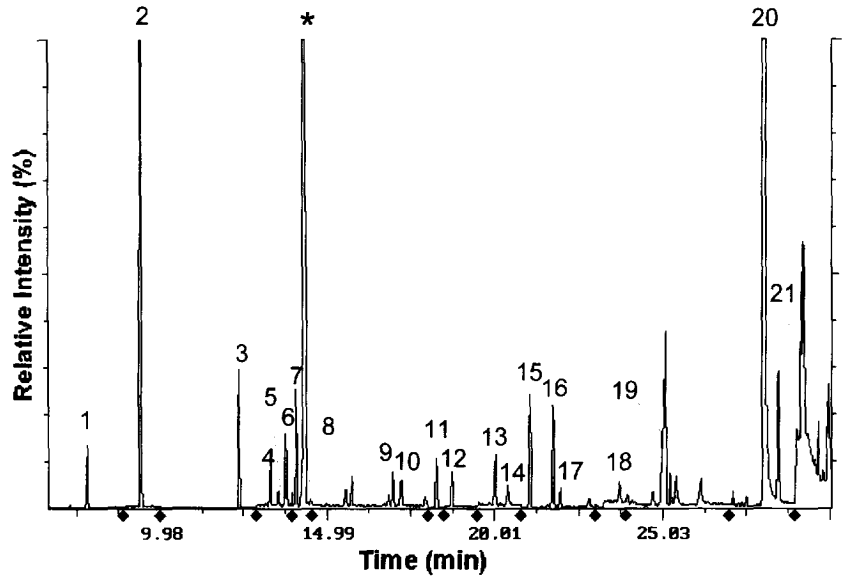

Fig. 5. GC–MS–MS product ion chromatogram of spiked carrot extract. Pesticides are present at 10 ppb (10 μg/kg). Target compounds predominate the total ion current trace. The peak numbers are listed in Table 1.

fruits and vegetables, with only minimal sample preparation required. The method is rugged and reliable, and provides for spectral confirmation of target analytes at low concentration. By injecting the standards only a few times, MS–MS conditions were determined for each pesticide and internal standard

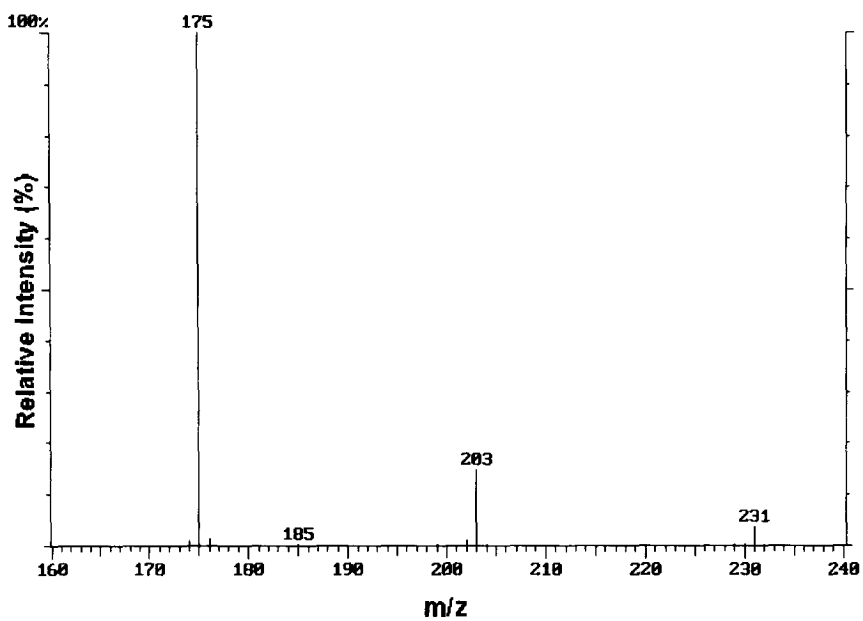

Fig. 6. CID MS–MS product ion spectrum of ethion in standard chromatogram. Ethion was present at 40 pg/μl. Spectrum is background subtracted.

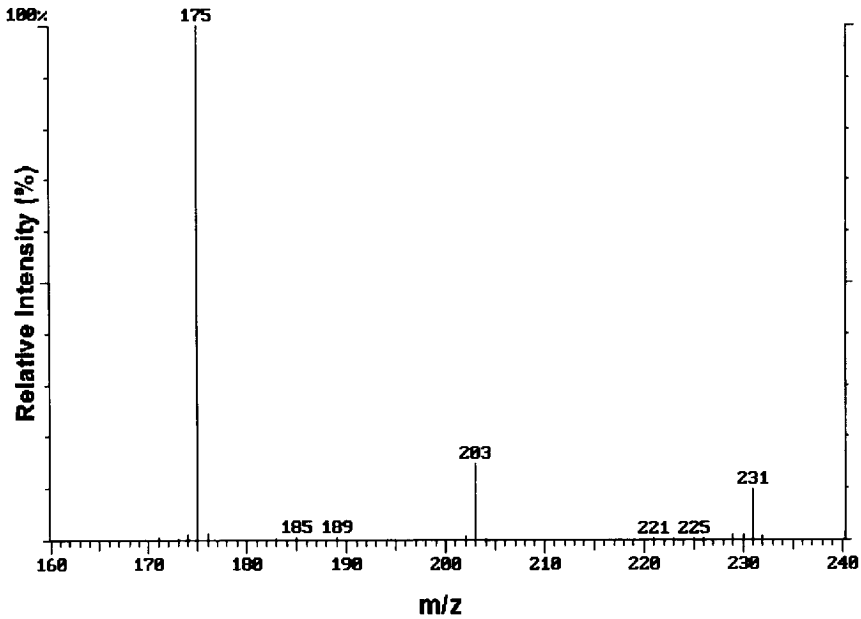

Fig. 7. CID MS–MS product ion spectrum of ethion in spiked carrot extract chromatogram. Ethion was spiked at 10 ppb (10 μg/kg). Spectrum is background subtracted.

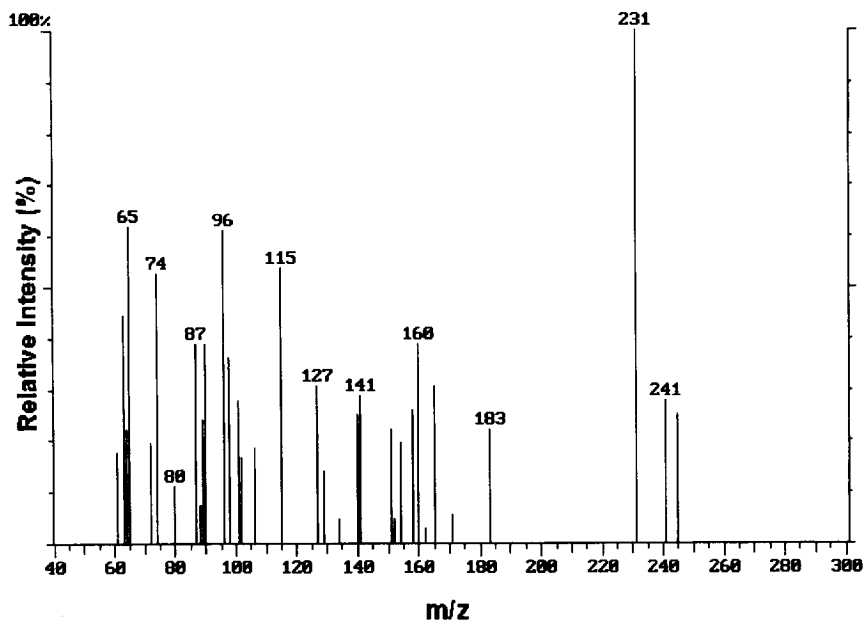

Fig. 8. Full scan EI spectrum of ethion in spiked carrot extract chromatogram. Ethion was spiked at 10 ppb (10 μg/kg). Spectrum is background subtracted.

used. GC–MS–MS provides linear calibration curves and good recovery for samples spiked at the 10 ppb level, with few interferences from the food extract matrix. As the technique is easy to automate, it is well-suited to routine pesticide analyses in a variety of agricultural products.

References

[1] A. Agüera, M. Contreras and A.R. Fernandez-Alba, J. Chromatogr. A, 655 (1993) 293–300.
[2] H.M. Pylypiw, Jr, J. Assoc. Off. Anal. Chem. 76 (1993) 1369–1373.
[3] G. Durand, P. Gille, D. Fraisse and D. Barceló, J. Chromatogr., 603 (1992) 175–184.
[4] J.V. Headley, K.M. Peru and M.T. Arts, Anal. Chem., 67 (1995) 4349–4353.
[5] S. Schachterle, R.D. Brittain and J.D. Mills, J. Chromatogr. A, 683 (1994) 185–193.
[6] J. Yinon, Rapid Commun. Mass Spectrom., 9 (1995) 532–536.
[7] G.C.Stafford, Jr, P.E. Kelley, J.E.P. Syka, W.E. Reynolds and J.F.J. Todd, Int. J. Mass Spectrom. Ion Processes 60 (1984) 85–98.
[8] J.N. Louris, R.G. Cooks, J.E.P. Syka, P.E. Kelley, G.C. Stafford and J.F.J. Todd, Anal. Chem., 59 (1987) 1677–1685.
[9] M. Wang, S. Schachterle and G. Wells, J. Am. Soc. Mass Spectrom., 7 (1996) 668–676.