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## High-performance liquid chromatography coupled with mass spectrometry applied to analyses of pesticides in water. Results obtained in HPLC/MS/APCI in positive mode

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**Abstract.** Determinations of pesticides and their degradation products in natural waters, given the great heterogeneity of the substances involved, conventionally demands the use of the following analytical methods:

- gas chromatography with different specific detectors such as the electron capture detector, NPD thermo-ionic detector, and mass spectrometry,
- high-performance liquid chromatography combined with a diode array ultraviolet detector or a spectrofluorimeter after derivatization,
- thin-layer chromatography (TLC) with detection of the isolated substances by UV.

With liquid chromatography, the most widely used detector is the diode-array UV detector. This method, recommended in French standard AFNOR T 90 123 (EN ISO 11369) [1], represents a significant advance in the approach to the identification of polar substances detected in unknown samples, compared with the results obtained by UV detection with a single wavelength. However, this method of detection does not guarantee the identification of the detected substances in absolute terms. Confirmation on a second column or by gas chromatography is therefore necessary.

The atmospheric interfaces equipped with APCI (Atmospheric Pressure Chemical Ionization) or ESI (Electrospray Ionization) ion sources help to broaden the field of application of the couplings of liquid chromatography with mass spectrometry, and have seen substantial developments in recent years [2–4]. They offer performance in agreement with environmental requirements in terms of quantification limits, sensitivity, simplicity of use and reliability [5]. They are accordingly suitable for the identification and quantification of pesticides and their conversion products in waters [6,7].

This article presents a summary of the results obtained on surface waters with the APCI interface in positive ionization mode, after extraction of the pesticides at neutral pH. The analyses were performed as part of a multi-residue approach applied to a priority list of 40 pesticides to be determined in the surface waters of the Centre region of France.

In addition to high-performance liquid chromatography combined with the diode array UV detector and coupled with mass spectrometry, gas chromatography coupled with mass spectrometry was used as a technical complement, because of its suitability for apolar substances such as lindane, organochlorinated pesticides, certain organophosphorus pesticides, trifluraline etc.

For the other substances investigated, such as triazines and some of their degradation products, phenylureas, triazoles, amides and carbamates, high-performance liquid chromatography coupled in series with a UV detector and a mass spectrometer was employed. The results obtained with the diode array UV detector were compared with those obtained with the mass spectrometer in order to validate the results obtained with the latter detector.

Acquisition and quantification methods optimized for HPLC/MS with APCI interface in positive ionization mode are presented in the article.

Results on samples of surface waters with preconcentration following the liquid/liquid or liquid/solid methods are described. The analytical approach is set for: preconcentration methods, HPLC/MS acquisition parameters, quantification methods, practical limits of quantification, and identification.

**Key words.** HPLC – mass spectrometry – atmospheric interface – APCI – pesticides – waters.

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## Introduction

The need to analyse waters in order to identify and quantify a growing number of pesticides and their conversion products, which are generally thermolabile, non-volatile and exhibit medium to high polarity, raises the question of the reliability of the instrumental methods currently used for their analysis. The analytical methods routinely used to determine these substances in waters employ gas chromatography, either in combination with specific detectors (ECD, electron capture detector; NPD, thermo-ionic detector) or coupled with mass spectrometry or thin-layer chromatography (TLC). Capillary electrophoresis with UV detection was also tested recently in this field.

High-performance liquid chromatography combined with a diode array UV detector has been established in the laboratories in recent years as the complementary technique to gas chromatography to analyse these substances. However, the only UV spectrum used as a means of identification proved to be insufficient, justifying the advantage of coupling mass spectrometry with liquid chromatography, the only device potentially capable of identifying the substances detected.

In the recent past, these couplings made with “particle beam” and “thermospray” type interfaces, aroused little interest in environmental analyses, due to their lack of sensitivity and the insufficient number of substances analysable by these methods, as compared with gas chromatography coupled with mass spectrometry.

The atmospheric interfaces (APCI, Atmospheric Pressure Chemical Ionization, and Electrospray), which have appeared in recent years, serve on the contrary to broaden considerably the field of substances to be analysed by liquid chromatography coupled with mass spectrometry, with a sensitivity in agreement with the requirements of the European Union for water analyses [8,9].

An increasing number of publications of results of investigations conducted with these couplings using atmospheric interfaces, illustrate the large potential of this technique combined upstream with liquid/solid preconcentration methods, in-line or off-line [10–15]. Results obtained with this coupling in connection with a study on the surface waters of the Centre region in France and dealing with a portion of the 40 pesticides or conversion products selected in accordance with the criteria of an approach inspired by CORPEN<sup>1</sup> [16] are presented here.

## Materials and methods

### ***Review of the operating principle of the atmospheric interfaces used in HPLC/MS coupling***

#### ***APCI (Atmospheric Pressure Chemical Ionization) interface***

The general operating principle of this interface is based on the pneumatic nebulization and the vaporization of the

mobile HPLC phase followed by ionization of the substances in solution by Corona discharge. The production mechanisms of the ions involved in the process are of various types.

- (1) Pneumatic and thermal for the nebulization and desolvation of the mobile phase.
- (2) Electrostatic for the ionization of the substances extracted: the Corona current measures a few  $\mu\text{A}$ , and the Corona discharge voltage is 2 to 5 kV.

The main characteristics of this ionization mode are the following:

- it is a mild ionization mode with possible degradation of the most thermolabile compounds (the temperature of the vaporizer is between 400 and 450 °C),
- it is compatible with the standard flow rates of liquid chromatography (2 mL/min),
- the analytes or the mobile phase must have good proton affinity,
- the mass spectrum mainly contains the molecular ion with possible formation of adducts (combination with one of the mobile phase components): there is little fragmentation.

#### ***ESI (Electrospray Ionization) interface***

The general principle is based on a spraying of the mobile phase combined with ionic evaporation. This causes the:

- formation of charged liquid droplets,
- reduction in the size of the charged droplets by evaporation/disintegration (Rayleigh instability limit) up to the ionized species directly transferable in the quadrupole.

The main characteristics of this ionization mode are as follows:

- no degradation of thermolabile compounds,
- need to operate at eluent phase flow rates of about 200  $\mu\text{L}/\text{min}$ ,
- suitability for polar and non-volatile products,
- the mass spectrum mainly contains the molecular ion: there is practically no fragmentation.

### ***Field of application of atmospheric interfaces in HPLC/MS coupling***

The choice of the atmospheric interface associated with that of the chromatographic mobile phase is dictated by the polarity of the substances to be analysed, and by the positive or negative character of the ions formed in the chromatographic conditions applied.

The main applications of atmospheric interfaces in the analysis of pesticides can be summarized as follows.

<sup>1</sup> CORPEN: Comité d'Orientation pour la Réduction de la Pollution des Eaux par les Nitrates, les phosphates et les produits phytosanitaires.

## (1) APCI interface

The signal is acquired:

- on the positive ions for the following families: organophosphorus [17], triazoles, triazines, amides, phenylureas, carbamates, morpholines,
- on the negative ions for: phenoxyalkanoics, chlorophenols, sulphonylureas.

## (2) Electrospray interface

The signal is acquired:

- on the positive ions for the following families: triazines, some phenylureas, hydroxylated derivatives of atrazine,
- on the negative ions for the following families: acidic substances (phenoxyalkanoics, nitrophenols, benzotriazoles), metabolites of amides (alachlore).

**Instrumentation and columns**

The HPLC/UV/MS chromatography circuit has the following components:

- Varian 9012 elution gradient pump,
- Varian 9100 automatic sample passer,
- Varian Polychrom 9065 diode array UV detector,
- computerized control station equipped with Varian LC-STAR software,
- Finnigan SSQ 7000 mass spectrometer with APCI (Atmospheric Pressure Chemical Ionization) placed downstream of the UV detector cell, controlled by the ICIS software.

The chromatography columns used are packed with silica grafted with LC-ABZ type amide groups (Supelco), or silica grafted with Kromasil (Touzart and Matignon) type 18-carbon groups, separating the compounds by reverse phase partition chromatography:

- length: 250 mm
- inside diameter: 4.6 mm
- particle size: 5  $\mu\text{m}$ .

A retaining column packed with silica grafted with LC-ABZ (Sigma Aldrich Supelco) type amide groups or Kromasil (Touzart et Matignon) type 18-carbon groups is placed in front of the chromatographic column. The only examples presented here are those concerning substances extractable at neutral pH and analysable by HPLC/MS with the APCI interface in positive ionization mode.

**Chromatography**

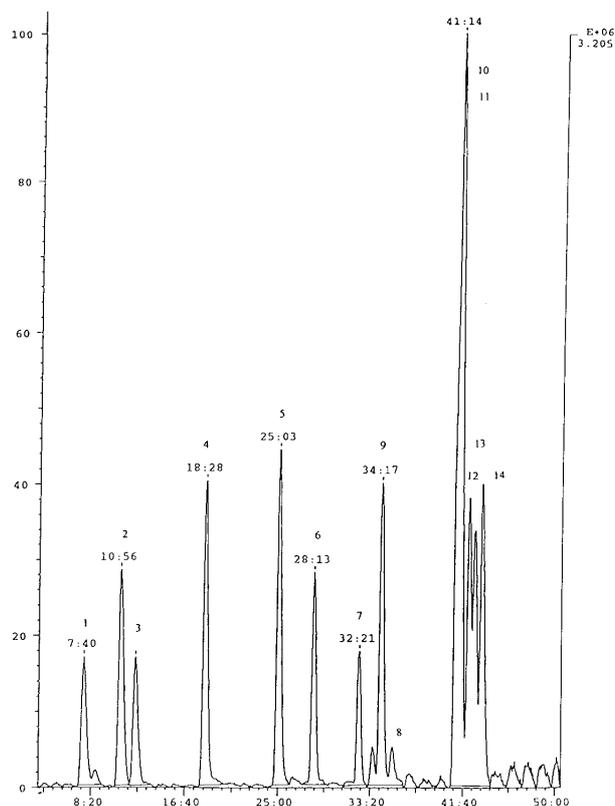
time (min)	% water	% acetonitrile
0	85	15
50	40	60
70	0	100
80	0	100
85	85	15

Flow rate of the mobile phase: 1 mL/min.

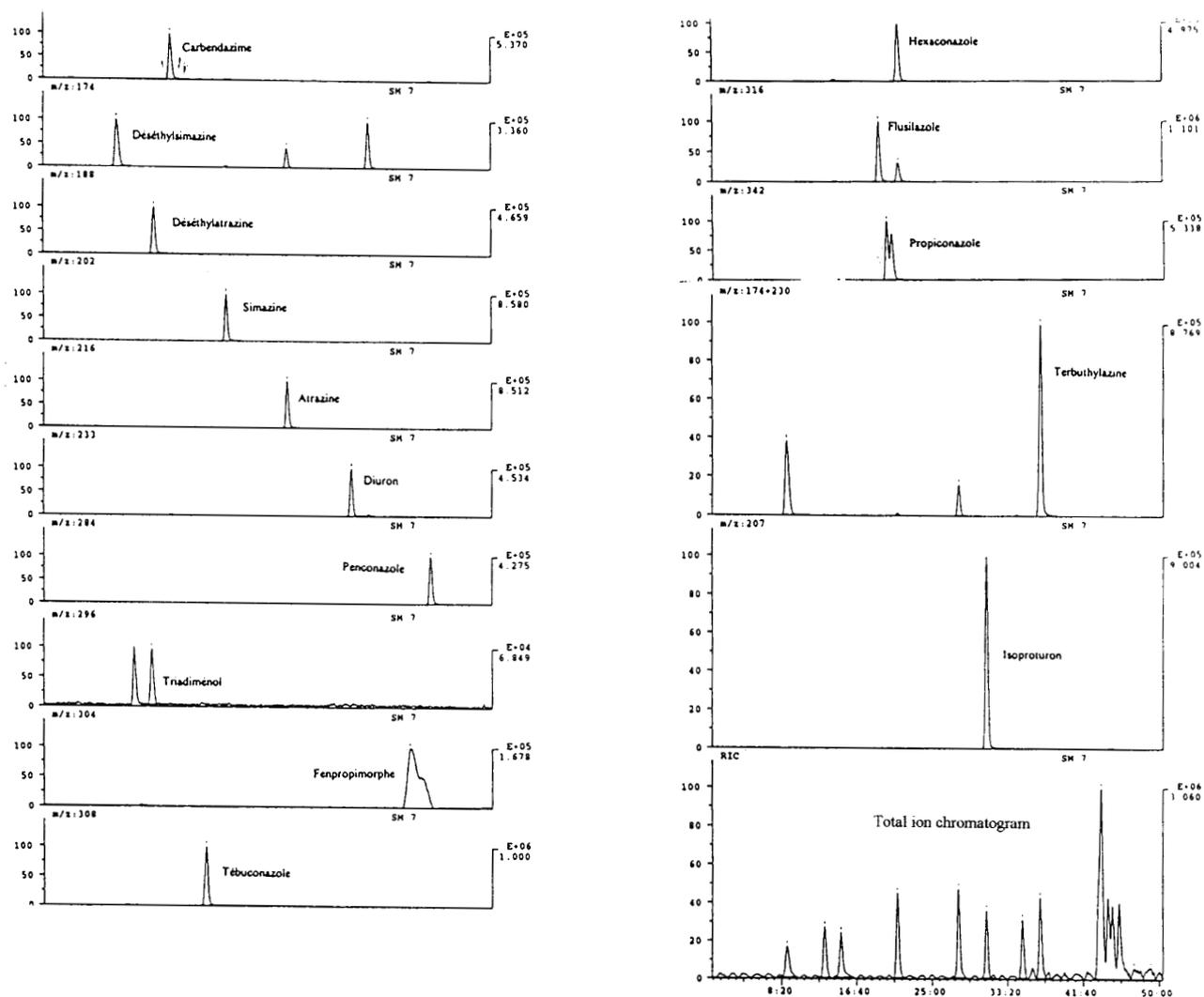
Volume injected: 20  $\mu\text{L}$ .

**Detection**

- (a) Diode array UV detector: scan from 190 to 360 nm.  
 (b) Mass spectrometry: APCI source.



**Fig. 1.** Total ion chromatogram of the selected pesticides obtained by HPLC/APCI/MS by injecting 20  $\mu\text{L}$  of a standard mixture solution containing the selected pesticides at a level of 5  $\mu\text{g/mL}$  each in acetonitrile. Peak numbering: 1. Desethylsimazine, 2. Desethylatrazine, 3. Carbendazime, 4. Simazine, 5. Atrazine, 6. Isoproturon, 7. Diuron, 8. Triadimenol, 9. Terbutylazine, 10. Tebuconazole, 11. Penconazole, 12. Flusilazole, 13. Propiconazole, 14. Hexaconazole.



**Fig. 2.** Extracted ion chromatograms corresponding to characteristic  $m/z$  of the selected pesticides using HPLC/APCI/MS from a 20  $\mu\text{L}$  injection of a standard solution mixture containing the pesticides at a level of 5  $\mu\text{g/mL}$  in acetonitrile.

Corona discharge: 5  $\mu\text{A}$ ,  
 Vaporizer temperature: 400  $^{\circ}\text{C}$ ,  
 Temperature of heated capillary: 225  $^{\circ}\text{C}$ ,  
 Buffer gas pressure of nebulizer: 70 lb/in<sup>2</sup>,  
 Mass range: 100 to 450 uma,  
 Scan time: 1 s,  
 Voltage applied to electron multiplier: 1750 V,  
 Collision voltage on octapole: +5 V,  
 Acquisition mode: signal acquired in total ionic current on positive ions in the range 100 to 400 uma.

## Calibration

Calibration solutions are made from fifteen different substances with certified purity, by dilution in methanol or acetonitrile. All of them were from Cluzeau Info Labo (Ste Foy

la grande France) The concentration interval of the calibration solutions ranges from 0.02 to 10  $\mu\text{g/mL}$  in the solvent.

The fifteen following substances belonging to the regional list and including some 40 pesticides extractable at neutral pH are analysable by HPLC/MS with the APCI interface in positive ionization mode.

<i>chemical family</i>	<i>substance</i>
triazines	atrazine, simazine, terbuthylazine, deséthylatrazine, deséthylsimazine
phenylureas	isoproturon, diuron, chlortoluron
triazoles	flusilazole, hexaconazole, tebuconazole, penconazole, propiconazole, triadimenol
benzimidazoles	carbendazime
morpholines	fenpropimorph

**Table I.** Calibration data obtained with HPLC/APCI/MS in a range 0.05 – 10 ng/μL in acetonitrile solution: – under full scan mode and signal determination on extracted ion chromatograms corresponding to characteristic  $m/z$  – and in SIM mode, for the studied pesticides after liquid-liquid extraction of 1 liter of sample with dichloromethane or 0.5 liter by solid phase extraction on 0.5 g C<sub>18</sub> silica cartridge.

Substances	$m/z$	$r^2$	equation $y = bx + c$ in TIC mode	TIC LOQ in μg/L	SIM LOQ in μg/L
<b>1. Regional priority list substances:</b>					
<i>Desethylsimazine</i>	174	0.9996	$y = 897.57 x - 29713$	0.02	0.005
<i>Desethylatrazine</i>	188	0.9996	$y = 1216.9 x - 41428$	0.02	0.005
<i>Simazine</i>	202	1.0	$y = 1876.3 x + 2565.4$	0.02	0.005
<i>Atrazine</i>	216	0.9999	$y = 1835.7 x - 621.8$	0.02	0.005
<i>Carbendazime</i>	134+192	0.9993	$y = 1392.9 x + 45114$	0.05	0.01
<i>Methabenzthiazuron</i>	222	0.9997	$y = 926.79 x - 31858$	0.02	0.005
<i>Chlortoluron</i>	213	0.9997	$y = 613.54 x - 19121$	0.05	0.005
<i>Isoproturon</i>	207	0.9999	$y = 2072.8 x + 11786$	0.02	0.005
<i>Diuron</i>	233	0.9997	$y = 950.14 x + 25721$	0.02	0.005
<i>Terbuthylazine</i>	174+230	0.9999	$y = 2336.7 x + 5776.4$	0.02	0.005
<i>Fenpropimorph</i>	304	0.9998	$y = 1685.3 x - 60691$	0.02	0.005
<i>Flusilazole</i>	316	0.9998	$y = 2291.2 x + 97243$	0.02	0.01
<i>Penconazole</i>	284	0.9992	$y = 1055.9 x + 48908$	0.02	0.005
<i>Propiconazole</i>	342	0.9997	$y = 1716.1 x + 123970$	0.02	0.005
<i>Tébuconazole</i>	308	0.9999	$y = 2202.9 x + 63778$	0.02	0.005
<i>Triadimenol</i>	296	0.9987	$y = 267.51 x + 19556$	0.1	0.05
<i>Hexaconazole</i>	314	0.9994	$y = 1087.9 x + 107785$	0.02	0.005
<b>2. Other substances:</b>					
<i>Tébutame</i>	234	0.9998	$y = 1237 x + 2707.6$	0.02	0.005
<i>Diflufenicanil</i>	395	0.9997	$y = 617.28 x - 4978.8$	0.03	0.01
<i>Napropamide</i>	272	0.9997	$y = 679.48 x + 19894$	0.02	0.005
<i>Métazachlore</i>	178+210	0.9992	$y = 444.98 x + 15651$	0.03	0.01

An example of chromatographic separation using the LC-ABZ column, in the above operating conditions and carried out on a calibration solution, is shown in figure 1.

HPLC grade acetonitrile and methanol, dichloromethane for pesticides residues analysis were obtained from Carlo Erba (Romilly sur Andelle, France). HPLC grade water was obtained from BDH (Merck, France).

## Preconcentration

### Preconcentration by liquid/liquid extraction

The liquid-liquid extraction with dichloromethane was chosen for the majority of the substances studied in the surface water samples due to the efficiency of this extraction method for a large number of these substances and the high level of the suspended materials present in these waters.

One litre of each sample is extracted at neutral pH by three times 60 mL dichloromethane and then concentrated

in the rotary evaporator and under nitrogen jet, and transferred to 0.5 mL acetonitrile for HPLC analyses.

### Liquid/solid (or SPE) preconcentration

Various media are used in liquid/solid extraction mode: the extraction cartridges are packed with silica grafted with C<sub>18</sub> octadecyl groups, and porous polymers, such as vinylbenzene/divinylbenzene copolymer, are used [18]. This extraction mode with C<sub>18</sub> cartridges is more suitable for the degradation products of atrazine and carbendazime in particular. It has been used for this study as followed.

#### Preconcentration at neutral pH on cartridges packed with 0.5 g C<sub>18</sub>-grafted phase (Supelco)

Cartridge conditioning:

- cause 6 mL of ethanol to percolate at a rate of 10 mL/min followed by 10 mL of de-ionized water.

Sample preconcentration:

- take 500 mL of water sample,

**Table II.** HPLC/APCI/MS mass spectra repeatability ( $n = 5$ ) for three substances obtained by collision ion-induced (CID) reactions under a 5 Volts octapole voltage.

Substances	Fragment masses	Relative abundances (%)		Complementary informations (adducts with acetonitrile)
		mean	cv (%)	
Terbutylazine (Base peak: 230)	230	100		271
	174	65	2.2	215
	176	20.4	8.2	
	232	35.2	5.5	
Carbendazime (Base peak: 134)	134	100		175
	192	90.2	2.9	233
	193	12	8.6	
Cyanazine (Base peak: 241)	160	67.4	4.9	201
	241	100	282	
	214	51.6	3.2	255
	216	16	9.9	
	242	12	11.8	
	243	34.2	7.6	

**Table III.** Recovery percentages obtained using the liquid-liquid method and the liquid-solid method for extraction of the selected pesticides and metabolites from one liter (LLE) and 0.5 liter (SPE) of surface water spiked with 0.5  $\mu\text{g/L}$  of each pesticide (1).

Substances	Extraction method	Recovery %
Atrazine	LLE	83.2 (9)
Simazine	LLE	92 (3)
Terbutylazine	LLE	92.7 (7.2)
Cyanazine	LLE	69.8 (10.5)
Desethylatrazine DEA	SPE	97.7 (2.3)
Deisopropylatrazine DIA	SPE	67 (3)
Isoproturon	LLE	88.3 (4.7)
Diuron	LLE	90.3 (3.8)
Chlortoluron	LLE	89.2 (4.1)
Flusilazole	LLE	96 (2.6)
Tebuconazole	LLE	92.2 (4.5)
Penconazole	LLE	88.6 (3.6)
Hexaconazole	LLE	89.4 (2.9)
Triadimenol	LLE	84.5 (5.6)
Tridemorph	LLE	82.8 (9.4)
Carbendazime	SPE	70.5 (4)

(1) Standard deviations (three replicates) are given in brackets.  
LLE: Liquid-liquid extraction.  
SPE: Liquid-solid extraction.

- check the pH: this must lie range between 6.5 and 7.5,
- cause 500 mL of water to percolate on the extraction cartridge at about 10 mL/min,
- dry the cartridge under vacuum for at least 10 min.

Elution of compounds fixed on the cartridge:

- add 2 mL of methanol, leave in contact for 2 min,
- cause to percolate at about 2 mL/min without going to dryness,
- collect the eluate in a 10 mL tube,
- repeat the operation with 2 mL of methanol

Concentrate the methanol extract by slow evaporation under nitrogen jet to a volume of 0.5 mL. This fraction can be analysed by HPLC/UV/APCI/MS.

The recovery percentages obtained using these two above extraction methods are given in the table IV.

## Results and discussion

### Calibration

The calibration curves obtained show very good response linearity on the signal of the ionic current extracted on the specific  $m/z$  ions of each substance (Fig. 2), in a wide range of concentrations (0.025 to 10  $\mu\text{g/mL}$ ).

The results are given in table I with the  $m/z$  values used for the quantification, the calibration equations and the correlation coefficients for each compound, the LOQ's in SIM and CIT modes.

### Sensitivity and quantification limits

The response sensitivities are affected by the ionization yield of the substances analysed in the instrumental conditions given above. They vary by a factor of 4, from the least sensitive substance (chlortoluron) to the most sensitive group including terbutylazine.

The practical quantification limits, determined by the signal corresponding to ten times the background noise on the chromatograms extracted on the specific ions of the substances investigated, range from 0.02 to 0.1  $\mu\text{g/L}$  in total ionic current. In single ion mode (SIM), the practical quantification limits are improved by a factor of 5 (Tab. II).

Diuron displays a better response sensitivity in negative ionization mode by HPLC/APCI/MS [19].

### Mass spectra

The mass spectra essentially show a pattern with the protonated molecular ion  $(M+H)^+$ , sometimes accompanied by the cluster ion with acetonitrile  $(M+CH_3CN)^+$  or  $(M+41)^+$ . This route of ionisation can be related with the high proton affinity of these compounds. Some substances undergo

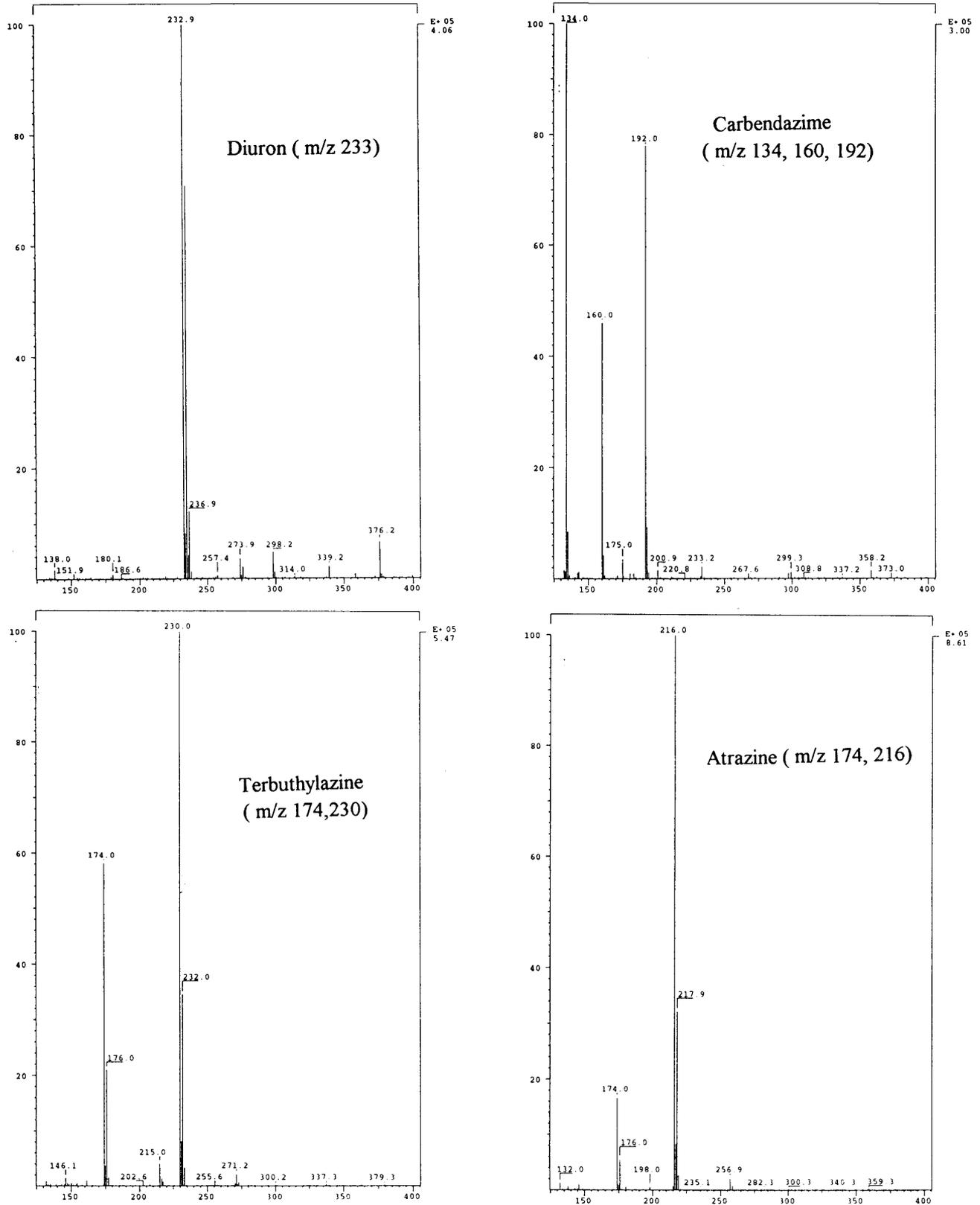


Fig. 3. Full scan HPLC/APCI/MS mass spectra of four substances obtained by applying a 5 volts CID voltage on the octapole.

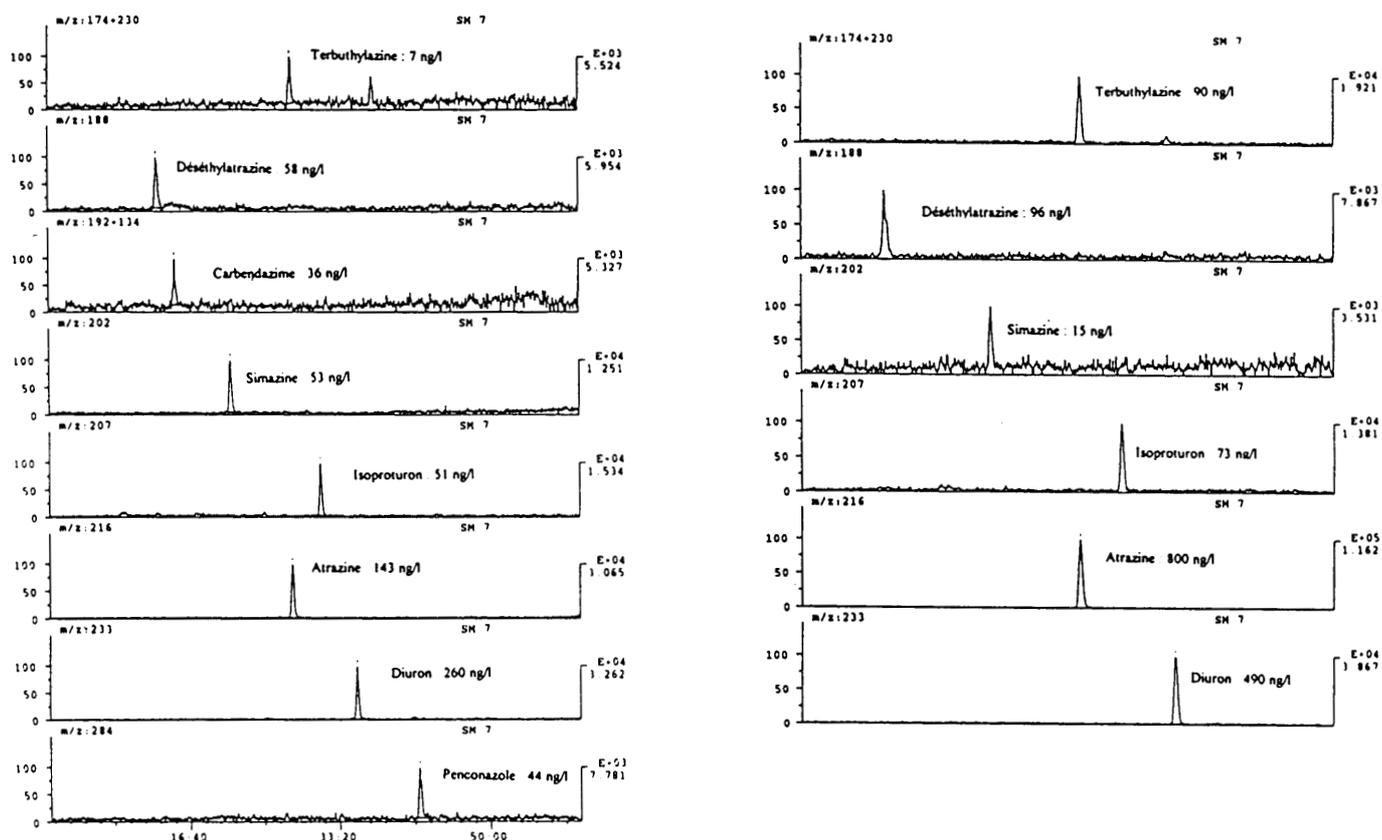


Fig. 4. Extracted ion chromatograms isolated at different  $m/z$  from two surface water samples using HPLC/APCI/MS under full scan mode.

fragmentation despite the mild ionization conditions. This is the case of carbendazime, atrazine, terbuthylazine, while others, like diuron, contain only the protonated molecular ion and the adduct (Fig. 3). The fragmentation can be accentuated by imposing a potential of a few dozen volts on the input octapole, thus generating fragmentations by collision. The repeatability of the mass spectra acquired in identical experimental conditions was confirmed (Tab. II), demonstrating the feasibility of the compilation of a library of reference spectra usable to identify the substances detected.

HPLC-APCI-MS has high potential as an identification method. Structural information is generated in the mass spectrum from the protonated molecule, the adducts and the fragments obtained by collision. The main limit for an unequivocal elucidation of some compounds is the insufficient fragmentation [20].

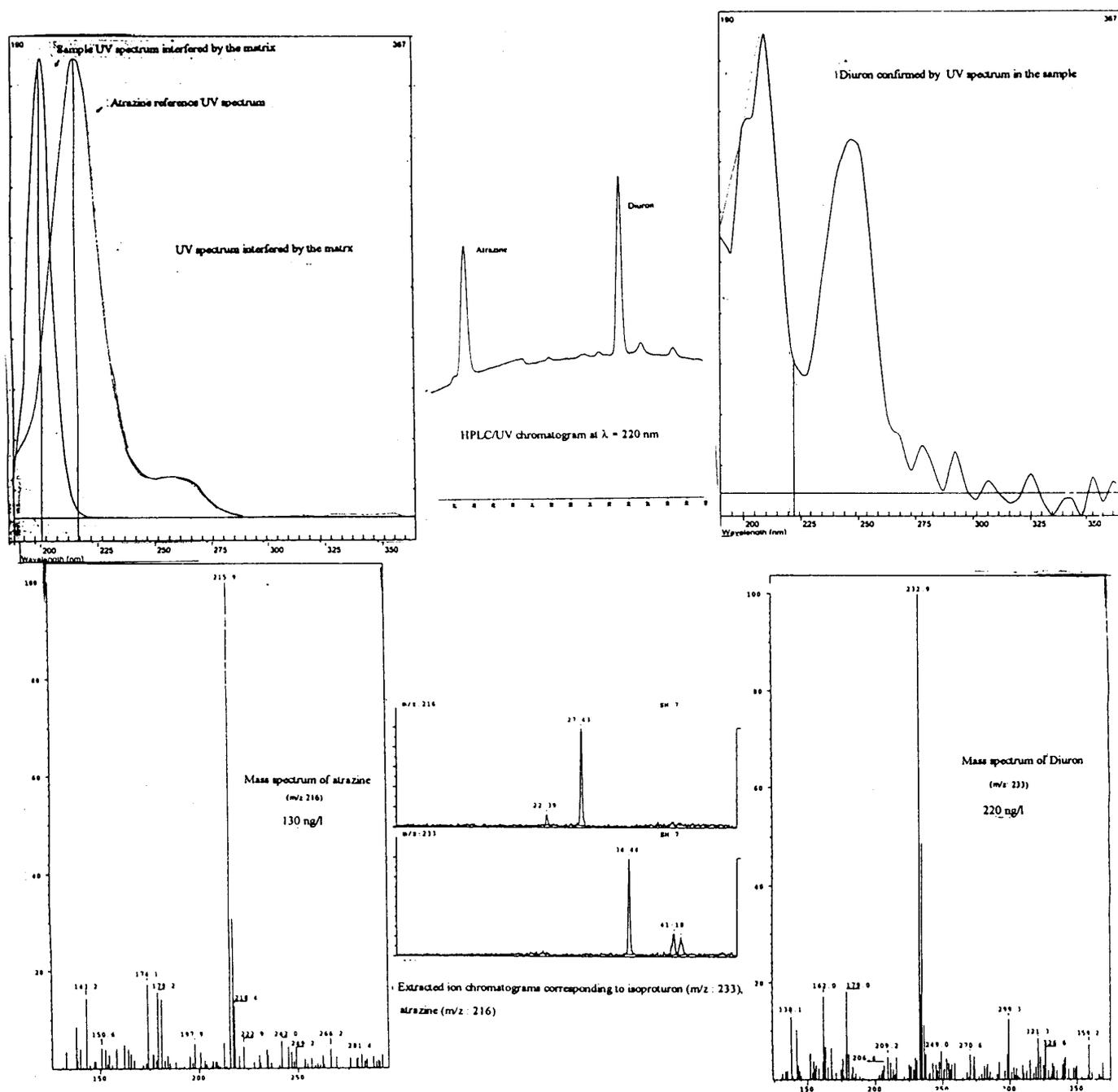
#### Results obtained on surface waters, UV/MS comparison

This method, applied to surface waters, was used to detect and identify positively, by associating their UV spectra and mass spectra, a number of substances of the regional list analysable by HPLC (Fig. 4). In this figure, the two surface water samples analysed show the following compounds

quantified on their specific extracted  $m/z$  ions chromatograms: terbuthylazine  $m/z$  174+230 (7 and 90 ng/L), desethylatrazine  $m/z$  188 (58 and 96 ng/L), atrazine  $m/z$  216 (143 and 800 ng/L), simazine  $m/z$  202 (53 and 15 ng/L), isoproturon  $m/z$  207 (51 and 73 ng/L), diuron  $m/z$  233 (260 and 490 ng/L), carbendazime  $m/z$  192 +134 (36 ng/L), penconazole  $m/z$  284 (44 ng/L).

It was possible to confirm the good correlation of the detection results obtained on the surface waters respectively by diode array UV and by mass spectrometry on specific ions in mass spectrometry. This good correlation has been particularly illustrated for two pesticides that are frequently detected in the surface waters investigated, diuron and desethylatrazine, one of the degradation products of atrazine.

Interference in diode array UV detection was controlled thanks to information from mass spectrometry (Fig. 5). In the example shown in figure 5, a very intense peak at the retention times of atrazine and the wavelength of 220 nm displays a different UV spectrum from that of atrazine. Mass spectrometry showed that a small fraction of the UV signal could be attributed to atrazine. The interfering substance in UV is not ionized in the instrumental conditions used, leading to an analytical signal in mass spectrometry derived exclusively from atrazine. Thus the quantification of atrazine



**Fig. 5.** Confirmation of atrazine and diuron in a surface water sample by simultaneous DAD and APCI/MS detections: – Diuron is identified by its mass spectrum and its UV spectrum – Atrazine is only identified by its mass spectrum, the UV spectrum is interfered by the matrix.

was possible without resorting to confirmation by another analytical method (GC/MS).

The main substances detected in this HPLC/MS study are atrazine, diuron, desethylatrazine, deisopropylatrazine or desethylsimazine, isoproturon, simazine, carbendazime, terbutylazine, penconazole, tebuconazole and fenpropimorph.

Other substances were detected in GC/MS, such as lindane and alachore, or confirmed by cross-checking with information for triazines.

The concentrations range are 0.1 µg/L to 4 µg/L for atrazine and diuron the two main present substances found.

## Conclusion

High-performance liquid chromatography coupled with mass spectrometry with atmospheric interfaces enables:

- the analysis and identification of pesticides and their conversion products, polar and thermolabile, with quantification limits compatible with European requirements for drinking water (0.02 µg/L for most of the substances determined in this study),
- confirmation of the substances detected in diode array UV,
- resolution of the problems of co-elution of certain substances in liquid chromatography,
- identification of certain substances or degradation products not included in the priority lists.

The prospects of this analytical method have expanded further, thanks to the coupling with the MS/MS tandem. However, it cannot substitute for the other analytical techniques, but rather adds to the range of organic substances analysable and identifiable by coupling methods.

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