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New Approach for the Analysis of Acidic Pesticides in Water by LC/MS with a Particle Beam Interface

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A new method for the determination of 18 acidic pesticides in water by liquid chromatography/mass spectrometry is presented. A liquid–solid extraction procedure for the isolation of the pesticides from the aqueous samples was employed. The method, which avails of a micro-flow rate particle beam interface, offers improved performance for the analysis of heat-sensitive compounds such as phenoxy acid herbicides. The new technique combines the benefits of a reduced mobile-phase flow rate (1–5 μL/min) with a modified vaporization surface inside the ion source of the mass spectrometer. The electron impact ion source was covered with a Teflon layer, which has been proven to minimize compounds' decomposition and adsorption. The improved vaporization of thermally unstable substances, accomplished by the modified surface, allows a higher signal response and an accurate reproduction of the original chromatographic profile. Electron impact ionization allows almost unambiguous identification of the analytes. The liquid chromatography, carried out with a C18 packed capillary column, was optimized to allow the injection of larger sample volumes, thus improving method sensitivity for trace level pollutants. The detection limits were in the range of 0.1–1 ppb, which is a considerable improvement in the analysis of these compounds with mass spectrometric detectors.

Introduction

The widespread use of new biologically active molecules for both agricultural and industrial purposes requires very accurate and sensitive analytical methods and techniques in order to ensure a valid environmental control. Reversed-phase high-performance liquid chromatography (HPLC) offers several advantages over classical gas chromatographic (GC) methods for the analysis of heat-sensitive compounds such as phenylureas, phenoxy acids, quaternary amines, and carbamates (*1–8*).

It is also well known that the potential of many chromatographic techniques is greatly enhanced when they are coupled with mass spectrometry. Unfortunately, the advantages gained by coupling HPLC and mass spectrometry are strongly obstructed by the inherent difficulties found for the ionization of chemically fragile solutes brought in by a complex liquid mobile phase.

In the last 15 years, several attempts have been tried in this field, and some radically different brilliant ideas have provided commercially viable solutions. Among them, thermospray (TS), particle beam (PB), and electrospray (ESI) are better suited for environmental applications (*9–20*). Each of these involves a different technical approach to sample ionization and solvent removal. From a mass spectrometric point of view, the rate of fragmentation and, therefore, the extent of structural information also differ significantly. Because of the extensive and reproducible fragmentation produced, the particle beam interface, which exploits electron impact (EI) and chemical ionization (CI), supplies very informative results and often allows undoubted identification of analytes. In recent years, most of the shortcomings claimed for the particle beam interface have been the object of deep investigation. As a result of this research effort, the interface has become a reliable and effective analytical tool.

Our research group has recently designed a micro-flow rate particle beam interface for capillary liquid chromatography/mass spectrometry (*21, 22*), which allows greater sensitivity and much simpler operation procedures. The approach consisted of reducing the mobile-phase flow rate to as low as 1 μL/min in order to eliminate most of the drawbacks associated with a massive solvent intake. A specifically designed nebulizer generates a homogeneous and fine aerosol allowing consistent transfer of the solute particles and perfect reproduction of the original chromatographic profile. Enhanced sensitivity was observed especially with a high concentration of water in the mobile phase. Overall performance using gradient analyses was also improved.

The new interface was successfully employed for the analysis of basic–neutral and acidic pesticides in water samples (*23*). In that work, the analysis of the acidic pesticides showed a noticeable loss of sensitivity and chromatographic resolution compared to that offered by the basic–neutral pesticides. This may be explained by the work of Betowski et al., who gave a very interesting description of a decomposition phenomenon activated by the host surface of the ion source during the solute vaporization process (*24*). The phenoxy acid herbicides were particularly vulnerable to heat and gave unpredictable mass spectral results.

In an effort to minimize the uncertainty of our method and to improve the performance with chemically delicate compounds, we have assessed the role played by different impact surfaces inside the ion source. Betowski pointed out the importance of ion source cleanliness on the extent and severity of any compound decomposition. In a preliminary study (*25*), we presented the advantages offered by covering the particle impact surface with Teflon. We

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tested the new ion source with some phenoxy acids and other compounds, and the results obtained clearly showed a higher sensitivity and more reproducible mass spectral results. The consistent adsorption of the phenoxy acids on the ion source surface was reduced by using the modified surface, thus allowing more substance to be converted into the gas phase. Superimposition of fragment ions for close-eluting peaks was minimized with a noticeable improvement in the analysis of complex mixtures.

In this work, we have revisited and improved our method for the analysis of acidic pesticides in water by LC/PB-MS using this new technology. Five more pesticides were added to this group. The water extraction procedure was not modified. Detection limits were lowered significantly with the new ion source, and chromatographic efficiency took a great advantage with the improved vaporization. Moreover, the reoptimization of the operating conditions with the packed capillary columns allowed larger volume injections with a higher method sensitivity.

Experimental Section

Particle Beam Interface and Mass Spectrometer. All the experiments were carried out with a Hewlett-Packard 59980B particle beam unit, coupled with a Hewlett-Packard 5989A quadrupole mass spectrometer. The original nebulizer was replaced by a laboratory-made micro-flow nebulizer. This device generates a mobile-phase aerosol using flow rates as low as 1 μL/min. A 50 μm i.d., 180 μm o.d. fused silica capillary tubing (Polymicro Technologies, Phoenix, AZ) was used as the nebulizer tip and used to connect the liquid chromatograph. The nebulizing gas was helium of 5.6 purity grade (>99.9996%) and was purchased from SOL (Milano, Italy). The helium pressure needed was 70–90 psi to supply 0.1 L/min. The desolvation chamber temperature was kept at 40 °C. The operating pressures were 0.5 Torr in the desolvation chamber, 0.3 Torr in the second stage of the momentum separator, and $8-10 \times 10^{-5}$ Torr in the manifold of the ion source.

Mass spectrometer tuning and calibration were performed automatically using perfluorotributylamine (PFTBA) as a reference compound and monitoring m/z 69, 219, and 502. The repeller potential was adjusted manually.

Mobile phase was allowed into the ion source during calibration. The dwell times during selected ion monitoring (SIM) analyses were adjusted in order to obtain 0.5 cycles/s and a mean of 10 acquisition samples for each HPLC peak. Quantitation and identification criteria, when possible, were based on the detection of three characteristic ions for each test compound. The run time was divided in several ion programs in order to enhance ion response sensitivity. Table 1 shows the SIM acquisition parameters used for the analysis of the acidic pesticides. The final transfer tube, prior to the ion source, was shifted to a fully retracted position after the tuning procedure only in EI ionization mode. The electron energy was set at 70 eV in positive ion mode for all the experiments.

Ion Source. A Teflon coating was applied to the particle impact area of a conventional Hewlett-Packard ion source (*25*). The GC inlet, located on the same side of the source housing, was closed with a stainless steel plug. Because of the positive results obtained in our preliminary study, fluoroethylenepropylene (Teflon FEP) was used in this work (Teflon is a trademark of the Du Pont Company). All Teflon polymers share a similar chemical inertia, but Teflon FEP better accomplished the vaporization of acidic pesticides, although its operating temperature range (−270 to 205 °C) was lower than those of similar polymers. Teflon layers were obtained from tubings of different thickness (0.5–2 mm) purchased from Cole Parmer (Niles, IL). The tubing was cut in short pieces (1 cm), split open, and then flattened under load and by heating slightly over the specified upper temperature limit. After the flat piece was cooled, it was precisely shaped into a 7-mm disk. The disk was inserted into the ion block between a dent engraved inside the GC inlet and the stainless steel plug (Figure 1). The disk was firmly fixed by tightening the plug. The ion source plunger, which hosts the ion repeller, could still move freely between EI or CI position without interfering with the Teflon insert. Because of the very limited area covered by the polymer and its remote location, no appreciable field distortion or electrostatic charging were noticed. The ion source was kept constantly at 200 °C. No need was found for higher source temperatures.

TABLE 1

SIM Acquisition Parameters for the Analysis of 18 Acidic Pesticides

time (min)	program	compound	m/z	dwell (ms)
0	1	4-nitrophenol	109, 139	1000
22	2	2,4-dinitrophenol	154, 184	400
		dicamba	173, 175, 220	400
25.8	3	bentazone	161, 198	200
		bromoxynil	275, 277, 279	200
		MCPA	141, 200	200
		2,4-D	162, 164, 220	200
28.5	4	3,5-dichlorobenzoic acid	173, 190, 192	120
		mecoprop	107, 142, 214	120
		dichlorprop	162, 164	120
		2,4,5-T	196, 198, 254	120
		warfarin	265, 308	120
		2,4-DB	162, 164, 198	120
		MCPB	107, 142, 144	120
		2,4,5-TP	162, 196, 198	120
33.5	5	dinoseb	163, 211	250
		dinoterb	177, 225	250
		pentachlorophenol	264, 266, 268	250

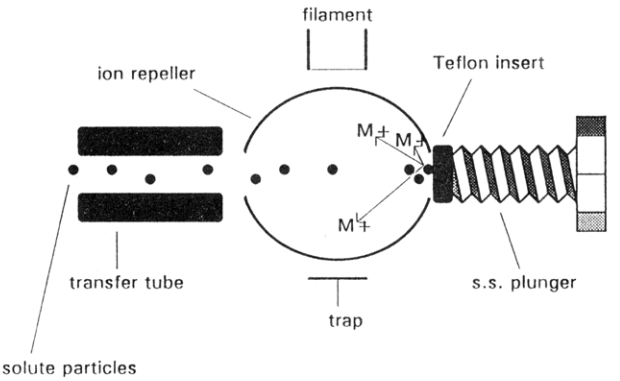

FIGURE 1. Scheme of the modified ion source with the Teflon insert.

Liquid Chromatography. Liquid chromatography was carried out with a Kontron Instrument 420 dual-pump, binary-gradient, conventional HPLC system (Kontron Instrument, Milano, Italy). Microliter flow rates were obtained with a laboratory-made splitter that was placed between the pumping system and the injector (*26*, *27*). The splitter allowed accurate and stable micro-flow rates and rapid delivery of solvent concentration changes for reliable and reproducible gradients. For sample injection, a zero-volume Valco injector, equipped with 60-nL and 0.5-μL

internal loops was employed (Valco, Houston, TX). A laboratory-made packed capillary column was used for the chromatographic separations (*28*). These columns are routinely made in our laboratory from 1/16 in. o.d., 250 μm i.d. PEEK tubing (Alltech Associates Inc., Deerfield, IL) and are packed with C18 reversed-phase 5-μm particle size purchased from Phase Sep (Queensferry, U.K.). A 25 cm long column has a mean of 20.000 theoretical plates at 1 μL/min of flow rate. Because of a favorable Van Deemter curve, only a slight loss of chromatographic efficiency is observed at higher flow rates (<5 μL/min). The column was coupled with the micro-flow nebulizer.

For the separation of phenoxy acids, a mobile phase composed of 100% water was linearly changed to 20:80 water/acetonitrile in 40 min. When loops larger than 60 nL were used, water promoted a solute focusing at the head of the column. The mobile-phase flow rate was increased up to 4 μL/min. The consequent column head pressure reached a maximum of 2240 psi during the gradient elution. A 60-nL loop was used only for concentration calibration experiments. A 0.5-μL loop was otherwise employed. A concentration of 0.05% of TFA in water and 0.025% in acetonitrile was found sufficient to suppress dissociation of the acidic pesticides. Although methanol usually gives a higher signal response using a particle beam interface, acetonitrile was preferred for its lower viscosity.

Extraction Procedure. A liquid–solid extraction procedure for the isolation of pesticides from aqueous samples was employed. A cartridge was filled with graphitized carbon black (Carbograph 1) and was capable of sampling up to 2 L of water. The extraction cartridge was made by using a polypropylene tube, 6.5 × 1.4 cm i.d., packed with 250 mg of Carbograph 1, 120–400 mesh (Alltech, Deerfield, IL). Polyethylene frits, 20 μm pore size, were located above and below the sorbent bed. Before a water sample was extracted, the cartridge was washed with 5 mL of methylene chloride/methanol (80:20 by volume) followed by 2 mL of methanol and 15 mL of 10 g/L ascorbic acid in HCl-acidified water (pH 2). Water samples were forced through the trap at a flow rate of 150–160 mL/min by using a vacuum apparatus placed below the cartridge. Distilled water (7 mL) was passed through the trap after all the sample was passed through.

Acidic pesticides were collected by percolating through the trap, drop by drop, 6 mL of methylene chloride/methanol (60:40 by volume) alkalinized with 0.016 mol/L KOH. The extract containing the acidic pesticides was acidified by adding 0.35 mL of 2% (v/v) trifluoracetic acid (TFA) in water and then concentrated to obtain a final volume of 100 μL. For a detailed discussion of the extraction procedure see ref 7.

Reagents. All solvents were HPLC grade from Farmitalia Carlo Erba (Milano, Italy) and were filtered and degassed before use. Pesticides were purchased from Riedel-De Haën (Hannover, Germany). TFA was purchased from Sigma Scientific (St. Louis, MO). Reagent water was obtained from a Milli-Q water purification system (Millipore Corp., Bedford, MA).

Results and Discussion

In Table 2, a list of selected pesticides is reported. Most of them are not suitable for GC/MS methods because of their thermal instability. On the other hand, the particle beam interface functioning is based upon vaporization of solute aggregates over a hot surface, and the compound stability has to accomplish this process. This limitation may seem serious for typical HPLC amenable compounds that are otherwise handled at near-ambient temperature, but fortunately, for the majority of the analytes of environmental interest, the heat transfer is so rapid that thermal decomposition is rarely observed. Phenoxy acids fall in the category of heat-sensitive substances for which conventional particle beam methods showed some limitations. We reported previously (*23*) that for the acidic pesticides (including phenoxy acids) chromatography efficiency was lost during ionization, with the appearance of an evident peak tailing in the mass chromatogram. Moreover, the average sensitivity was noticeably lower compared with that observed for the basic–neutral pesticides.

TABLE 2

Selected Pesticides and Their Instrument Detection Limits

pesticide	class	CAS RN[a]	ng
4-nitrophenol	phenol	100-02-7	1.5
2,4-dinitrophenol	phenol	51-28-5	4.5
dicamba	methoxybenzoic	1918-00-9	4.5
bentazone	thiadiazinone	25057-89-0	0.7
2,4-D	phenoxy acid	94-75-7	5.0
MCPA	phenoxy acid	94-74-6	2.1
bromoxynil	phenol	1689-84-5	0.6
3,5-dichlorbenzoic acid	phenoxy acid	51-36-5	0.7
mecoprop	phenoxy acid	7085-19-0	3.0
dichlorprop	phenoxy acid	120-36-5	1.5
2,4,5-T	phenoxy acid	93-76-5	4.5
warfarin	coumarin	81-81-2	5.0
2,4-DB	phenoxy acid	94-82-6	0.7
MCPB	phenoxy acid	94-81-5	1.5
2,4,5-TP	phenoxy acid	93-72-1	1.5
dinoseb	phenol	88-85-7	1.5
dinoterb	phenol	1420-07-1	1.5
pentachlorophenol	phenol	608-93-5	0.7

[a] Chemical Abstracts Service registry number.

In trying to improve this method, we noticed a consistent adsorption of all phenoxy acids on the source surface that was only partially relieved at higher temperature. This phenomenon led to significant memory effect, noticeable as a slowly fading mass spectral background after every injection. The background signal was considerably strengthened by any substance subsequently injected into the system, resulting in a superimposition of different mass spectra. In other words, the impact of new solute particles strips aliquots of the adsorbed compound from the source surface to the gas phase, thus involving them in a new ionization process. This drawback was particularly troublesome when performing gradient analyses of complex mixtures of acidic pesticides with a multitude of near-eluting compounds. Each component gave a mass spectrum that was influenced by the preceding compound.

Coating the ion source surface with a Teflon polymer has consistently improved the mass spectral and chromatographic results by minimizing the adsorption of the analytes and, therefore, reducing the chance of multiple ionization. Figure 2 shows the m/z 198 ion profile, characteristic only of bentazone, extracted from a SIM analysis of a mixture of three acidic pesticides. Figure 2a shows the three adjacent peaks relative to a chromatogram obtained with a conventional ion source. The first and most intense peak comes from bentazone, while the last two originate from the same compound released when the target surface is hit by the two other compounds, MCPA

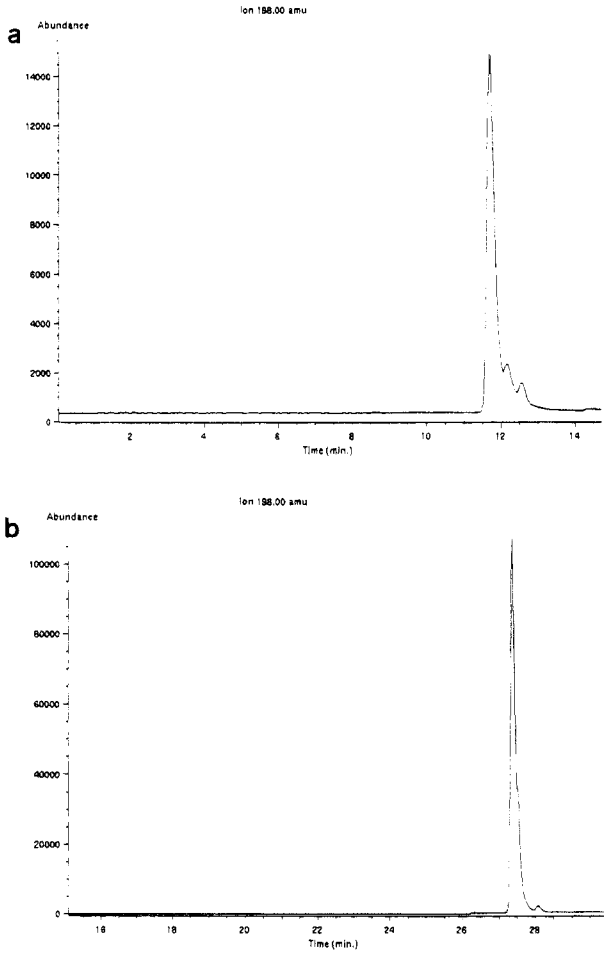

FIGURE 2. *m/z* 198 ion profile relative to the separation of bentazone, MCPA, and bromoxynil obtained with a conventional ion source (a) and with a Teflon-modified ion source (b).

and bromoxynil, neither of which has m/z 198 in its mass spectrum. Figure 2b reports the same analysis performed with the modified ion source. Alien signals are almost totally suppressed, and peak tailing is consistently reduced. The shift in the retention time is due to a different solvent program.

As stated previously, the micro-flow nebulizer largely contributes to the improved performance of the particle beam interface. Several aspects benefit from the scaled-down liquid intake, allowing a better and easier utilization of the interface. The reduced size of the solute particles generated by the micro-flow nebulizer offers a higher and more favorable surface to mass ratio. Under these conditions, the solute vaporization occurs faster, with less chance of thermal decomposition. At the same time, reliable and efficient capillary columns are able to resolve very complex mixtures. The injection volume of these columns is limited by the very low operating mobile-phase flow rate. At 1 μL/min, the correct injection volume does not normally exceed 100 nL, while 60 nL is the rule at the present time. A larger volume usually leads to a consistent loss of chromatographic efficiency and distorted peaks. A 60-nL injection is consistent with very small samples but represents a severe limitation for low concentrated samples. For this reason, even the good instrument sensitivity, accomplished by the new interface, can be insufficient for real sample extracts. In this work, we have developed a balanced modification of mobile-phase composition and flow rate in order to efficiently transfer larger loop volumes

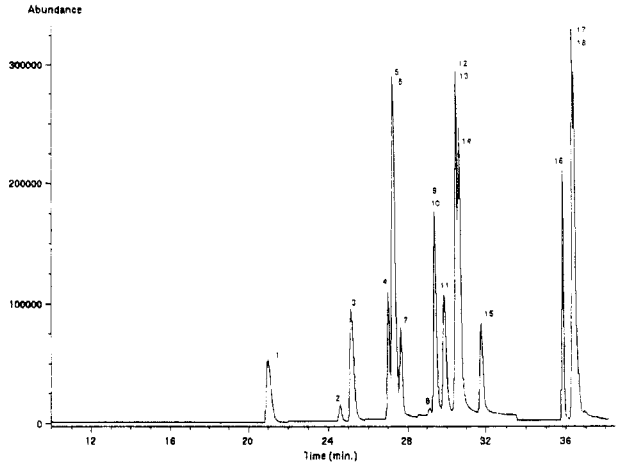

FIGURE 3. Reconstructed ion chromatogram relative to the separation of a standard solution of 18 acidic pesticides: (1) 4-nitrophenol, (2) 2,4-dinitrophenol, (3) dicamba, (4) bentazone, (5) 2,4-D, (6) MCPA, (7) bromoxynil, (8) 3,5-dichlorobenzoic acid, (9) mecoprop, (10) dichlorprop, (11) 2,4,5-T, (12) warfarin, (13) 2,4-DB, (14) MCPB, (15) 2,4,5-TP, (16) dinoseb, (17) dinoterb, and (18) pentachlorophenol.

(<1 μL) to the chromatographic column. The mobile-phase flow rate was increased 4-fold (up to 4 μL/min) with an upper pressure limit of 2500 psi. The higher flow rate was required to speed up the transfer of larger sample volumes to the head of the column. An initial mobile phase composition of 100% water focused the sample and limited the band spreading to a minimum. The solvent composition was then linearly changed to 20:80 water/acetonitrile in 40 min for the best separation of the 18 components. This procedure is feasible because of the superior performance of the micro-flow interface with a high concentration of water in the mobile phase. The new interface can tolerate a much wider choice of solvents and buffers, offering an easier approach to the convenient chromatographic requirements (*22*). Moreover, the optimization of some crucial nebulizer parameters is better accomplished by the new interface. Gas pressure and nebulizer position fine tuning are not influenced by a changing solvent composition or with different analytes, thus eliminating tedious optimization procedures. Such characteristics allow the maximum response for all the components of the mixture.

Figure 3 shows the reconstructed ion chromatogram obtained from a standard solution of the 18 acidic pesticides. A list of the eluted compounds is reported in Table 2. Two- or three-ion detection for each compound ensures undoubted identification even for co-eluted pesticides. The amount injected was between 120 and 500 ng for each compound. The injection was performed using a 0.5-μL loop, 2 min after the gradient was started. This procedure takes into account the delay between the electronic start of the gradient ramp and the effective modification of the solvent concentration perceived by the column. The improvement in the pesticides separation is clearly shown in the figure. Most of the peaks are much better resolved, and the tailing is no longer present.

A concentration calibration and an evaluation of the results reproducibility using the new method were performed. Bentazone, 2,4-DB, and pentachlorophenol (respectively a thiadiazinone, a phenoxy acid, and a phenol) were chosen for the test. A given amount of each pesticide was injected five times for each concentration. The concentration range was kept sufficiently wide to fit most trace analysis applications, and the lowest value was chosen

close to the detection limit. Each sample was introduced directly into the mass spectrometer without the column via the particle beam interface (flow injection) with a mobile phase composed of equal concentration of water and acetonitrile. TFA was added to the mobile phase. The use of buffers, as pointed out by Bellar and co-workers (*29, 30*), improves the transport of the solute particles throughout the interface and may extend response linearity toward lower concentration of the analyte. Linear regression plots for the concentration calibration data and correlation coefficients were calculated as follows: $y = 17.56x - 36.16$ (0.9936) for 2,4-DB; $y = 17.04x - 5.47$ (0.9989) for pentachlorophenol; $y = 52.81x - 101.64$ (0.9962) for bentazone. The mean standard deviations calculated using the average of all peak area values for each concentration experiment are 12.66% for bentazone, 17.99% for 2,4-DB, and 5.16% for pentachlorophenol. The mass spectrometer was operating in SIM at m/z 198 for bentazone, m/z 162 for 2,4-DB, and m/z 266 for pentachlorophenol. A 60-nL loop was used instead of a larger one for the calibration experiments. This choice was motivated by the fact that test samples were injected without the column, and no band focusing was thus achieved. The mobile-phase flow rate was kept at 2 μL/min for all the calibration experiments. Excellent linearity can be observed in all calibration plots even at the lowest concentrations. It is important to point out that with this method the response linearity is extended over a wide range of concentrations (up to 30 ng). These results are comparable with respect to other LC/MS coupling techniques used in environmental applications (i.e., thermospray, ESI, API).

Detection limits for the analytes considered in this work were evaluated injecting dilute solutions of each compound in operative chromatographic conditions using the column and a larger injection loop (0.5 μL). The mass spectrometer was operating in the SIM mode according to specific programs made considering two or three characteristic ions for each compound. The dwell time was adjusted in order to record 10 acquisition samples for each chromatographic peak. The lowest amount was calculated for a signal-to-noise ratio of 5:1 for the TIC peak. Table 2 reports the instrument detection limits for the acidic pesticides considered. An overall improvement of the instrument sensitivity with respect to the previous method is observed. In particular, phenoxy acids such as MCPA and 2,4,5-T had their detection limits lowered from 40 to 2.1 and 4.5 ng, respectively. The new material in the ion source reduced the amount of substance subtracted from the ionization process, increasing sensitivity particularly at very low concentrations. The use of a larger loop also contributed to improve the method detection limits by a factor of 8. Assuming a 100% extraction recovery for all pesticides from a 2-L water sample and with a concentration factor of 20 000, the instrument detection limits correspond to a method detection limit of 0.1−1 ppb. This range satisfies the detection requirements for environmental pollutants in water and wastewater. Actual recoveries for most pesticides are reported in ref 7.

A water sample from a river near Urbino was spiked with 4 μg of MCPA and 2,4,5-T. The compounds were dissolved in 50 μL of methanol and then dispersed in 1 L of filtered river water, obtaining a final concentration of 4 ppb. Blank extraction of the same river water was also performed. Figure 4 reports the ion profiles for the analysis of MCPA in the spiked water. Figure 5 shows the analysis

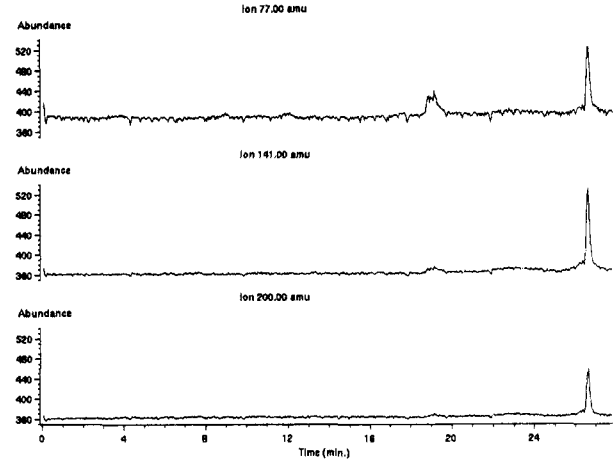

FIGURE 4. Ion profiles relative to MCPA in the spiked sample.

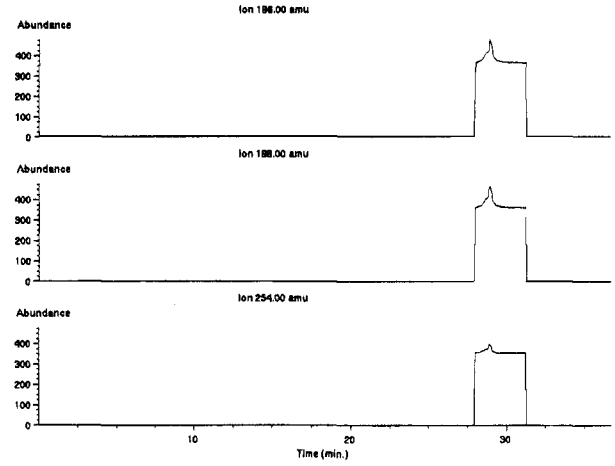

FIGURE 5. Ion profiles relative to 2,4,5-T in the spiked sample.

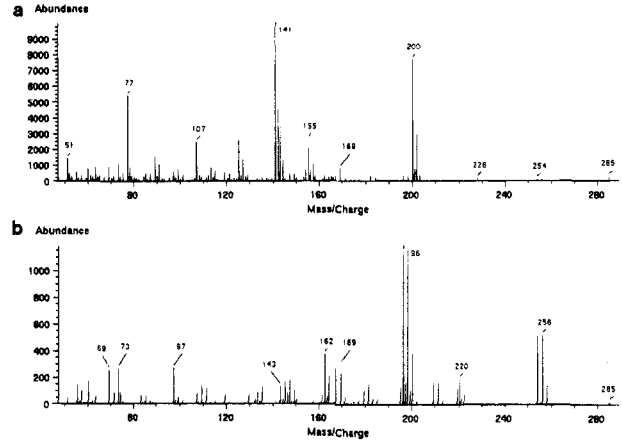

FIGURE 6. Mass spectrum of MCPA (a) and 2,4,5-T (b).

of 2,4,5-T in the same sample. A specific SIM program was used for the two substances. The concentration was calculated comparing the total ion current (TIC) peak area of the sample with that obtained injecting a 67 ppm standard solution. Figure 6 reports the mass spectra relative to the two compounds acquired separately with the particle beam interface. The peak abundances in the ion profiles match the relative abundances of the corresponding ions in the respective mass spectrum.

In summary, this work demonstrates the existence of a wide margin of further developments for LC/MS techniques in general and for the particle beam interface in particular. The innovations discussed in this paper suggest a valid and

more competitive role of the particle beam interface in the analysis of environmental pollutants at trace levels. Conventional electron impact mass spectra for almost undoubted identification of the analytes and a more reliable and easier use of the interface with thermally sensitive compounds are the highlights of this method.

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