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Structural elucidation and trace analysis with combined hyphenated chromatographic and mass spectrometric methods Potential of using hybrid sector mass spectrometry–time-of-flight mass spectrometry for pesticide analysis

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Abstract

The development of methods for analysis of triazines and their hydroxy metabolites in humic soil samples with combined chromatographic and mass spectrometric techniques is described. A two-way approach was used for separating interfering humic substances and for performing structural elucidation of the herbicide traces. Humic soil samples were extracted by supercritical fluid extraction and analysed both by HPLC–particle beam MS and a new MS–MS method. The new MS–MS unit is of the tandem-sector field-time-of-flight-MS type.

1. Introduction

Herbicides are widely used in agriculture and are subject to differing registration policies in several countries within the European Union (EU). Important is the group of triazine herbicides, some members of which are moderately toxic and environmentally persistent for several months. These triazines are readily soluble in water. Their leaching from cropland into subsoil water can be considerable. Therefore, one compound of this group (atrazine) is not permitted for use at all in Germany and others (terbuthylazine) are restricted in water protection areas. In order to confirm abuse of those compounds, metabolite concentrations in the soil have to be determined.

In our department (Biological and Biotechnical Plant Protection) triazines and their metabolites are usually quantified in leaching water and soil samples with a previously described LC method coupled with UV detection [1] or with GC–MS methods [2,3].

GC–MS is a common and sensitive method for the determination of triazines and their non-polar metabolites [2,3]. However, the polar hydroxy metabolites must also be detected in order to confirm illegal application of triazines [4,5]. HPLC separation techniques are convenient for determining polar hydroxytriazines [6].

With LC and MS detection, triazines can be determined via direct liquid introduction (DLI) [7], thermospray (TSP) in “filament on” or

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"filament off" modes [8–14], particle beam (PB) [12–17] or with an atmospheric pressure ionisation (API) [18] interface. Although triazines have been extensively studied [1–18], few data on analysis of hydroxytriazines in soil with high humic acid content are available.

In less complex samples, the use of tandem mass spectrometry (MS–MS) permits rapid analysis of specific compounds without the need for chromatographic separation [19,20]. In more complex samples like humic soils the necessary chromatographic effort can be reduced significantly. The overall limit of detection is usually higher in this approach, but the improved signal-to-noise ratio in the secondary mass spectrum facilitates structural elucidation. Although environmentally important compounds have been studied [19–30], few data on MS–MS examinations of pesticides in soil have been reported.

In this study, it was our aim to develop an analysis method for hydroxytriazines in complex soil samples. We combined modern methods of analysis for achieving fast and reliable results. This goal was approached from two different ends of the analytical chain. On one hand we developed a short procedure for extraction and separation of triazines from humic soil by supercritical fluid extraction (SFE) and on the other hand we tried to achieve structural elucidation of preseparated hydroxytriazines by using a MS–MS method.

SFE is a technique used to extract non-polar substances preferably from semi-solid samples with an unnoxious solvent [31,32]. Supercritical CO_2 is usually employed as the extraction solvent of choice, with varying solvent strength depending on applied pressure, temperature and modifiers added.

In an attempt to extract atrazine of medium polarity [33] and its polar hydroxy metabolites in the same process, application of high pressure (50 MPa) and addition of 10% methanol as a modifier is necessary. When compared to conventional extraction [34] and static SFE methods [35] the use of the principle of "fractionated extraction" [36] in a dynamic extraction mode results in a considerable gain of extraction selectivity. Co-extraction of humic acids is suppressed significantly under these conditions. Therefore, usually applied clean-up procedures like gel permeation chromatography [37] and solid-phase extraction [38] can be circumvented at considerable savings in time and cost.

The hybrid tandem mass spectrometer consists of a double-focusing sector field mass spectrometry (BE-MS) system, a collision cell working with surface-induced dissociation (SID) and serving as a detector for the first MS system, and a time-of-flight (TOF) MS system [39–43].

2. Experimental

2.1. Reagents

High-purity gases He (99.999%) and CO_2 (SFC grade) were obtained from Messer-Griesheim (Düsseldorf, Germany), water from a Milli-Q system (Millipore, Bedford, MA, USA). HPLC-grade methanol, acetonitrile, analytical-reagent grade ammonium acetate, and analytical-reagent grade perfluorotributylamine (PFTBA) were obtained from Merck (Darmstadt, Germany) and triazines and their hydroxy metabolites from Riedel-de Haen (Seelze, Germany).

2.2. Sample handling

Stock solutions of the triazine herbicides and their hydroxy metabolites were prepared by dissolving 25 mg of each compound in 50 ml methanol. From these solutions mixed standard solutions were prepared and diluted with methanol.

Standard samples were prepared by spiking Kieselgur (Merck) with a liquid standard solution followed by vigorous mixing. Spiked soil samples containing 500, 50, 5, 2 or 0.5 μg/g of each analyte were produced from a sandy humic soil in the same way.

The spiked soil samples were stored for two days at 4°C and kept at intermediate humidity in the dark.

Moreover, real soil samples selected from pesticide degradation studies of our laboratory

(Biological and Biotechnical Plant Protection) were employed, but these results will be published elsewhere [44].

2.3. Extraction

A Dionex (Sunnyvale, CA, USA) Model SFE 703 apparatus was used to perform SFE of standard and soil samples in 10-ml sample cartridges. Conditions of the dynamic extraction of triazines and polar hydroxy metabolites from soil were as follows: flow-rate of 1 ml/min with a modifier content of 10% methanol, extraction time of 15 min and extraction pressure of 50 MPa at 40°C. The collection vessels (stainless steel) were charged with 3.5 ml methanol and fitted with heat-exchange jackets which were adjusted to ca. 20°C via a circulating-water bath during collection.

2.4. Chromatography

The liquid chromatograph consisted of a Hewlett-Packard (Palo Alto, CA, USA) Model HP 1050 pump and a Rheodyne (Cotati, CA, USA) Model 7125 injector fitted with a 20-μl sample loop. The conditions for the chromatographic separation of triazines and polar hydroxy metabolites from co-extracted humic acids were set at a flow-rate of 0.30 ml/min with an isocratic 1 m*M* ammonium acetate–acetonitrile (50:50) mobile phase on a RP18 Supersphere 200 × 2.1 mm (4 μm particle size) separation column obtained from MZ Analysentechnik (Mainz, Germany).

The PB interface from Hewlett-Packard (Model 5998 A) was used to couple the electron impact (EI) source of the mass spectrometer to the liquid chromatograph. The PB interface desolvation chamber temperature was 40°C, the helium pressure of the nebulizer was 45 p.s.i. (1 p.s.i. = 6894.76 Pa), and the capillary position of the nebulizer was optimized daily.

2.5. Mass spectrometry

The experiments were performed both on a HP 5989 quadrupole mass spectrometer with a mass range of 1000 u and on a new tandem mass spectrometer.

The hybrid tandem mass spectrometer was constructed by the Second Physical Institute [39–43]. It consists of a double focusing sector field mass spectrometer (mass range 10000 u, mass resolution 10 000), a collision cell working with SID and a TOF-MS system with a mass range above 10 000 u and an energy-limited mass resolution of 1000 (Fig. 1).

Because of differences in construction, EI sources of both mass spectrometers have to be operated under different optimum conditions.

The source temperature of the quadrupole MS was 250°C, ionisation energy 70 eV and the mass range scanned was 90–240 u in the positive ion full scan mode.

The source temperature of the tandem MS was 100°C, ionisation energy 200 eV and the mass range scanned by the primary MS was 5–300 u in the positive ion full scan mode. In the tandem mode, the first stage MS is set to transmit a specific molecular ion (parent ions/primary beam). As a matter of operation, one complete daughter ion mass spectrum is recorded within every time of flight (μs). Therefore, for TOF-MS no scanning is needed.

The energy of the primary beam is 3 keV, the potential of the SID target surface is 1.4 keV. The incident angle of colliding ions is 2° and the potential gradient across the channel plate 1 kV. The potential of the drift tube of the TOF-MS

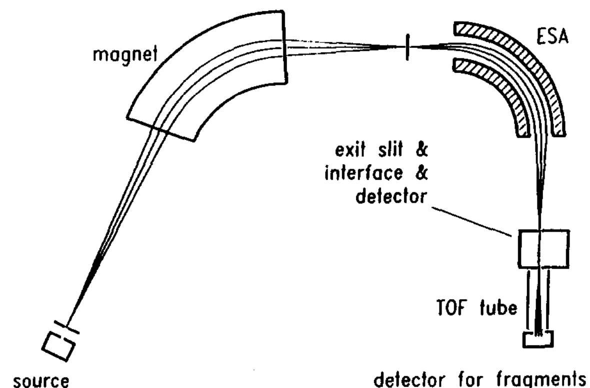

Fig. 1. Overall construction scheme of the tandem BE-MS–SID-TOF-MS.

system is 0 V, the detector potential −3 kV in order to improve the sensitivity of the channel plate. The mass scale of TOF-MS was calibrated by MS–MS measurement of the H_2O, N_2, O_2 and perfluorotributylamine signals.

3. Results and discussion

3.1. Extraction and chromatography

Recoveries of Soxhlet extractions from humic soil (2 h, methanol) were compared with recoveries of extraction from humic soil by SFE (15 min, CO_2 10% methanol).

The yields for atrazine and terbuthylazine were comparably high for both methods. Recoveries for the hydroxy metabolites on the other hand were significantly better with SFE than with Soxhlet extraction (Table 1). Moreover, SFE yields clearer extracts with up to 80% lower background of humic coextracts.

Chromatographic separations with UV detection of triazines and their metabolites require prolonged gradient programs [1]. The possibility of gaining additional structural information by a quadrupole MS or a MS–MS detector facilitates performing chromatography within a few minutes and with an isocratic program (see Fig. 3) because complete separation of every compound of the mixture is not absolutely necessary.

These simplifications both increase the lifetime of mesobore columns significantly and facilitate the optimization of PB operating conditions. The mesobore column thus may run on isocratic separation conditions. This results in a gain of sensitivity of the LC–PB-MS method when compared to a gradient program.

4. Mass spectrometry

(1) SFE extracts from soil and standard mixtures of triazines and their hydroxy metabolites were measured with LC–PB-MS in the SCAN mode. This strategy results in readily interpretable mass spectra of each component (Fig. 2). However, the sensitivity of this method in the SCAN mode is poor (5 mg/kg soil) for these compounds (Fig. 3).

Structural information of measurements with LC–PB-MS in the selected ion monitoring (SIM) mode is sometimes equivocal and is confined to target analysis, especially in the determination of structurally similar compounds like metabolites of one herbicide. The sensitivity of this method in the SIM mode is increased by a factor of 10 to ca. 0.5 mg/kg soil.

Table 1
Comparison of recoveries of SFE and Soxhlet extraction from spiked soil

Spiked (ppm, w/w)	Recovery (%)											
	SFE						Soxhlet extraction					
	T	A	OHT	OHA	OHDEA	OHDIA	T	A	OHT	OHA	OHDEA	OHDIA
0.5	91 ± 7	93 ± 9	83 ± 5	81 ± 11	80 ± 9	79 ± 17	95 ± 9	93 ± 10	53 ± 11	50 ± 7	57 ± 9	40 ± 9
2.0	95 ± 3	90 ± 5	78 ± 7	78 ± 4	70 ± 6	76 ± 2	94 ± 4	92 ± 7	50 ± 6	48 ± 10	50 ± 8	37 ± 13
5.0	88 ± 5	87 ± 4	73 ± 7	66 ± 3	81 ± 8	70 ± 8	90 ± 5	94 ± 3	48 ± 8	39 ± 7	43 ± 9	48 ± 7
Overall	91.7	90.0	78.0	75.0	77.0	75.0	93.0	93.0	50.3	45.6	50.3	41.7
Range	82–101	84–104	64–88	63–90	75–83	61–96	84–103	83–102	41–64	32–56	36–66	24–55

$n = 3$. SFE: 15 min, 1 ml/min, 10% methanol, 50 MPa. Soxhlet extraction: 2 h, 150 ml methanol. Spiked soil: sandy humic soil stored at 4°C for two days after spiking. T = Terbuthylazine; A = atrazine; OHT = hydroxyterbuthylazine; OHA = hydroxyatrazine; OHDEA = hydroxydeethylatrazine; OHDIA = hydroxydeisopropylatrazine = hydroxydeterbutylterbuthylazine.

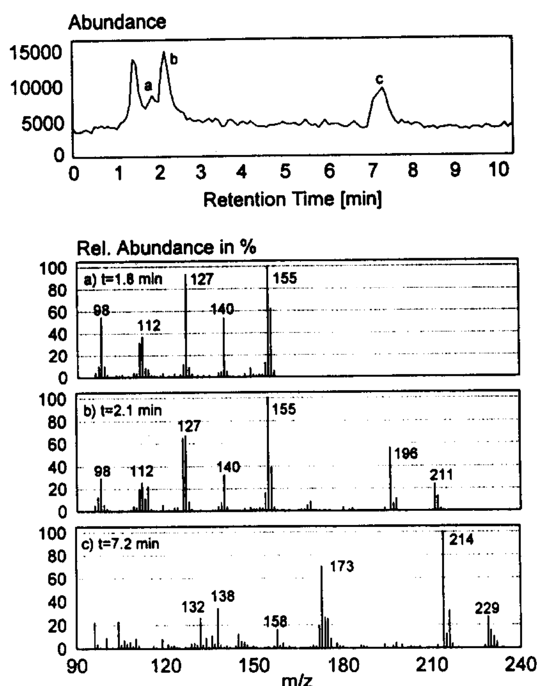

Fig. 2. (Top) Total ion chromatogram (SCAN mode) of a sample containing 20 mg/kg of (a) deterbutyl-2-hydroxyterbuthylazine (b) 2-hydroxyterbuthylazine and (c) terbuthylazine. (Bottom) Resulting mass spectra of the analysed components a–c.

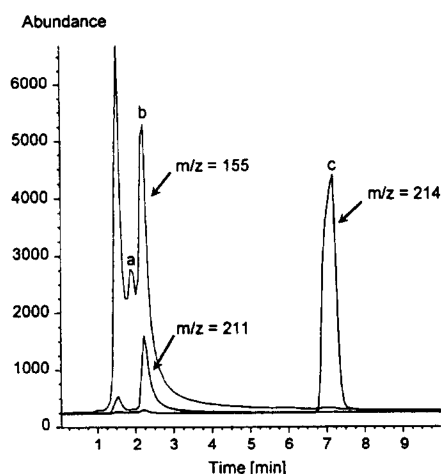

Fig. 3. Ion chromatogram (SIM mode) of a sample containing 20 mg/kg of (a) deterbutyl-2-hydroxyterbuthylazine (b) 2-hydroxyterbuthylazine and (c) terbuthylazine. Mass 155 corresponds to a or b, mass 211 to b and mass 214 to c.

The comparably high limits of detection can be explained by increasing losses of analytes with decreasing molecular mass, especially below 200 u, due to co-volatilisation with the solvent into the vacuum system during the desolvation step.

(2) Measurements with the DLI-MS–MS of triazines and their hydroxy metabolites result in reliable tandem mass spectra down to 0.2 mg/kg soil. The interpretation of the secondary mass spectra is difficult because of the low mass resolution of the second stage mass spectrometer ($M/\Delta M = 10$). In spite of this shortcoming the interpretation of these mass spectra is possible because of the similarity of their fragmentation pattern to those resulting from EI ionisation (Fig. 4). Therefore, characteristic masses appearing in EI mass spectra can be used for interpretation of SID-TOF mass spectra. This is an important advantage, because of already existing EI-MS libraries (for instance NIST, National Institute of Standards and Technology, Gaitherburg, MD, USA).

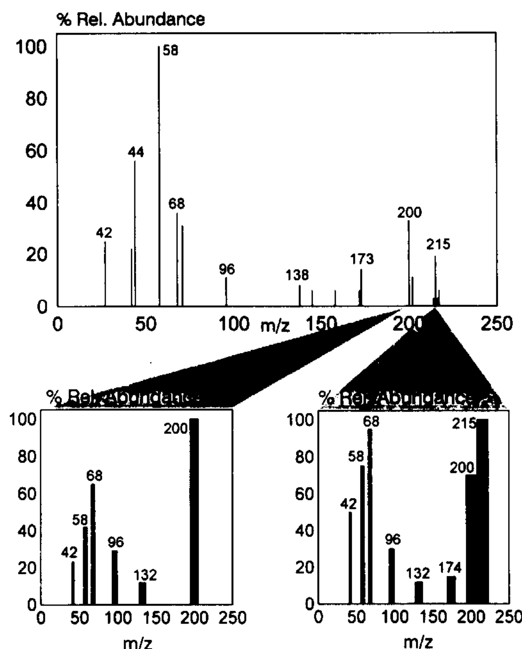

Fig. 4. Tandem mass spectra of atrazine. The primary mass spectrum is a typical EI fragmentation mass spectrum, the secondary mass spectra are SID-fragmentation mass spectra of the parents ions m/z 200 and 215. The widths of the mass bars in the secondary mass spectra correspond to the half widths of the mass peaks.

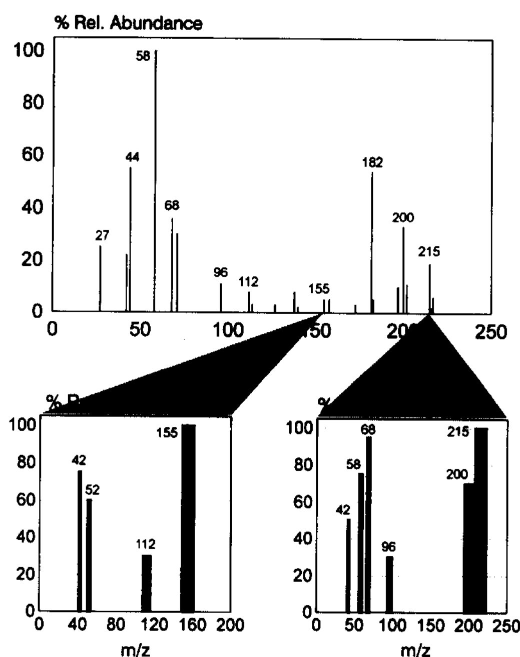

Fig. 5. Tandem mass spectra of a sample containing a surplus of atrazine and 20 ng deisopropyl-2-hydroxyatrazine. The secondary mass spectra are SID-fragmentation mass spectra of the molecular ions of atrazine (m/z 215) and its metabolite (m/z 155).

The identification of deisopropyl-2-hydroxy-atrazine ($m/z = 155$) in the presence of high atrazine ($m/z = 215$) concentrations by means of the characteristic fragment with 112 amu in the secondary mass spectrum (Fig. 5) may serve as an example. The time required to get a statistically correct secondary mass spectrum of about 50 000–100 000 counts depends on the intensity of the selected parent ion in the primary spectrum. In the measurements presented this analysis time was shorter than 1 min.

Because of the so far unsatisfactory mass resolution, the main advantage of the MS–MS method, its sensitivity, is nearly leveled down, because more counts are necessary to fit a reliable mass bar into a broad peak. Moreover, useful secondary mass spectra are confined to low masses ($m/z = 20$–200) because of the difficulty of peak matching of higher masses. The theoretical mass resolution of TOF-MS is $M/\Delta M = 1000$. Therefore, understanding the process within the collision cell [45–50] is crucial for an improvement of the mass resolution of this hybrid MS–MS method. Further investigations will be discussed elsewhere.

The performances of two different methods of structure-elucidating trace analysis with MS detectors are compared (Table 2). Normally, an increase in structural information is accompanied by a decrease of sensitivity. The DLI-MS–MS method keeps the advantage of obtaining structural information in form of mass spectra similar to EI mass spectra down to a lower limit of detection (20 ng) and a significantly lower limit of quantification. Nevertheless, LC–PB-MS and DLI-MS–MS can be used complementarily because of their different preferred mass ranges (LC–PB-MS: $m/z = 200$–2000; DLI-MS–MS: $m/z = 20$–200). Other methods like LC–diode array detection (DAD) and LC–TSP-MS do not

Table 2
Comparison of LC–PB-MS and DLI-MS–MS

	LC–PB-MS (SIM)			LC–PB-MS (SCAN)			DLI-MS–MS		
	T	OHT	OHDIA	T	OHT	OHDIA	T	OHT	OHDIA
Limit of detection (ng)	50	50	100	400	400	1000	20	20	20
Limit of quantification (ng)	400	500	1200	1000	1200	2500	50	50	50
Linear range	10^3	10^3	10^3	10^2	10^2	10^2	10^2	10^2	10^2
Structural information	Target analysis			Yes, intermediate masses			Yes, low masses		

Abbreviations as in Table 1.

Table 3
Comparison of other methods for the analysis of hydroxytriazines OHT and OHA

	LC–DAD [52]	LC–TSP-MS (SCAN) [51]	DLI-MS–MS	LC–PB-MS (SIM)	LC–PB-MS (SCAN)
Limit of detection (ng)	0.2	1–2	20	50	400
Structural information	UV spectra	Molecular ion	SID mass spectra	Three selected ions	EI mass spectra

Abbreviations as in Table 1.

suffer from those limitations and are significantly more sensitive. However, the structural information obtained from those methods are poor (Table 3). Therefore, our MS–MS method appears useful as supporting tool for structural elucidation of hydroxytriazines in humic soil.

5. Conclusions

A method for structural elucidation and trace analysis with combined chromatographic (LC–MS) and mass spectrometric (MS–MS) techniques was developed to facilitate reliable determination of triazines and hydroxy metabolites in humic soil down to 0.5 mg/kg soil.

Using selective dynamic SFE yields remarkably clean extracts with good recoveries down to 0.5 mg/kg triazine and hydroxy metabolites in humic soil. This simplifies the chromatographic separation and introduction into the MS system by PB interface. Comparison of PB-quadrupole MS measurements (SCAN and SIM modes) with measurements of a hybrid MS–MS with DLI shows comparative sensitivities within 10-min runs. The advantages of the new MS–MS method, i.e. increased sensitivity and structural information, are nearly compensated due to the low mass resolution of 10 in the secondary MS system.

Comparing the performance of LC–PB-MS and the actual DLI-MS–MS method results in an advantage of the MS–MS method in analysing polar metabolites of low molecular masses and high polarities, i.e. those substances not easily analysed by LC–PB-MS with sufficient sensitivity. Moreover, the relative mass uncertainty is not as disturbing when examining low masses as opposed to high masses. In examining compounds of intermediate molecular masses, both methods can be used complementarily because of their different advantages and disadvantages. For instance, DLI-MS–MS was found to provide a rapid and comprehensive survey of metabolites present without HPLC losses, while LC–MS succeeded in resolving isobaric species present [53].

Both strategies are not really routine methods, MS–MS less than LC–MS. Most analysed real soil samples with herbicide residues result from application according to good agricultural practice. Therefore, an additional preconcentration step will be necessary for obtaining reliable quantitative results in most cases of metabolite analysis, where the metabolite concentration is smaller than the parent compound. Nevertheless, the described methods are successfully used to confirm LC–DAD results of soil analysis from field trials [44]. If it is possible to increase the mass resolution of the second stage MS to $M/\Delta M = 100$ to 1000, the hybrid MS–MS method will be at least 10- to 100-fold more sensitive while yielding secondary mass spectra for reliable structure elucidation.

Moreover, because of the construction of the hybrid MS–MS system with a TOF-mass spectrometer as secondary MS system, every emerging daughter ion is detected with highest sensitivity. No selection of special daughter ions is necessary in this experiment for achieving best sensitivity. In contrast, MS–MS experiments working with quadrupole or sector field MS as secondary MS have to select one daughter ion (single reaction mode) in order to achieve full sensitivity [54].

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