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Simultaneous pulsed flame photometric and mass spectrometric detection for enhanced pesticide analysis capabilities

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Abstract

Analysis of pesticides by simultaneous pulsed flame photometric detection (PFPD) and mass spectrometric (MS) detection was performed with column-effluent splitting between these two detectors. The resulting PFPD chromatograms were always much simpler due to the PFPD selectivity and were further characterized by better sensitivity than that of MS. Accordingly, the PFPD chromatogram served as a marker for the exact elution time of the suspected pesticide. At this exact elution time, the resulting mass spectra were examined for unique high-mass peaks and a precise background subtraction was performed for improved library identification. If no definite identification was achieved, reconstructed mass chromatograms were performed, inspected for suspected major ions and confirmed with the PFPD chromatogram. A sequential search was then performed with the NIST library. The presence of P or S atoms was introduced into the search algorithm and two of the major suspected fragment mass peaks were included with an estimate of their minimum relative abundance. Under these conditions, the library search provided the correct pesticide identification, at a considerably lower concentration than achievable with standard GC–MS analysis. If only information on a single ion was available, such as with very pronounced matrix interferences, or with single-ion monitoring MS analysis, the NIST library sequential search was operated with this single-ion information and PFPD provided information on both P and S (the majority of organophosphorus pesticides contain both P and S). The incorporation of one major ion and two heteroatoms' (P and S) information enabled an effective library identification, at an even further reduced pesticide concentration. The simultaneous PFPD–MS analysis approach is demonstrated and discussed with several examples of authentic pesticides in vegetable and spices. The merits of this method are analyzed and discussed with an emphasis on the unique suitability of PFPD for combination with MS.

Keywords: Detection, GC; Food analysis; Pesticides

1. Introduction

The effective analysis of pesticides in fruits, vegetables and other food products is a challenging analytical procedure which is of considerable and growing importance. Typical analyses are based on high resolution gas chromatography (GC) with selective detection methods [1] such as flame photometric detection (FPD or pulsed FPD (PFPD), nitrogen–phosphorus detection (NPD or TSD) and/or electron-capture detection (ECD). Once a pesticide is detected, confirmation and identification is performed with gas chromatography–mass spectrometry (GC–MS). It has long been recognized that the pesticide identification step with GC–MS is the bottleneck in pesticide analysis, with the lowest

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practical sensitivity. Since MS is a universal detection method without selectivity, its actual detection limits are considerably reduced by matrix interferences, especially those encountered in fruit, vegetables, spices and other food items. As a result, in the analysis of trace levels of pesticides in complex matrices, mass spectral library identification is often hampered by the coelution of several matrix compounds. Furthermore, complex and lengthy sample clean-up procedures are often required which make pesticide analysis a long and expensive procedure [2,3].

Recently, a new direct/dirty sample introduction device (DSI) was described [4–6] that enables extract-free fast pesticide analysis. This DSI device is available from Varian as the ChromatoProbe. Sampling with the DSI is based on the introduction of acetone blended fruit or vegetable in a small glass vial into a temperature programmable GC injector. Initially, the solvent is gently evaporated at about 100°C for 1 min and then the injector temperature is ramped to 250°C for the vaporization and 'thermal extraction' of the pesticides that are cryo-focused on the GC column. The GC analysis is then performed as usual, after which the vial with the nonvolatile 'dirt' and residue is removed and disposed of. Fast pesticide analysis with this DSI device combined with pulsed flame photometric detection has been demonstrated and discussed elsewhere [6].

PFPD [7–9] is a very sensitive and selective detection method for organophosphorus pesticides. It also enables sulfur pesticide analysis and can provide information on sulfur and phosphorus atoms simultaneously, including the S/P ratio for a given pesticide that contains both S and P [6].

In this paper, we describe a new and more effective method of pesticide analysis, based on simultaneous PFPD and MS detection. We found that this simultaneous detection procedure results in a greatly improved pesticide identification capability, which is much superior to the information obtained by performing this analysis with these two detectors separately. The use of two GC detectors simultaneously is not new and has proved to be informative and effective with several detector combinations also for pesticide analysis [10,11]. Over 28 years ago, Grice et al. described dual-wavelength FPD that was also operated simultaneously as an flame ionization detection (FID) [12]. More recently Morello et al. described pesticide analysis using simultaneous NPD and MS, mounted on the same GC, but acting as detectors for the output from two different columns [13]. FPD was used to help MS speciation and analysis of tributiltin in aquatic matrices [14], but without simultaneous operation. We note that only recently has advanced software been developed that enables an effective and accurate comparison of the results obtained from the two detectors.

2. Experimental

A schematic diagram of the experimental setup is shown in Fig. 1. Two experimental systems were used in the experiments described here. The first system was a Hewlett-Packard model 6890 GC system equipped with a model 5972 mass-selective detector and an O.I. Analytical model 5380 pulsed flame photometric detector. The sample was injected as an extract solution using the standard HP split/

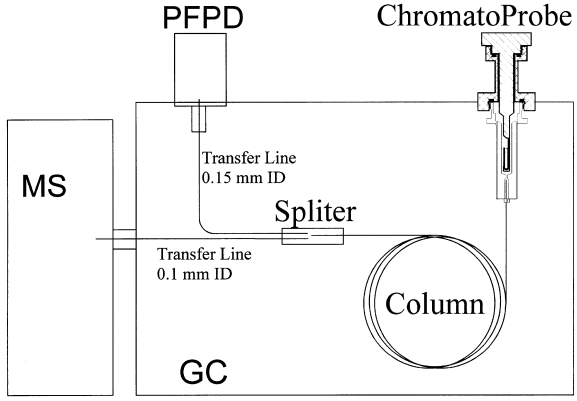

Fig. 1. The PFPD–MS experimental setup. The column output was split between the PFPD and MS systems, using an SGE column-flow splitter. The MS and PFPD were connected via a 20- or 30-cm microbore column (0.1 mm I.D., 0.1 μm DB-1 film), and a 35-cm microbore column (0.15 mm ID and 0.1 μm DB-1 film) respectively. Under these conditions, the column output was at atmospheric pressure, the flow-rate to the MS system was 0.5 ml/min for a 30-cm connecting column length (0.8 ml/min if the column length is 20 cm) and the rest of the column flow-rate was transferred to the PFPD. The PFPD chromatogram is obtained simultaneously with the MS one with a constant, compound independent, delay time of about 1 s plus the electronic processing delay, if such a delay exists.

splitless injector (with electronic flow control), and a 30×0.25 mm I.D. HP-5 capillary column with 1 μm film thickness was used. The end of the column was connected into an SGE (SGE, Ringwood, Australia) model VSOS column output splitter. The VSOS splitter was supported with a proper clip to the column holder. The splitter output was connected to the mass spectrometer vacuum system with a 30-cm long microbore capillary column (SGE 0.1 mm I.D., 0.1-μm BP1 film thickness) and to the PFPD system with a 35-cm long microbore column (SGE 0.15 mm I.D., 0.1 μm BP1 film thickness). We used columns with a thin film coating as transfer lines since we feel that they provide better deactivation than deactivated fused-silica transfer lines, but standard transfer line columns can probably also be used. The details of the output columns length and I.D. are important for determining the split ratio. Since the output of the PFPD transfer line column is at atmospheric pressure and this column is 86 times shorter than the analytical column, the pressure at the column splitting point can be considered as one atmosphere for all practical applications. Thus, the flow-rate to the MS system is determined by the helium conductivity from ambient pressure into vacuum, and by the transfer line temperature, length and I.D. This was calculated to be about 0.5 ml/min with the configuration described above. We have tested it experimentally by reducing the column flow-rate until the mass spectrometer showed the onset of an air leak through this transfer line. A flow-rate of 0.5–0.6 ml/min was indeed experimentally observed. The 0.15 mm I.D. of the transfer line to the PFPD system was a compromise value intended to minimize the retention time difference between PFPD and MS on the one hand (smaller I.D.), and the need to establish a known and close to ambient column output pressure which prevented us from using a 0.1 mm I.D. column. Under these experimental conditions and using a column flow-rate of 1.6 ml/min, a split ratio of 2 (PFPD) to one (MS) was established (1:1 split ratio with the Varian system). The calculated carrier gas transit time in the MS transfer line is less than 0.1 s, while that in the transfer line of the PFPD system was about 0.5 s. However, we observed a 0.07-min time delay between the MS and the PFPD signals, predominantly due to the digital buffer time delay of the O.I. Analytical PFPD electronics. This time delay was measured as 0.069±0.001 min and was found to be compound independent. Thus, the pesticide elution times were taken as 0.07 min earlier in the mass chromatogram in comparison with the PFPD chromatogram. The SGE splitter was found to be inert and did not produce any observable peak tailing. Dagan reported [15] that the SGE splitter produced some solvent tailing and thus he used a glass Y splitter. This solvent tailing was not observed by us. Penton also reported [16] on the use of a 'Press Fit' glass splitter for splitting the column effluent between a mass spectrometer and a GC detector. We found the 'Press Fit' glass Y column effluent splitters to be less reliable and capable of developing a leak after some time and thus highly recommend the SGE (or another) metal-based Y splitter. Dagan also reported [15] on the effective use of deactivated fused-silica columns as transfer lines and on having less than a 1-s, compound independent, time difference between MS (earlier) and PFPD in the Varian GC–PFPD–MS system.

Extract samples were injected splitless for 1 min at 60°C GC oven temperature, followed by temperature programming at a rate of 15°C/min to 310°C with a waiting period of 3–5 min at that temperature. The Hewlett-Packard ChemStation software was upgraded with a new Windows 95 based ChemStation software in order to enable the simultaneous PFPD and MS detection. With this software, the two chromatograms were placed one on top of the other and they shared a common zoom magnification.

The second experimental system was a Varian model 3800 GC system and a Saturn 2000 ion-trap mass spectrometer, and the chromatograph was equipped with a Varian PFPD system. The model 3800 GC system contained three 1079 temperature (and flow) programmable injectors. One such injector was used for standard extract solution injections at an injector temperature of 250°C, while the second contained the ChromatoProbe direct/dirty sample introduction device, as shown schematically in Fig. 1. The ChromatoProbe and its applications for the analysis of dirty samples, including blended food items only, is described in detail elsewhere [5,6]. Sampling with the ChromatoProbe was initiated (3 μl sample volume) at an injector temperature of 100°C for 1 min, followed by heating at a rate of 200°C/min to 250°C, holding the injector at 250°C

for 0.5 min, and continuing with a rapid cooling back to 100°C after this thermal extraction time. The column flow-rate during the first 2.25 min was 5.1 ml/min (splitless) and was reduced to 1.6 ml/min (He flow) after that time of thermal extraction with a split flow of 30 ml/min (split opened only after 2.25 min). A pressure program maintained a constant column flow-rate of 1.6 ml/min during the chromatographic analysis. The analytical column was an 18 m×0.25 mm I.D. J&W DB-1 narrow-bore capillary column with 1 μm film thickness. The GC oven temperature program was initiated at 50°C for 1 min with the injection of extract samples, or 2.25 min with ChromatoProbe sampling. The temperature was then increased at a rate of 15°C/min to 300°C with a waiting period of 6 min with injected samples or 3 min with ChromatoProbe sampling, since the less volatile compounds were retained in the vial.

The column output splitting was performed with an SGE VSOS column output splitter (as described above). The ion trap was connected with a 20-cm long microbore column having 0.1 mm I.D. and 0.1 μm BP1 film thickness. The PFPD was connected with a 35-cm long standard narrow bore J&W column with 0.25 mm I.D. and 0.1 μm DB1 film thickness. Admittedly, a PFPD transfer line with 0.15 mm I.D. could have been preferable, but the experiments performed here were done with this standard column as a transfer line due to availability reasons only. In this Varian GC–PFPD–MS system, the mass chromatogram was obtained 0.04 min earlier than the PFPD chromatogram (pesticide independent).

Samples of oregano, rosemary, cucumber, tomato and squash extracts were obtained from the Israel Plant Protection Center [17] and were prepared with standard liquid extraction methods using the Luke procedure [2]. The concentration of the extracts was 4.7 g/ml for the cucumber, tomato and squash and 1 gram/ml for the oregano and rosemary spices. Samples of the original tomato and rosemary that were used for the preparation of their extracts were also given to us by the Israel Plant Protection Center and were prepared for ChromatoProbe sampling by weighing, addition of 2 ml/g of acetone and blending for 3 min with an Osterizer blender. After one additional minute a few ml of the supernatant liquid of the blended tomato or rosemary were transferred into a sample vial and were used without further cleaning. The pesticides dimethoate in cucumber, malathion in rosemary, endosulfan in tomato and dichlorovos in rosemary were all authentic pesticides with the indicated levels as measured by the Israel Plant Protection Center [17]. The oregano extract was spiked with 200 ppb each of five pesticides (diazinon, methylparathion, parathion, methyltrithion and ethion) and the squash extract, that was at a concentration of 4.7 g/ml, was spiked with 5 ppb of ethion thus simulating approximately 1 ppb ethion in the squash.

The PFPD temperatures were 300°C and the detectors were operated at 3 Hz. The MS transfer lines were at 280°C and the mass spectral range was usually m/z 50–450 with a scan-rate of about 1.5 Hz.

3. Results

3.1. Marking of the pesticide

The simplest and most obvious merit of the simultaneous combination of a selective detector and a mass spectrometer is that PFPD, as an element selective detection system, considerably simplifies the chromatogram and enables an immediate marking of the pesticide for its fast mass spectrometric identification. In Fig. 2, we show the simultaneous PFPD and MS analysis of 0.12 ppm dimethoate in cucumber (Varian GC–MS system was used here). Since this is an extract with 4.7 g/ml, the actual pesticide concentration was 0.56 ppm (1 μl injected amount). While the mass spectrometer chromatogram (upper trace A) is very complex, the PFPD chromatogram (lower trace B) immediately indicates the pesticide elution time. In the insert at the lower right side, we show a magnified portion of these chromatograms which shows a clean single PFPD peak indicating the exact elution time of the pesticide. The mass chromatogram was shifted 0.04 min to obtain the same elution time as in the PFPD chromatogram. A small, but observable, pesticide chromatographic peak is observed and is easily identified by the library as dimethoate. Several remarks are made in order to further illuminate this result:

(1) Only one GC–PFPD–MS system was used

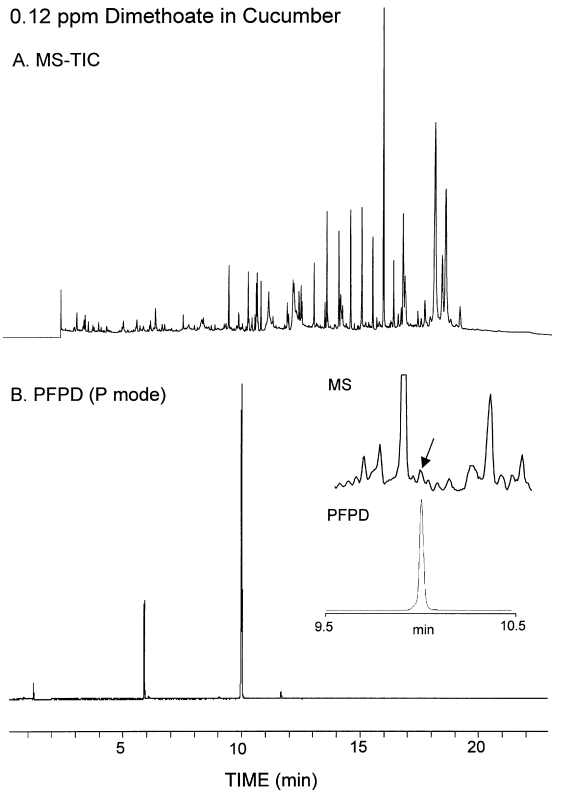

Fig. 2. PFPD–MS marking of a target compound. A cucumber extract, containing 0.12 ppm authentic dimethoate (4.7 g/ml resulting in 0.56 ppm in the extract) was analyzed simultaneously with the PFPD in its P mode and MS (Varian 3800 GC system plus Saturn 2000 MS system). While the observed total-ion chromatogram is very complex, the PFPD chromatogram is simple due to its selectivity. The magnified trace marks the exact elution time of the pesticide that is easily identified by the library search. The PFPD peak at 6 m is from a natural sulfur compound (benzothiazole) and its sulfur origin is identified by the time delay of its pulsed flame emission.

and the results serve for dual simultaneous screening and confirmation, thereby saving the cost and bench space of an additional GC system.

(2) Time is saved by performing a single chromatographic analysis instead of two analyses one after the other.

(3) The simultaneous PFPD–MS analysis with a single column provides the ultimate elution time precision for locating the pesticide in the mass chromatogram. The actual precision is a small fraction of a second, and depends on the mass scanning frequency.

(4) The smaller additional PFPD chromatographic peak at close to 6 min elution time was identified to originate from naturally occurring benzothiazole. While PFPD was in the P detection mode, it is well known [6,9,12,18–20], that sulfur compounds at large amounts are observed with both FPD and PFPD since the sulfur emission under the phosphorus spectral window is about 3% of its maximum. However, with the PFPD post-run software, the pulsed flame emission is recorded and stored for post-run observation (similarly to mass spectra in GC–MS software) and the emission time immediately identifies this GC peak as originating from a sulfur compound. The use of dual gate software can eliminate this peak but we prefer to leave it and identify it post-run .

(5) As observed, the split ratio of 1 to PFPD and 1 to MS is justified since the MS sensitivity is limited due to matrix chemical noise and not instrumental limitations, thus adding more sample to the MS system will not enhance its sensitivity. On the other hand, PFPD serves for the quantitative determination of the pesticide and thus can benefit from an increased relative portion of the sample flux. We shall further discuss this aspect with other examples.

3.2. Finding the needle in the haystack

The example above is considered to be relatively easy, and fast pesticide identification and quantitation was demonstrated with dimethoate in cucumber. However, with lower concentrations and/or with more complex matrices, the situation is more difficult and no pesticide chromatographic peak may be observed. In Fig. 3, we show the GC–PFPD–MS analysis of pesticides in oregano extract (1 g/ml) (using the HP GC–MS system). The oregano extract was spiked with an MX-5 pesticide mixture (from Nanogen) containing 200 ppb each of diazinon, methylparathion, parathion, methyltrithion and ethion, in that order of elution. Clearly, the total ion chromatogram (TIC) is very complex and no pesticide peaks can be located. Furthermore, even a library search on each mass spectrum cannot reveal any of these five pesticides. We further note that while the mass chromatogram was magnified and many peaks were saturated in it, its concentration scale (y axis) was far higher than that in the PFPD

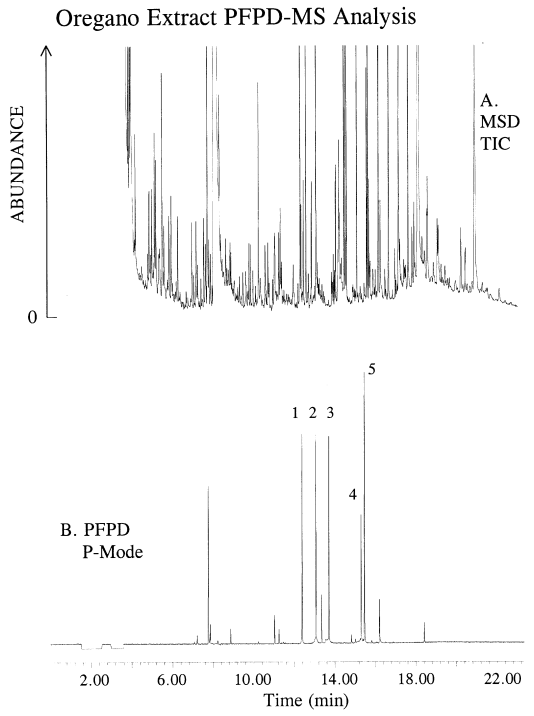

Fig. 3. Finding the needle in the haystack. An oregano extract (1 g/ml), spiked with 200 ppb each of diazinon, methylparathion, parathion, methyltrithion and ethion in order of their elution time, was analyzed (HP 6890 GC system plus 5972 mass-selective detector). The observed total ion chromatogram (upper trace) is very complex, rendering the identification of any of these pesticides impossible. The lower chromatogram was obtained simultaneously with PFPD in its P mode. All the pesticides are clearly observed as the five major peaks in the 12–16-min time window, together with a few additional phosphorus and sulfur compounds.

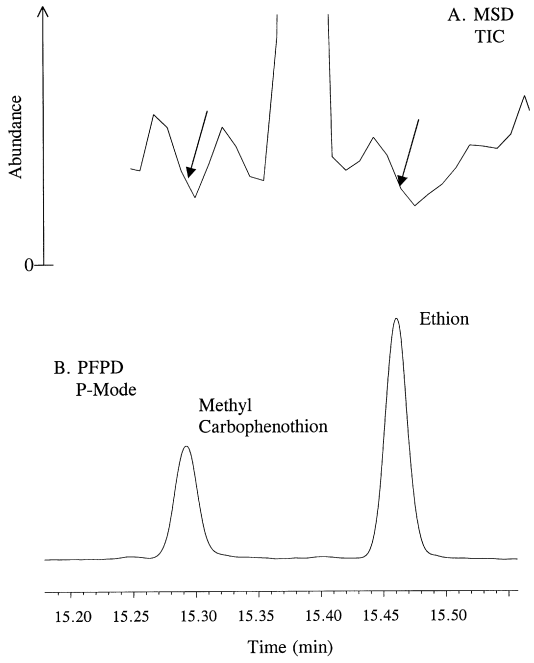

Fig. 4. Locating the precise pesticide elution times. The PFPD and MS chromatograms of oregano shown in the previous figure were magnified (zoom) around the elution time of methylcarbophenothion and ethion. While the PFPD chromatogram shows two peaks, the total ion chromatogram shows only valleys and no peaks at all for these elution times. Accordingly, the PFPD chromatogram is essential for the precise location of the pesticide elution times.

chromatogram. The PFPD chromatogram, on the other hand, is relatively simple, showing the five pesticides (marked in numbers 1–5) as the highest chromatographic peaks. A few additional peaks are observed in the PFPD chromatogram, mostly due to natural sulfur compounds (although PFPD was in the P mode) and a few due to low level phosphorus compounds or low level authentic pesticides. As mentioned above, an unambiguous classification to sulfur and/or phosphorus compounds can be achieved with PFPD. In order to identify these pesticides, we magnified the two PFPD and MS chromatograms around the ethion and methylcarbophenothion (another name for methyltrithion) as shown in Fig. 4. In Fig. 4, the mass chromatogram was shifted 0.07 min in order to compensate for the electronic delay so that the two chromatograms would have the same elution time. Clearly, neither pesticide reveals itself in any chromatographic MS peak. Coincidentally, they are very close to being at a ‘chromatographic valley’. However, the PFPD chromatogram is clearly characterized by a nice chromatographic peak shape which enables the precise location of the pesticide elution time in the mass chromatogram. In Fig. 5, we show the mass spectra obtained for the ethion pesticide. The upper mass spectrum is the raw mass spectrum obtained at the exact pesticide elution time of 15.46 min as indicated by PFPD (15.39 min in the actual mass chromatogram). The two prominent relatively high-mass fragments at m/z 231 and 153 were revealed only at this mass spectrum and at a nearby mass spectrum and thus were attributed to the pesticide. However, with this mass spectrum, a library search failed to

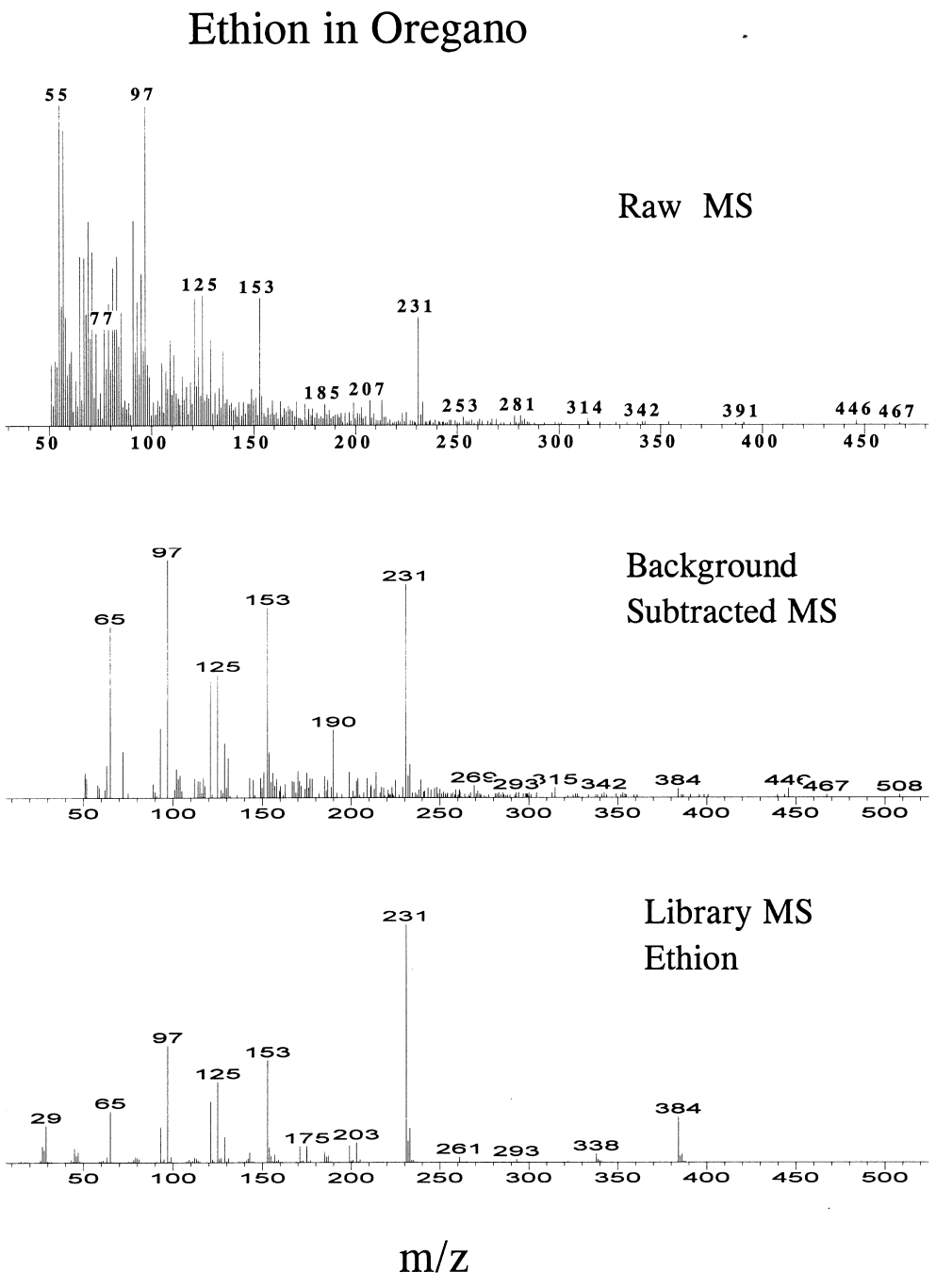

Fig. 5. Precise PFPD-given elution time for accurate mass spectral background subtraction and pesticide identification. The upper mass spectrum was obtained at the exact elution time of ethion in the oregano sample. While the major ethion ions at m/z 231 and 153 are clearly observed, this mass spectrum did not result in a library identification of ethion. However, after performing proper background subtraction (middle MS) ethion was the first hit in the library search with a 0.92 matching factor, well above any other possibility. This precise background subtraction is based on averaging three mass spectra around the exact PFPD determined pesticide elution time, averaging a background from nine mass spectra around this time and performing mass spectra subtraction.

identify any pesticide, and ethion was the third compound with a matching factor of 0.27 (27 in the ChemStation software). Accordingly, this case is a demonstration of a failed direct pesticide identification. On the other hand, after performing a careful background subtraction, ethion was identified as the first four hits with a 0.92 matching factor. Mass spectral background subtraction was performed by averaging three sample mass spectra around the PFPD-indicated pesticide elution time and nine background mass spectra at the two sides of the PFPD-indicated elution time, followed by its subtraction from the averaged sample mass spectrum. The result is shown in the middle-mass spectrum and is compared with that of the library shown at the bottom of Fig. 5. Final confirmation can be achieved, if this library identification is not completely convincing, by plotting reconstructed mass chromatograms of central ethion ions at m/z 231 and 153, its molecular ion at m/z 384 and on a suspected matrix ion at m/z 190. Indeed, all three ions of ethion showed clear reconstructed mass chromatogram peaks at exactly the same elution time and peak shape shown in the PFPD trace, while the m/z 190 mass chromatogram peak was shifted to longer elution times and had a peak tail. We note that the molecular ion intensity was always found to have lower relative intensities than the library mass spectra due to ion-source temperature effects [21,22]. All five spiked pesticides were similarly identified after careful background subtractions, except the methyltrithion whose mass spectra was too congested and could not be adequately cleaned by background subtraction.

3.3. NIST sequential search with two ions and one element for pesticide identification at lower concentrations

When the pesticide concentration is further reduced, while the matrix interference remains, the standard library search procedures may fail to identify the pesticide, even after careful background subtraction. In this case, the PFPD elemental information can help when combined with the NIST (National Institute of Standards and Technology) sequential search method. The NIST library sequential search is a library search with constraints according to additional available information. Let us assume a case where the background subtracted mass spectrum of ethion looks like the upper trace MS in Fig. 5. In that case, we suspect the two high-mass peaks at m/z 231 and 153 to be fragments of the pesticide. This assumption is supported by the fact that only background subtracted mass spectra that use the PFPD pesticide elution time result in mass spectra which contain these two ions. It can be further confirmed by obtaining computer reconstructed mass chromatograms of these two ions and observing that these mass chromatograms fully overlap with that of PFPD. Thus, we assume that the pesticide contains both these ions and the element phosphorus. In Fig. 6, we show the implementation of this PFPD and MS-derived information in the NIST sequential search mode. The NIST library was loaded independently, outside the GC–MS software. The ‘search’ was clicked and the ‘sequential method’ was initiated. A separate window appeared as shown in the middle of Fig. 6. The ‘elements’ section was selected and as shown at the bottom, $P>0$ and ‘some’ of these elements were inserted. After the ‘OK for all’ button was clicked the ‘peaks’ window was activated and both fragments m/z 231 and 153 were introduced with over 30% estimated normalized abundance. After acceptance and OK, the ‘OK’ button in the middle window in Fig. 6 was clicked and the search was initiated. Ethion appeared as the only compound that fulfils the sequential search requirements and thus a definite pesticide identification was achieved from the combined PFPD and MS-derived information, in a case where the standard library search failed. We have applied this sequential search method in many cases, including all of the five pesticides of Fig. 3, and it always provided an unambiguous pesticide identification. In a few cases, unlike in the example of ethion above, a few library compounds may appear. The final identification in these cases is based on the existence or nonexistence of additional major ions. For example, methyltrithion in Fig. 4 could not be identified by the library. However, it showed clear m/z 157 and 125 ions at over 30% normalized abundance. The sequential search with these ions and P atom provided five possible candidates. Only methyltrithion (methylcarbophenothion in the library) also shows a

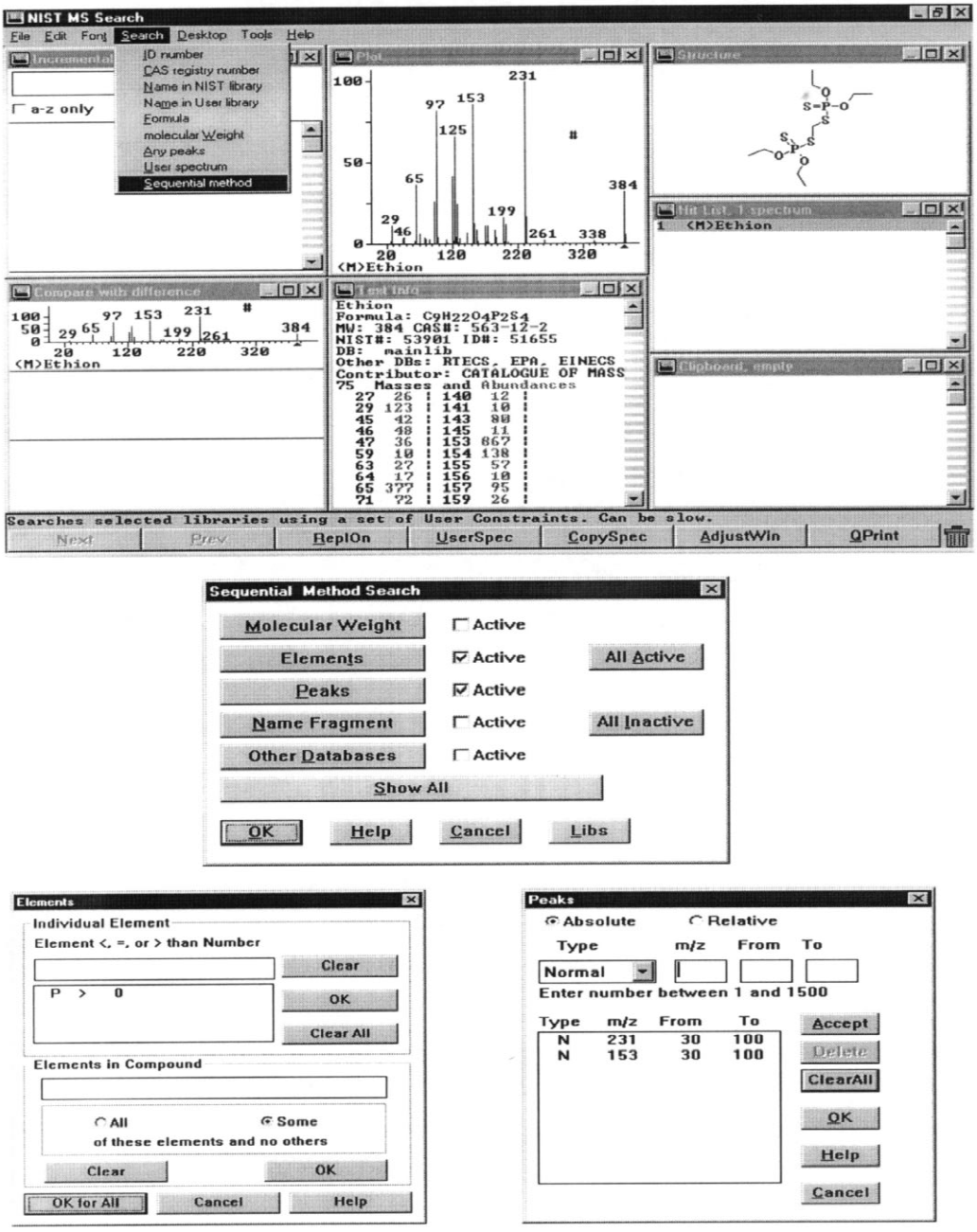

Fig. 6. NIST sequential search for obtaining pesticide identification at lower pesticide concentrations. When the pesticide concentration is too low, even precise background subtraction does not provide adequate mass spectrum quality for library identification. In that case, as shown, the NIST library has a sequential search mode that enables a search with constraints to those compounds in the library that contain one or more phosphorus atoms (PFPD-derived information, written as P>0 and as 'some of these elements') and m/z 231 and 153 fragments at above 30% normalized abundance. Under these search conditions, ethion is positively identified as the only compound that meets these constraints.

small m/z 314 (molecular ion) and the correct order of peak heights of the m/z 157 and 125 ions.

We have studied this mode of sequential search and our conclusions are that the inclusion of the P atom limits the search to about 2% of the library content (sulfur is found in 11% and nitrogen in 45% of the library compounds) while the inclusion of a fragment with over 30% normalized abundance further restricts the search by a factor of 50. However, while the P atom information is orthogonal and does not relate to the fragment information, the second fragment information may relate to the first ion. Furthermore, the ion information constraint is better with higher mass ions. Thus, on average, P atom and two ions result in 1–5 possible compounds that enable unambiguous pesticide identification (if it exists in the library). Actually, this conclusion can be tested by anyone with the NIST library and on any pesticide. The only assumption that needs to be made pertains to the safe ion abundance constraint that should be inserted, in view of the original abundance and matrix interference. A few such computer 'games' can quickly prove our point.

3.4. Sequential search with one ion and two elements for library identification at the lowest concentrations

In Fig. 7, a harder case of pesticide identification is shown. Fig. 7 demonstrates the analysis of authentic malathion in rosemary. The pesticide concentration was found to be lower than 100 ppb using standard extraction procedures. In Fig. 7, we used the ChromatoProbe sample introduction device for sampling. We found that the sample cleanliness was similar to that achieved with standard liquid extraction procedures while the pesticide recovery efficiency was higher by a factor of 2.4 with the ChromatoProbe.

In Fig. 7, the mass chromatogram is shown (upper trace) together with the PFPD P mode chromatogram (middle trace) and the PFPD S mode chromatogram. The malathion peak is indicated by the arrows and clearly contains both sulfur and phosphorus atoms. Furthermore, from a comparison of the P mode and S mode chromatograms we conclude that malathion has two sulfur atoms for each phosphorus atom since, for the same malathion peak height, the P

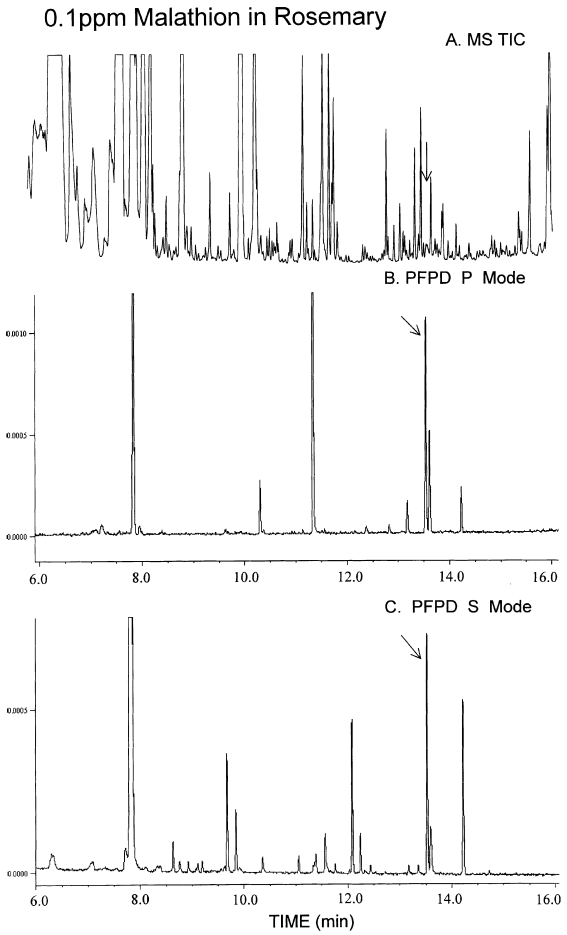

Fig. 7. ChromatoProbe–GC–PFPD–MS identification of malathion in rosemary. Three μl of blended rosemary in acetone were sampled with the ChromatoProbe (DSI) and analyzed with GC–PFPD–MS (Varian 3800 GC system plus Saturn 2000 MS system). The rosemary sample was independently found to contain below 0.1 ppm of malathion by the Israel Plant Protection Center using standard extraction procedures. Malathion is indicated by the arrows and contains both S and P. By comparison to another compound in the chromatograms at 10.3 min, one can learn that it contains more than one sulfur atom per phosphorus atom. We note that the PFPD chromatogram contains a few additional peaks and the PFPD capability of elemental identification (P and or S) is valuable for the effective combination of the PFPD-derived information with that of MS.

mode peak at 10.3 min is a factor of four higher than for that compound in the sulfur mode. The issue of PFPD-derived S/P intra-compound elemental information has been discussed elsewhere [6]. In Fig. 7, two consecutive runs were performed, but with post-

run software, a P+S mode could be used and the two chromatograms could be generated by the software after the run [6]. Since this software was not commercially available at the time of performing this experiment, we performed two consecutive chromatographic runs.

In Fig. 8, we show the time axis expanded TIC and mass chromatograms of several ions together with the background-subtracted mass spectrum of the suspected malathion pesticide, using its exact elution time as obtained with PFPD. No library identification

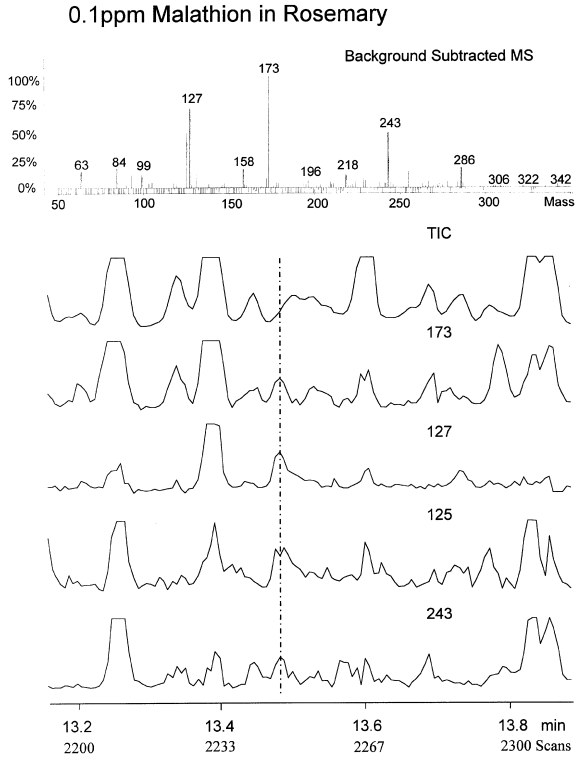

Fig. 8. Sequential search with one ion and two elements for the ultimate low concentration identification limits in a complex mixture. In this sample of rosemary, the malathion is 'buried' in the matrix chemical noise. Precise background subtraction (top trace MS) did not provide library identification. The lower traces show the reconstructed mass chromatograms of the major ions in the background subtracted mass spectrum. Due to the congested nature of these traces they could not be trusted. Accordingly, a NIST sequential search was performed using P>0, S>1 elemental information as derived from PFPD and the dominant m/z 173 as an existing ion with more than 50% normalized intensity. Malathion was extracted and identified as the only compound that fulfilled these requirements.

was achieved with this background subtracted MS. Accordingly, we performed computer-reconstructed mass chromatograms of all the major ions revealed in this spectrum namely m/z 243, 173, 127 and 125 as shown in Fig. 8. While the TIC trace shows the pesticide elution time on the left side of a non-pesticide peak or peaks, all the mass chromatograms show an exact co-elution with the GC–PFPD peak. However, each mass chromatogram was heavily congested and thus could not be trusted due to the occurrence of elution-time overlap of several compounds in the time window presented in Fig. 8. Furthermore, a standard three-ion search of malathion as a target compound could easily provide at least four additional false 'malathion' peaks within this 0.7-min time window. A NIST sequential search with two ions that include the high mass m/z 243, an additional ion and the element P failed to provide any hit. Thus, we performed a sequential search using PFPD providing two-element information as P>0 and S>1 and m/z 173 with over 50% natural abundance. Malathion is exclusively identified as the only NIST library compound that fulfils these constraints. Apparently, the m/z 243 ion belongs to a non-pesticide matrix compound that coelutes with malathion, and this coelution made the sequential search mode of two elements and one ion essential. We studied this type of sequential search and found it very effective, yielding only 1–5 compounds as candidates, with further confirmation of the correct pesticide provided by additional mass spectral information of the existence or nonexistence of additional MS ions. Since PFPD is more sensitive than MS due to its *selectivity* and lower chemical noise, the sequential search method with one ion and two elements is a more sensitive method than the use of two ions and one element since one major ion is easier to observe than two (by definition the second ion is the ion that is smaller or less clearly identified). However, this mode requires two elements and only PFPD, unlike any FPD method, has the required sulfur sensitivity for this purpose. Note that the sulfur chromatogram in Fig. 7 has about the same S/N as the phosphorus chromatogram, while FPD is expected to show no sulfur peaks at all for malathion at these sulfur elution fluxes. Furthermore, PFPD can provide this two element information in a single run.

A statistical analysis of this approach of two

elements and one ion shows that it can be applied to all the elements except C, H, O, N as these elements are ubiquitous and found in 45% or more of the library compounds. In the world of pesticides, the important elements for this search method are P, S and Cl while nitrogen is not as useful for this procedure. Note that the majority of all phosphorus pesticides also contain one or more sulfur atoms and thus can be identified using this method.

3.5. Sulfur pesticide analysis

About 20% of the USA Environmental Protection Agency (EPA) list of pesticides contain sulfur without phosphorus [23]. Usually these pesticides are analyzed by the detection of a nitrogen atom that is found in most of them. It has been shown [6], that the selective detection of sulfur is preferable compared to nitrogen since the amount of sulfur matrix interference is considerably smaller than that of nitrogen, which is widely abundant in natural compounds, especially in plant-related matrices. In Fig. 9, we show the PFPD–MS detection of the sulfur pesticide endosulfan in tomato. A tomato sample containing 80 ppb of authentic endosulfan was blended with acetone and sampled with the ChromatoProbe for GC–PFPD–MS analysis. The upper TIC mass spectrum is very complex while the lower PFPD sulfur mode trace is much simpler and clearly indicates the two endosulfan pesticide isomers, each at 40 ppb concentration level. We used 3 μl of a tomato sample containing 1/3 g/ml (2 ml acetone per 1 g tomato), therefore, 40 pg of each endosulfan isomer pesticide was introduced into the column. The observed signal-to-noise ratio is a little higher than expected for this concentration and thus we feel that the real concentration is somewhat higher than the estimate of the Israel Plant Protection Center. In any case, this level of concentration is too low for FPD.

We found that the thermal extraction efficiency was higher with the ChromatoProbe for endosulfan in tomato, than the standard extraction efficiency, by about one order of magnitude. The issue of the effectiveness of the ChromatoProbe in thermal extraction is beyond the scope of this paper, but all our current results suggest higher thermal extraction efficiencies than with the standard liquid extraction

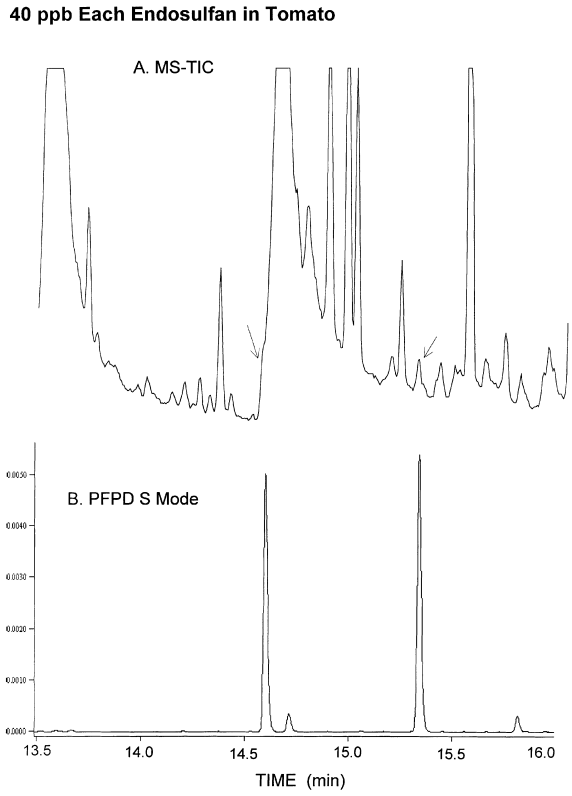

Fig. 9. PFPD–MS analysis of a sulfur pesticide. A tomato sample was found to contain 80 ppb of endosulfan (40 ppb each isomer). We analyzed this tomato after blending it with acetone and sampling 3 μl of the 'acetone ketchup' with the ChromatoProbe (Varian 3800 GC system plus Saturn 2000 MS system). As demonstrated, the two endosulfan isomers are clearly identified by the PFPD and precise background subtraction yielded library identifications with matching factors over 0.92. Similarly the endosulfan pesticide was identified with the NIST sequential search using two ions and sulfur atom information.

procedures. We observed clearer and cleaner endosulfan identification in this tomato matrix with the ChromatoProbe sampling than with a standard extract injection, despite its 4.7 g/ml concentration.

Note that the PFPD chromatogram clearly indicates the elution times of endosulfan in the mass chromatogram and after background subtraction, unambiguous library identification of each endosulfan isomer as one of the two endosulfan isomers was achieved. Furthermore, endosulfan could also be identified with the NIST sequential search using the sulfur elemental information and any two major ions, such as m/z 195 and 337.

3.6. Trace level target pesticide confirmation

Below a certain pesticide concentration level, which depends on the amount of matrix interferences, even the sequential search mode with one ion and two elements fails due to a lack of any clear pesticide ion information. In Fig. 10, we demonstrate such a case of authentic dichlorovos at a concentration level of less than 5 ppb in rosemary. In this case, even the PFPD chromatogram has some baseline noise while the mass chromatogram has no peak at the pesticide elution time, which is 'buried' in the high-time side of a matrix peak (note the 0.07-min time shift with the HP GC–MS system). In this case, even the most careful background subtraction failed to provide a meaningful and trustworthy mass spectrum and thus the NIST sequential search could not be employed. However, the elution time in the PFPD P mode chromatogram hinted towards dichlorovos as a possible pesticide candidate. Consequently, we performed computer reconstructed mass chromatograms on the dichlorovos major ions of m/z 109, 185 and its molecular ion m/z 220. As shown in Fig. 10, all three mass chromatograms gave a chromatographic peak at the expected pesticide elution time, as derived from the PFPD chromatogram. Furthermore, the relative intensities of the ions were as expected based on the library MS and only a single ion was observed for the molecular ion. While admittedly this case is not a clean library identification, the dichlorovos identification is strongly supported by the combination of the PFPD and MS given information. In another similar case of suspected dichlorovos in dill extract at this level, the result was a clean rejection of dichlorovos and the identity of the organophosphorus compound remained unsolved. Thus, we conclude that even when the sequential search fails, the PFPD–MS strategy enables target compound identity confirmation or denial.

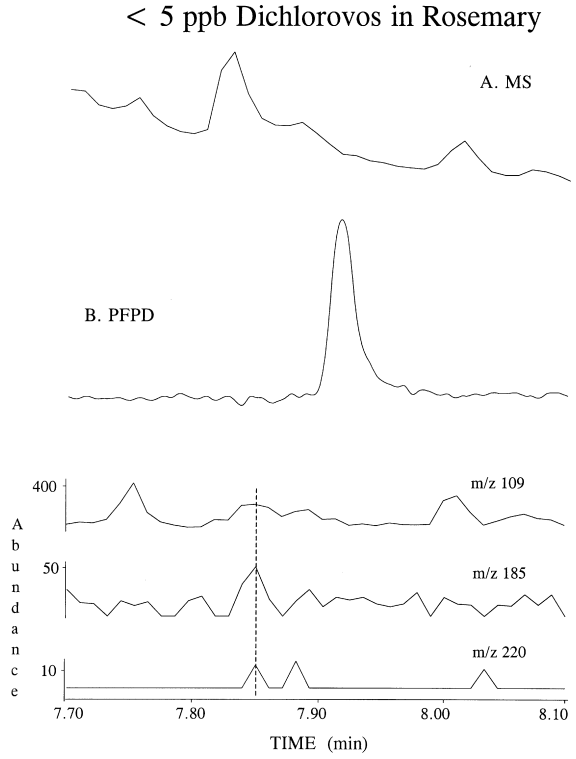

Fig. 10. Trace level target pesticide confirmation. Trace level analysis of dichlorovos (<5 ppb) in rosemary is shown (HP 6890 GC system plus 5972 mass–selective detector). When the pesticide concentration is too low, or the matrix interference is too high, the PFPD–MS information can be used for the confirmation of a target pesticide identification. In the rosemary sample above, dichlorovos was suspected based on its GC–PFPD elution time. Computer reconstructed mass chromatograms are shown at the bottom using the dominant dichlorovos m/z 109 and 185 fragment ions as well as its molecular ion at m/z 220. All three mass chromatograms show peaks at the expected elution time of 7.85 min (0.07 min earlier than in the PFPD chromatogram) and at the expected, albeit low, relative intensities.

3.7. Simultaneous PFPD and single-ion monitoring MS for the ultimate trace level pesticide analysis

Selected-ion monitoring (SIM) with a quadrupole mass spectrometer enables the lowest pesticide detection limits albeit with a major sacrifice in the content of mass spectral information. Time-shared SIM enables several target pesticides to be detected in the same chromatographic run by time programming of the monitored selected ion. A few ions can be simultaneously monitored (such as three ions) with some trade-off in the detection sensitivity.

In Fig. 11, we demonstrate the simultaneous PFPD–MS–SIM detection of 1 ppb ethion in squash extract. The squash extract having 4.7 g/ml was spiked with 5 ppb ethion, simulating 1 ppb ethion in the squash. PFPD was in the P mode while MS was

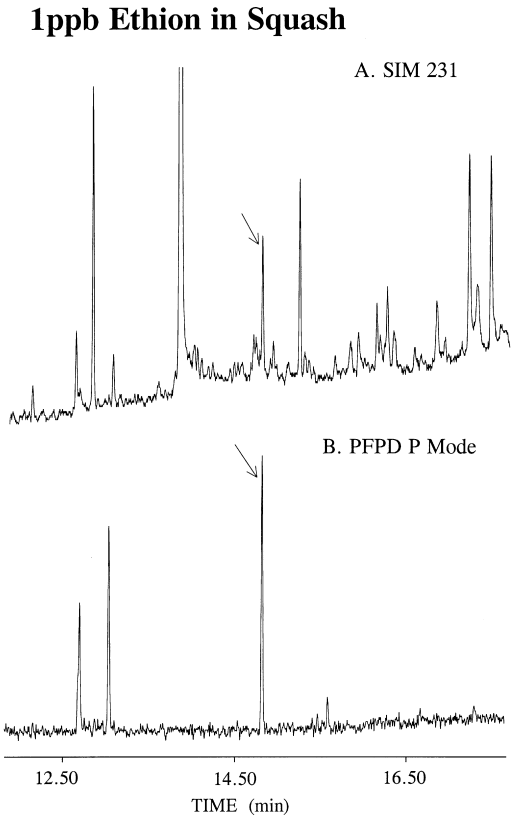

Fig. 11. Pesticide identification with single-ion monitoring sensitivity. A PFPD–MS analysis of 1 ppb of ethion spiked in squash is shown (5 ppb spiked in a 4.7 g/ml squash extract). PFPD (O.I. Analytical 5380) was in the P mode and MS (HP 6890 GC+5972 MSD) was in the SIM mode at m/z 231. Note that the PFPD P mode is much more selective than the MS–SIM mode. Only the spiked ethion PFPD peak is correlated with a corresponding SIM peak at exactly the same elution time. While a single ion and two elements can establish pesticide identification, identification is not claimed here but is strongly supported, *and at the lowest possible detection limits*.

in the SIM mode on the ethion major m/z 231 ion. The following conclusions are derived from Fig. 11:

(1) The PFPD P mode sensitivity matches or even exceeds by a little the mass spectrometry SIM mode sensitivity.

(2) The PFPD P mode selectivity is considerably greater than that of the mass spectrometer SIM mode as observed in the complex SIM chromatogram.

(3) Ethion is identified as the only compound with full coelution of the mass chromatogram and any of the PFPD peaks. After introducing the 0.07-min time shift, the other two PFPD peaks did not overlap with any MS–SIM peak.

(4) The MS–SIM peak intensity is as anticipated from its PFPD peak height.

While a clear identification is not claimed here, the combination of one major-ion information, P elemental content and the exact elution time can serve for a high confidence level pesticide identification, at the lowest possible concentration. This identification can be further supported by sulfur atom information if available.

4. Conclusions and discussion

As shown above, the combination of PFPD and MS and simultaneous operation in a single GC system, greatly enhances pesticide detection and identification capabilities. In this case, a single system with both of these detectors outperforms the combination of two separate systems, each with a single detector. The small loss of up to a factor of two, encountered with the splitting of the column output does not hamper the detection sensitivity. This situation exists because the MS is the bottleneck of the system detection sensitivity and its practical sensitivity depends on matrix rather than on instrumental noise. This chemical noise is reduced in a manner similar to the actual pesticide signal upon column effluent splitting. As a result, the overall detection sensitivity remains unchanged while the pesticide identification concentration limit is considerably improved through the combination of both the PFPD and MS generated information. The simultaneous PFPD and MS detection with its resulting column effluent splitting is also involved with several additional minor experimental aspects. A steady column flow-rate is required in order to avoid a leak of air through the short microbore transfer line, but such a small air leak is tolerable by the MS system if its ion source is turned off and the transfer line is cooled down (during a change of septum etc.). On the other hand, this column splitting has some minor benefits in the ability to replace columns without venting the MS vacuum system and a much

greater freedom of column flow-rate and column I.D. is experienced.

4.1. Enhanced pesticide detection and identification capabilities

The merits of simultaneous PFPD and MS detection are several fold:

(1) PFPD marks the elution time of a suspected pesticide for fast zooming on the pesticide peak in the mass chromatogram, followed by its standard library identification (dimethoate in cucumber in Fig. 2).

(2) In cases where no mass chromatogram peak is observed and/or no library identification is achieved, the exact PFPD-derived pesticide elution time enables a careful and accurate background subtraction for enhanced library identification capability (ethion in rosemary in Figs. 3–5).

(3) The pesticide identification capability is further enhanced and exists even when standard library identification fails, due to excessive matrix interferences, through use of the NIST sequential search method. The sequential search is based on the provision of information on two ions and one element such as P or S. (Fig. 6).

(4) The NIST sequential search sensitivity is further improved by the provision of information on one ion and two elements, such as S and P and m/z 173 in malathion as shown in Figs. 7 and 8.

(5) A unique sulfur pesticide detection capability is provided by PFPD and demonstrated in the analysis of endosulfan in tomato (Fig. 9). Again, a sequential search can be performed with a sulfur atom and information on two ions.

(6) In cases where a careful mass spectral background subtraction fails in the reliable provision of information on even a single major pesticide ion, the PFPD chromatogram can serve for the confirmation of a suspected pesticide, based on its elution time. This was demonstrated in Fig. 10 for dichlorovos in rosemary through a time overlap of mass chromatograms of major dichlorovos ions with the PFPD P mode chromatogram.

(7) The ultimate detection sensitivity in a quadrupole GC–MS system is achieved by using MS in the SIM mode simultaneously with PFPD as demonstrated for 1 ppb ethion in squash in Fig. 11.

4.2. Simultaneous GC selective detector and MS operation

While this paper deals with simultaneous combination of PFPD and MS detection, this method can clearly be generalized as simultaneous selective and MS detection which can be extended to any other selective GC detector. The central merit of a precise elution time marking for accurate library search is shared by all the selective GC detectors as is the savings in bench space, cost and analysis time through the use of a single system with two detectors. However, we believe that the combination of PFPD and MS is particularly beneficial for several reasons as discussed in its comparison with each of the other major GC selective detectors that are used for pesticide analysis:

(1) NPD. The combination of NPD and MS can be useful as a supplementary combination to PFPD–MS for pesticide analysis. However, due to the wide distribution of natural nitrogen compounds, its combination with the NIST sequential search has a limited value since 45% of the NIST library compounds contain one or more nitrogen atoms. Furthermore, NPD fails to provide unambiguous elemental information due to its simultaneous N and P detection.

(2) ECD. ECD is incompatible with the NIST sequential search as it does not provide elemental information. Even worse is its limited and ill-defined selectivity that results in too many searches of pesticide suspects.

(3) Atomic emission detection (AED). AED can be used in combination with the MS and with a very broad range of elements. However, it is a complex and costly detector that requires special maintenance. Its sensitivity with a few elements such as the halogens is limited and incompatible with that of the MS. Furthermore, separate computers are currently required that makes mutual zooming less convenient. On the other hand, when its sensitivity is sufficient, it is highly compatible with the single-ion, two or more elements NIST sequential search method.

(4) Halogen-selective detection (XSD or ELCD).

XSD [24] can be a particularly suitable detection method for simultaneous detection with MS, and will share the benefits of the NIST sequential search as discussed. A minor limitation is that the nature of the detected halogen is not well defined and only halogens are suspected. The XSD and PFPD triple combination with MS can be considered when suitable software will be available or with two separate computers. The total abundance of halogen compounds in the NIST library is a little over 13% but their natural abundance in plant matrices is very limited.

4.3. PFPD versus FPD

FPD can certainly be effectively used for simultaneous detection with MS and it shares some of the benefits previously outlined for PFPD. However, the FPD–MS combination is inferior to the PFPD–MS combination in the following important aspects:

(1) The FPD selectivity is limited and it is especially susceptible to major interferences from natural sulfur compounds [6,12,18–20]. The availability of a multitude of GC peaks with uncertain elemental origin makes the task of careful pesticide library search on each GC peak tedious and less effective. With PFPD, these sulfur interferences can be avoided with the dual gate subtraction mode [6] or identified as belonging to sulfur compounds.

(2) The phosphorous elemental information might be ambiguous with FPD due to sulfur interferences, thus, precluding the use of the NIST sequential search with one element and two ions.

(3) The FPD sulfur detection sensitivity is inadequate for pesticide analysis and is incompatible with the sensitivity of the MS. A detection limit of 20 pg S/s is translated into 400 pg pesticide, far more than that of the MS. The PFPD specification of 1 pg S/s detection limit translates into 400 times greater sulfur detection signal-to-noise ratio than that of FPD due to its quadratic sulfur response.

(4) The NIST sequential search with one ion and two elements is precluded due to the incompatibility of the sulfur channel of FPD in terms of the sensitivity requirements.

(5) The superior PFPD P mode sensitivity is valuable in making the confirmation of a target pesticide identity and/or combination with the MS-SIM mode possible. These modes require the highest selective detector sensitivity. SIM mode detectivity of 0.1 pg pesticide per second is translated into a selective detector sensitivity requirement of 10 fg P/s.

(6) PFPD, unlike FPD, can simultaneously detect and identify 13 elements including S, P, N, Sn, Se, As and Ge [25,26]. Elemental identification requires the dual gate approach [9] or post-run processing software which we have and will soon be available from O.I. Analytical as ‘PFPD View’.

4.4. GC–MS–MS versus GC–PFPD–MS

In comparison with MS–MS, we note that the PFPD–MS is an effective method for unknown pesticides, unlike MS–MS which although very effective, is limited to target compounds. When target compounds are searched, MS–MS might be a superior alternative to PFPD–MS, as it displays a broad applicability to all compounds and not only to those with a specific element. However, for universal pesticide residue analysis where unknown pesticides must be considered, MS–MS cannot be employed and the PFPD–MS method should be preferred. Furthermore, PFPD–MS, especially when combined with the ChromatoProbe sample introduction device, enables combined screening and confirmation in one fast chromatographic analysis if a short column is used. The use of a short column may limit the number of target pesticides amenable for MS–MS in a single run. We also note that the NIST sequential search, in contrast to and unlike MS–MS, provides a true library search that also excludes all the other library compounds. On the other hand, PFPD–MS and MS–MS can supplement and complement each other. In all the MS–MS examples that we observed we found that the MS–MS daughter ions also appear in the EI mass spectrum, although at vastly different relative abundances. Consequently, we found that the NIST sequential search can be employed with MS–MS information through the incorporation of the parent ion and its estimated abundance and two MS–MS daughter ions with an estimated abundance of 2% or more only. The sequential search with one ion at 30% or more, two ions with 2% or more and

one element such as P or S enables an unambiguous pesticide identification. In that case, the identification is with a higher confidence level of NIST library identification which is superior to the limited user-provided MS–MS library. Furthermore, PFPD–MS and MS–MS can complement each other so that PFPD–MS is used for unknown pesticide analysis while MS–MS is used for target compound analysis and/or for further MS–MS confirmation of compounds identified by PFPD–MS, with the ultimate confidence level in the identification.

4.5. Nonpesticide PFPD–MS applications

We have also briefly studied the PFPD–MS approach with two additional applications and found that:

(1) The PFPD–MS was useful in the analysis of sulfur compounds in coffee. Elite Turkish coffee powder was introduced as is with the ChromatoProbe, and the PFPD–MS (S mode PFPD) provided clear detection of all the major sulfur compounds in the coffee. However, library identification was not achieved in many cases due to the lack of these compounds in the NIST library. Accordingly, these sulfur compounds could be characterized by their mass spectra or by a few major ions and the presence of a sulfur atom while their identification requires further study, perhaps with MS–MS.

(2) The PFPD–MS was employed for the attempted identification of sulfur compounds in Diesel fuel and kerosene. While very nice chromatograms were achieved, the combined PFPD and MS failed to identify any of the major sulfur compounds in these fuels due to excessive mass spectral chemical noise. Thus, even PFPD–MS fails to identify sulfur compounds in very complex matrices, such as Diesel fuel, when the sulfur compound concentration is too low. Accordingly, sulfur analysis in complex petrochemical fluids will probably continue to rely on sulfur-selective detectors alone and not on mass spectrometry which renders itself inapplicable for this purpose.

4.6. Quantitative aspects of the PFPD–MS method

As demonstrated above, a lower pesticide identification concentration can be achieved with the PFPD–MS method in comparison with standard GC–MS analysis. However, the magnitude of this improvement factor is hard to quantify. Furthermore, this improvement factor may depend on prior available information, the use or disregard of the GC elution time information, the analysis of target or unknown pesticides, the amount of time allocated for post-run pesticide search and the nature and degree of matrix interferences. Even without any matrix interference, simultaneous PFPD–MS detection enables lower pesticide identification concentration since the reliable determination of the single most prominent ion is much easier than the determination of the whole mass spectrum, including the few low amplitude ions. In addition, background subtraction with clean samples is limited due to poor ion statistics.

When no prior information is available from GC with selective detection, the PFPD–MS method easily improves the MS identification concentration limit of a pesticide in a complex mixture by more than an order of magnitude. We found that precise mass spectral background subtraction enables pesticide identification at a concentration which is a factor of three lower compared with experiments without such background subtraction. The use of the NIST sequential search with two ions and one element further reduces the concentration that can be identified by another factor of two, and the sequential search with two elements and one ion is estimated by us to enable library identification at four times or more lower concentration than is enabled by background subtraction with PFPD–MS. Accordingly, we claim that the PFPD–MS method enables about an order of magnitude lower pesticide identification concentration. Admittedly, this statement is rather loosely defined and not well supported and thus future dedicated experiments will be required to establish a better quantified improvement factor. On the other hand, in pesticide analysis, the mass spectrometry identification step is the bottleneck with the lowest sensitivity in comparison with GC with any of the selective detectors, mostly due to the lack of selectivity. Thus, we hope that any improvement in this bottleneck, as demonstrated and discussed in this paper, will prove itself useful.

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