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Journal of Chromatography A, 1090 (2005) 126–132
JOURNAL OF CHROMATOGRAPHY A
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Possibilities and limitations of quadrupole mass spectrometric detector in fast gas chromatography

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Received 4 January 2005; received in revised form 16 June 2005; accepted 22 June 2005
Available online 19 July 2005

Abstract

In this work the application and limitations of a common bench top quadrupole mass spectrometer was evaluated for the qualitative and quantitative measurement of *n*-alkanes and pesticides of a wide range of volatilities and polarities with fast GC separations using 0.15 mm I.D. narrow-bore capillary columns. It was found that the spectra acquisition rate has a great impact on sensitivity (peak areas, peak shapes and S/N ratios). The quality of the obtained spectra is not significantly influenced in the full scan monitoring mode for the fastest scan rates. For quantitative analysis a selected ion monitoring mode is able to acquire the sufficient number of data-points for the proper peak shape reconstruction and good repeatability of peak areas measurements expressed by RSD (<5%) for all tested dwell times shorter than 75 ms. However, for shorter dwell times, S/N ratio is lower, while peak areas are not influenced.

Keywords: Fast GC–MS; Fast gas chromatography; Mass spectrometry; *n*-Alkanes; Pesticides

1. Introduction

Utilisation of fast gas chromatography (fast GC) on narrow-bore capillary columns is advantageous for the use in routine laboratories due to the higher sample throughput, the same and even higher separation efficiency than conventional capillary GC (CGC), higher sensitivity and/or precision and simultaneous reduction of operating costs of a GC analysis [1,2].

For proper operation of any "fast" column with MS, the peak broadening caused by extra-column effects must be small enough to preserve the column efficiency. The sampling frequency of a detector must be high enough to provide the sufficient number of data points across the peak for the accurate representation of a peak. Trends in GC are the ever increasing need for the positive identification and the need for more flexible systems that allow the analysis of a wide variety of samples in one system. These trends clearly results in the need of mass spectrometric detection [3]. In fast GC mostly time of flight (TOF) mass spectrometers are preferred due to their fast data acquisition rates reaching up to 500 Hz and the subsequent possibilities of chromatographic and spectral peak deconvolution [4,5]. Quadrupole instruments have been most widely used in conventional CGC. Proving their abilities for adequate detection of narrow peaks without the loss of sensitivity would therefore help to extend the use of the fast GC to routine laboratories.

Only few papers are dealing with questions arising, such as the influence of fast MS operation on sensitivity, repeatability of measurements and quality of mass spectra, when slower scanning quadrupole MS instruments are utilized for detection of narrow peaks in fast GC on narrow-bore capillary columns. Hada et al. [6] and Korenková et al. [7] have used quadrupole MS as detectors in fast GC on narrow-bore columns for determination of pesticide residues. In both papers satisfactory results were obtained with regards to analytes quantitation in full scan and selective ion monitoring

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doi:10.1016/j.chroma.2005.06.090

modes, but there is neither specification and/or discussion on settings of MS parameters and its impact on satisfactory chromatogram reconstruction when narrow peaks are detected, nor data on the measured peaks width. Dallüge et al. [8] utilized quadrupole MS as a detector in the resistively heated GC and published the results of quantitative analysis. Also the relationship between the peak area measurements repeatability (expressed as the relative standard deviation (RSD)) and the question of data points across the peak is discussed. The number of scan data points—six obtained across the peak was considered as satisfactory [8].

In literature there are general discussions concerning how many data points are actually needed to define the chromatographic peak; the values in the ranges of 15–20 was found to be the minimum for the accurate representation of a peak [9], but in other papers [4,10,11] also three to four data points are published that work well enough for quantitative analysis.

In this work possibilities of commercial quadrupole MS detector Agilent 5973N coupled to fast GC on a 0.15 mm I.D. narrow-bore column are studied for analytes of the wide range of physico-chemical properties. The 0.15 mm I.D. columns will allow more flexibility in loadability, sample introduction (flow rate) and operate at lower inlet pressures when compared to 0.1 mm I.D. columns [12]. Important searched parameters are the relationship between scan rate and sensitivity and repeatability of measurements (peak area, signal to noise ratio (S/N)) and the quality of the obtained spectra in full scan mode. In selective ion monitoring (SIM) the relation between dwell time and peak shape, response and S/N ratio were searched.

2. Experimental

GC–MS measurements were performed on an Agilent 6890N GC equipped with a programmed temperature vaporizer (PTV) connected to 5973N MSD (Agilent Technologies, Avondale, PA, USA) providing maximal scan range 1.6–800 amu with maximal scan rate 5650 amu/s. For tuning autotune procedure available through ChemStation software was used, perfluorotributylamine (PFTBA) was default calibration standard. Chromatographic column CP-Sil 8 low bleed/MS 15 m long, 0.15 mm I.D., film thickness 0.15 μm, Varian (Middleburg, The Netherlands) was connected to 1 m long 0.32 mm I.D. retention gap (Supelco, Bellefonte, USA) with press-fit connector (Agilent Technologies, Switzerland) and polyimide resin (Supelco, Bellefonte, USA).

Helium with purity 5.0 (Linde Technoplyn, Bratislava, Slovak Republic) was used as a carrier gas in the constant flow mode 1.2 ml min^{-1}. PTV inlet was operated in a cold splitless mode with the following temperature programme: initial temperature 150 °C, ramp 400 °C min^{-1} to 350 °C and splitless time 1.13 min. The injection volume was 1 μl. The following oven temperature programme was used: initial temperature 100 °C hold 1.13 min, ramp 24 °C min^{-1} to 300 °C hold 1.29 min. In this study, six *n*-alkanes and 21 pesticides belonging to different chemical classes were used. Their list with chemical class, retention time and target ions for full scan and target ions and qualifiers for SIM is given in Table 1. Standards of the used *n*-alkanes (C_{12}, C_{14}, C_{16}, C_{18}, C_{22} and C_{26}) were obtained from Fluka (Buchs, Switzerland), standards of pesticides were obtained from different sources and were of purity >95%. Stock solutions of *n*-alkanes and pesticides was prepared at approximate concentration 0.5 mg ml^{-1} and were stored in a refrigerator (−18 °C). Working solutions were prepared by dilution of stock solutions in toluene.

3. Results and discussion

3.1. Full scan experiments

In Agilent 5973N mass selective detector, the data acquisition rate—scan rate in full scan mode is given by the number of samples (abundance measurements of each mass before going on to the next mass during the measurement of one cycle) that are taken and afterwards saved as one data point. The number of measurements of each mass is given by 2^N, where N is the number set by operator in the ranges of 0–7 only for integers. The other parameter controlling scan rate is the range of scanned masses. The gain in speed of a data acquisition rate by narrowing the scanned mass range is advantageous only up to the highest mass of an expected molecular ion to prevent the loss of information for the proper compound identification. However, the gain in scan rate controlled by narrowing the range of masses to be scanned is less powerful than by setting the number of samples.

In our experiments scans were performed over the range of masses 50–510 *m/z* (molecular ion of deltamethrine is at *m/z* 503 with ion cluster up to *m/z* 509). A solution of *n*-alkanes and pesticides in toluene with approximate concentration 3 ng μl^{-1} was used. For the data acquisition the following sampling rates were used: 0–4 resulting in scan rates 10.68, 5.98, 3.18, 1.64 and 0.84 scan s^{-1}, respectively, indicated by the ChemStation software. However, from the obtained data, slightly lower scan rates were calculated; 10.60, 5.93, 3.17, 1.63 and 0.83 scan/s for samples 0–4, respectively.

Peak widths at half heights were dependent on a compound and elution time and were in the range of 0.5 s for *n*-C_{12} with retention time 2.67 min to 1.07 s for deltamethrin with elution time 9.94 min; elution times and peak widths at half height are presented in Table 1. Measured peak widths are below the range 1–3 s used for defining the fast GC according to van Deursen et al. [3]. Chromatogram with all measured compounds obtained in full scan mode is presented in Fig. 1. Chromatographic conditions were optimized (column carrier gas flow according to Blumberg [13] and oven temperature gradient was set to 10 °C per void time [14]). In Fig. 2, the average peak areas (eight replicates), its RSDs and (S/N) ratios of *n*-alkane C_{22} and selected pesticides are

Table 1
The list of the used *n*-alkanes and pesticides, their retention times, peak widths, monitored ions and SIM group start times

Compound	Chemical class	Retention time (min)	Peak width at half height (s)[a]	Monitored ions in SIM target ion[b]	Group start time in SIM (min)
n-C_{12}	*n*-Alkane	2.67	0.50	**57**, 71, 85	2.50
Dichlorvos	Organophosphate	2.89	0.53	**109**, 79, 185	2.80
n-C_{14}	*n*-Alkane	3.60	0.55	**57**, 71, 85	3.20
n-C_{16}	*n*-Alkane	4.58	0.60	**57**, 71, 85	
Dimethoate	Organophosphate	5.22	0.80	**87**, 93, 125	5.00
Simazin	Triazine	5.28	0.77	**201**, 186, 173	
Terbuthylazine	Triazine	5.43	0.70	**214**, 173, 229	5.39
Diazinon	Organophosphate	5.47	0.64	**179**, 137, 152	
n-C_{18}	*n*-Alkane	5.49	0.66	**57**, 71, 85	
Pyrimethanil	Anilinopyrimidine	5.53	0.66	**198**, 199	
Chlorpyrifos-methyl	Organophosphate	5.89	0.61	**199**, 286, 288	5.70
Fenitrothion	Organophosphate	6.16	0.62	**277**, 125, 109	6.02
Chlorpyrifos	Organophosphate	6.28	0.65	**199**, 197, 314	5.49
Cyprodinyl	Anilinopyrimidine	6.57	0.68	**224**, 225	6.40
Penconazole	Triazole	6.61	0.83	**159**, 161, 248	
Captan	Phtalimide	6.73	0.74	**79**, 149, 264	
Methidathion	Organophosphate	6.81	0.71	**85**, 145, 93	
n-C_{22}	*n*-Alkane	7.11	0.70	**57**, 71, 85	7.00
Kresoxim-methyl	Oximinoacetate	7.14	0.66	**116**, 131, 206	
Myclobutanil	Triazole	7.16	0.75	**179**, 150, 245	
Tebuconazole	Triazole	7.85	0.84	**125**, 250, 252	7.50
Phosalone	Organophosphate	8.38	0.73	**182**, 121, 367	8.10
n-C_{26}	*n*-Alkane	8.48	0.95	**57**, 71, 85	
Bitertanol	Triazole	8.83, 8.87	0.89, 1.13	**170**, 168, 141	8.70
Cypermethrin	Pyrethroid	9.20–9.29	0.83–0.94	**163**, 181, 181	9.15
Etofenprox	Non-ester pyrethroid	9.34	1.00	**163**, 376, 135	
Deltamethrin	Pyrethroid	9.94	1.07	**253**, 181, 255	9.70

[a] Peak widths were measured in SIM at dwell time 10 ms.
[b] The same target ion used also in full scan monitoring, target ions printed in bold font.

presented in the dependence on the utilized sampling rates. For all compounds studied all three parameters provided very similar information. Peak areas were evaluated by integration of extracted ion chromatograms. For each compound one target ion for quantification was selected (Table 1). As can be seen peak areas—responses are significantly increasing with increasing the number of samples up to the sampling rate of 3, which provides the scan rate 1.68 scan s^{-1}. At the higher

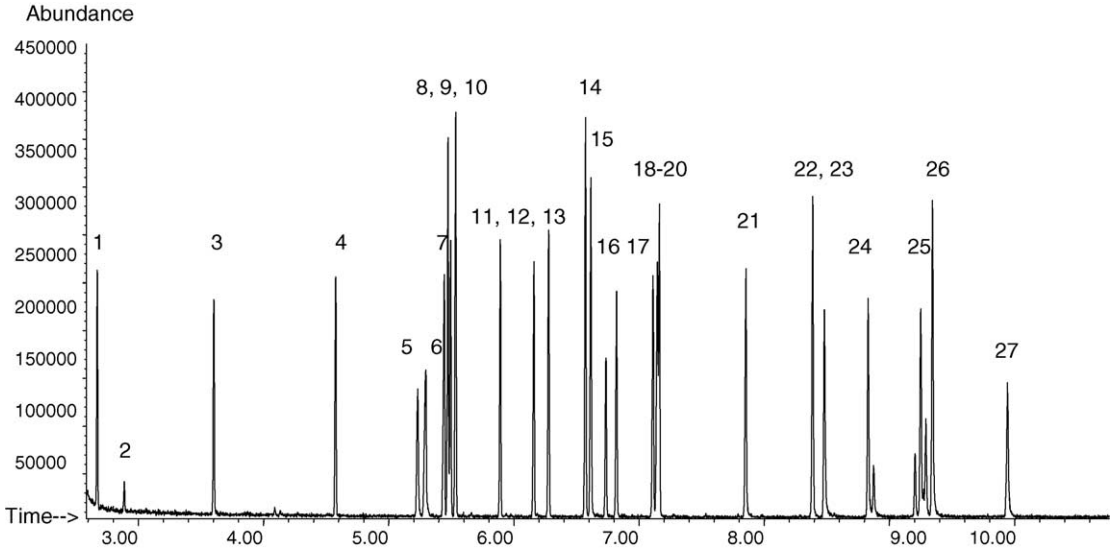

Fig. 1. Chromatogram obtained in full scan mode with samples set to 0 with resulting scan rate 10.68 scan s^{-1}, separation conditions are described in experimental (1) *n*-C_{12}, (2) dichlorvos, (3) *n*-C_{14}, (4) *n*-C_{16}, (5) dimethoate, (6) simazin, (7) terbuthylazine, (8) diazinon, (9) *n*-C_{18}, (10) pyrimethanil, (11) chlorpyrifos-methyl, (12) fenitrothion, (13) chlorpyrifos, (14) cyprodinyl, (15) penconazole, (16) captan, (17) methidathion, (18) *n*-C_{22}, (19) kresoxim-methyl, (20) myclobutanil, (21) tebuconazole, (22) phosalone, (23) *n*-C_{26}, (24) bitertanol, (25) cypermethrin, (26) etofenprox and (27) deltamethrin.

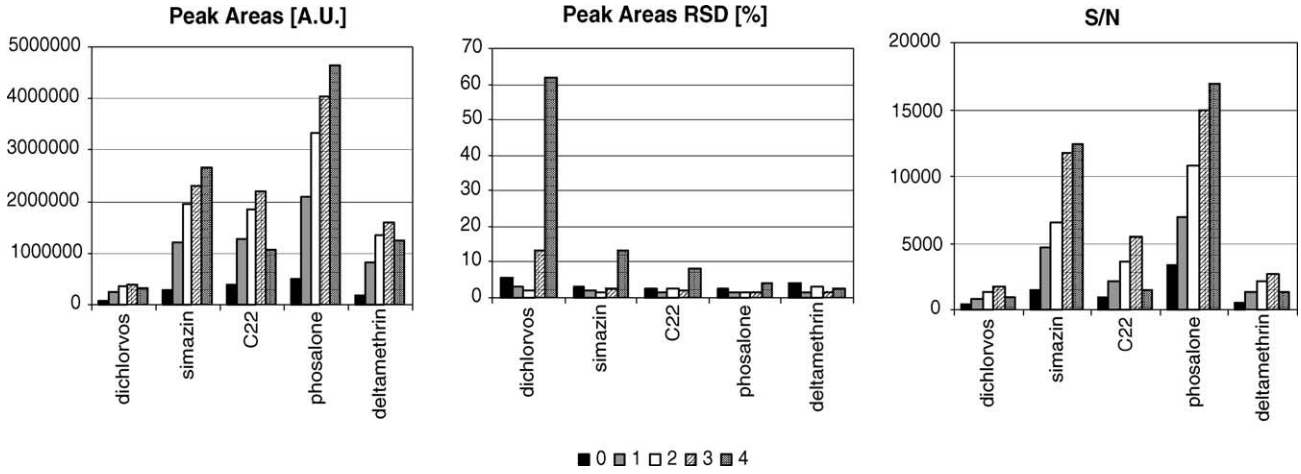

Fig. 2. The dependence of average peak areas, RSDs of peak areas and S/N ratio ($n = 8$) of selected compounds in full scan mode on the number of samples taken for measurement 0–4 (scanned range of masses 50–510 *m*/*z*).

number of samples peak areas significantly decreased due to spectra skewing and insufficient number of points for the proper peak shape reconstruction and subsequent integration. Repeatability of peak areas expressed as RSDs of peak areas were typically below 4% for samplings in the range 0–2, for the highest sampling RSDs of peak areas were significantly higher. In Fig. 3, overlaid extracted ion chromatograms of chlorpyrifos-methyl obtained at different sampling rates is presented for *m*/*z* 286. As can be seen, peak shapes obtained at samples set to 0, 1 are satisfactory and at higher number of samples (3, 4) peak shapes are distorted by the low number of data points for its proper reconstruction. For the highest scan rate 10.68 scan s^{-1} about 17–25 data-points were obtained per peak, for scan-rates 5.98, 3.18, 1.64 and 0.84 in the ranges of 9–14, 5–7, 3–4 and 1–2 data-points were obtained, respectively. However, full scan experiments utilizing quadrupole mass spectrometers are usually performed for qualitative analysis purposes; even one point per peak with spectrum of acceptable quality is sufficient for positive compound identification [4].

Quality of the obtained spectra was evaluated as similarity of spectra measured in the maximum of the peak with the library spectra (NIST 02 library). For chlorpyrifos, fenitrothion and chlorpyrifos-methyl better values of similarity were obtained for the samples set to values 1–3 than for the spectra acquired at the samples set to 0 or 4, for samples 4, no proper match for fenitrothion was found in the mass spectra library (Table 2). In Fig. 4, raw mass spectra taken from different parts of chromatographic peak measured at samples set to 1 are presented. As can be seen, spectral skewing is at acceptable level. The different observation was found when spectra are taken from ascending or descending parts of the peak acquired at samples set to 2–4, strong spectra skewing occurs.

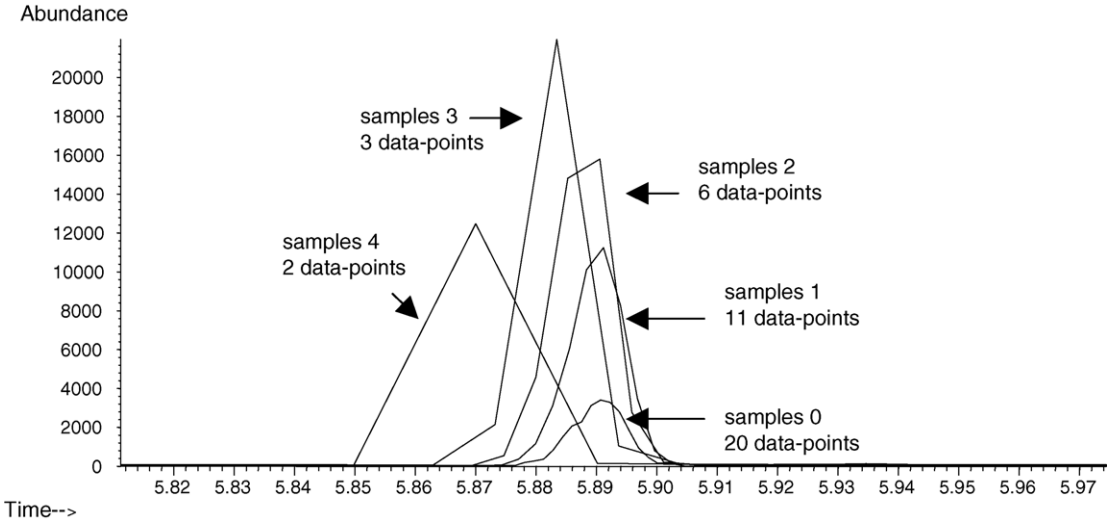

Fig. 3. Overlaid ion chromatograms of chlorpyrifos-methyl *m*/*z* 125 measured at different settings of samples with the number of datapoints obtained.

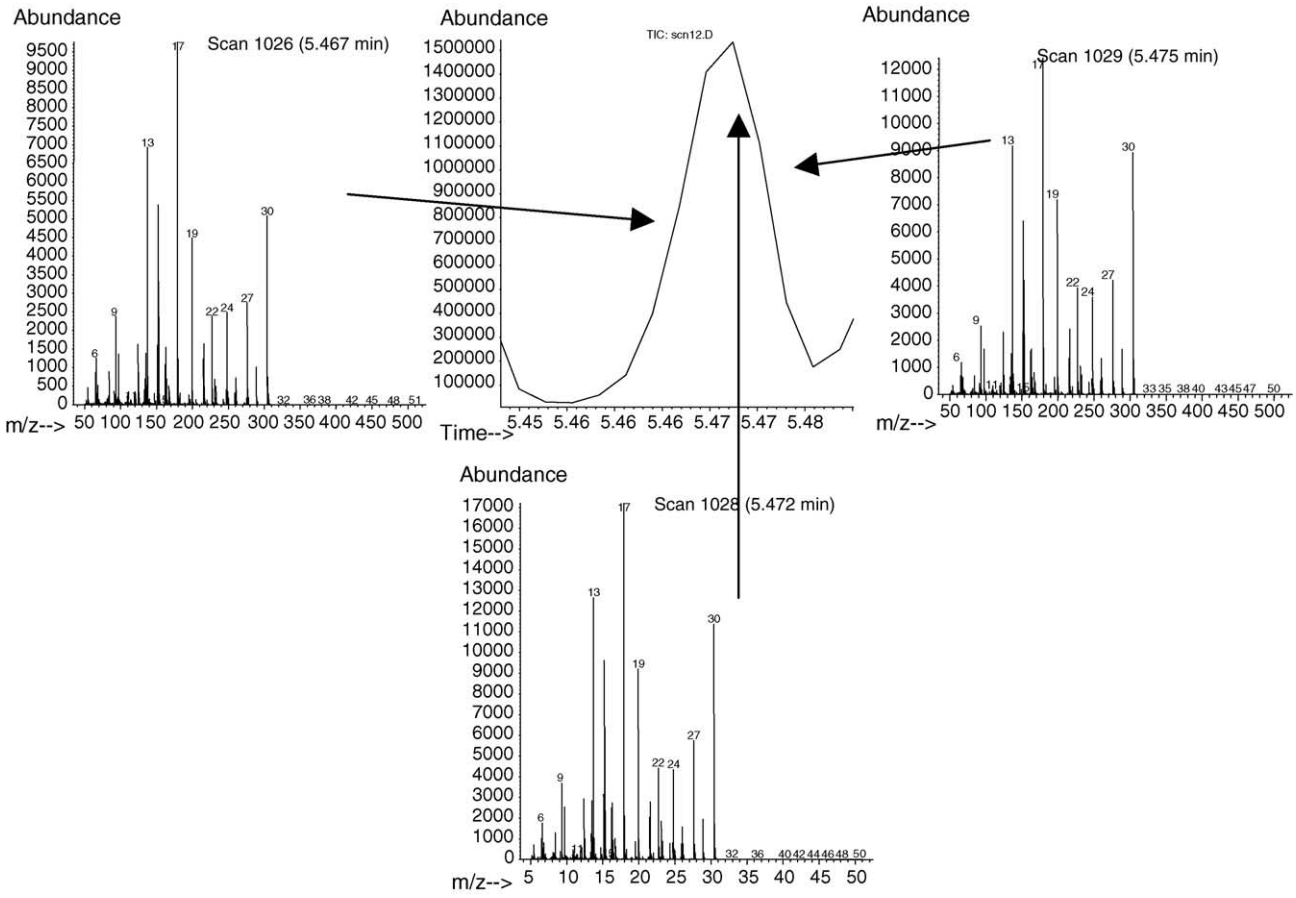

Fig. 4. Comparison of spectra skewing in full scan mode at sampling set to 1, with scan rate 5.98 scan s^{-1}, diazinon, injected amount 3 ng.

3.2. Selected ion monitoring (SIM)

For quantitative analysis with quadrupoles, especially at low concentration levels, selected ion monitoring mode is preferred mainly due to its higher sensitivity. The dependence of average peak areas ($n = 8$) as the measure of response was searched for the following dwell time 10, 25, 50, 75 and 100 ms. Solution of *n*-alkanes and pesticides in neat toluene with approximate concentration 0.3 ng μl^{-1} was used. Compounds were sorted into groups for SIM according to their elution times and three ions were selected for each compound (except for pyrimethanil and bitertanol with two ions).

Each SIM group contained selected ions for one to four compounds, therefore 3–11 ions were monitored for each group, as shown in Table 1. For peak area integration the same target ions were used as in the full scan experiments. The change of responses with different dwell times applied is not significant. The repeatability of peak areas was dependent on the compound nature and the applied dwell time and was found below 3% of RSD for dwell times 25 and 50 ms, for dwell time 10 ms, repeatability of peak areas expressed as RSD was up to 5%. For dwell times 75 and 100 ms, significantly worse repeatability of peak area measurements was obtained, reaching up to 80%. S/N ratios calculated for target ions were increasing with increasing dwell time. In Fig. 5, average peak areas (obtained from the integration of target ion peaks), repeatability of peak area measurements and average S/N ratio ($n = 8$ for all) are presented for selected compounds. Very similar trend was observed for all compounds under study. The peak widths in half heights were slightly increasing (about 3%) with increasing dwell time, but the significant increase was observed for the dwell time 100 ms due to the strong peak shape distortion. Also target to qualifier ion ratios and its repeatability were searched. For the shorter dwell times in the range of 10–50 ms, target to qualifier ion ratios were constant with the repeatability in the range of 1–2%. At the higher applied dwell times target to qualifier ion ratios changed and also their repeatability was significantly worse (RSD up to 35%), due to the insufficient

Table 2
The dependence of match factor expressing the similarity of the measured spectra at different number of samples taken for spectra acquisition, compared to the spectra library NIST'02

Compound	Average spectra match quality samples				
	0	1	2	3	4
Chlorpyrifos-methyl	83.75	96.25	95.75	96	83.625
Fenitrothion	91.875	92	92	96.125	–
Chlorpyrifos	91.5	91.5	95	91.125	84.75

(–) No proper match in mass spectra library.

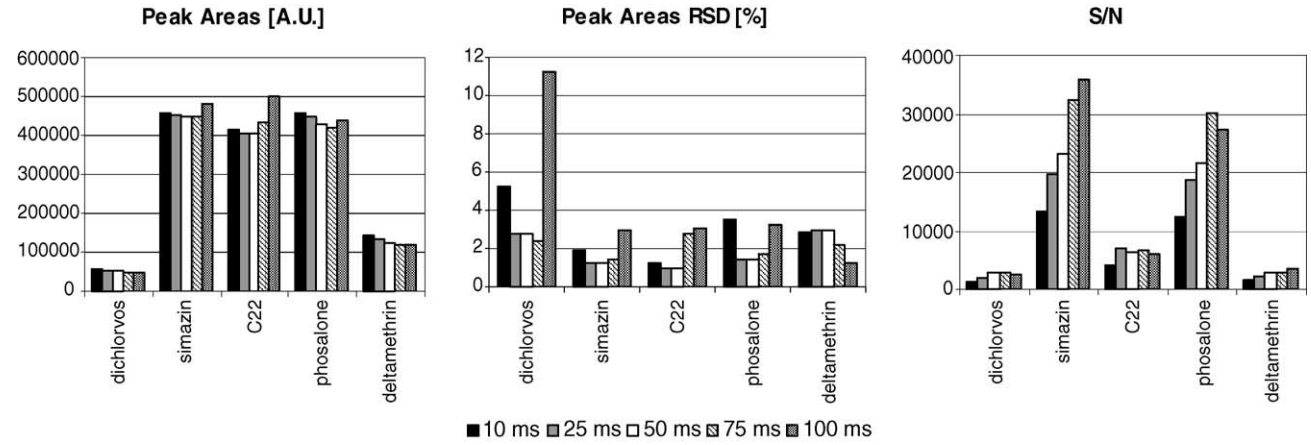

Fig. 5. The dependence of average peak areas, RSDs of peak areas and S/N ratios ($n = 8$) on different dwell times applied for SIM for selected compounds.

number of data points for the proper peak reconstruction and integration.

Calculation of the minimum peak width applicable for the required number of data points per peak at necessary number of ions monitored can be performed. It is important to realize, that to measure the dwell time of a selected duration for a given mass, MSD must set up parameters of quadrupole allowing the acquisition of a signal what takes approximately 15 ms for the parameters of quadrupole for a given measured mass, 10 ms for measurement (dwell time) and another approximately 5 ms at the end of SIM cycle to return back to the cycle starting settings. These values were calculated by the linear regression of different dwell time settings vs. the duration of one data-point measurement (the given time divided by the number of datapoints measured during the given time) for the given dwell time. The minimum peak half width detectable can be calculated by taking some minimum number of data-points per peak, e.g. six and minimum delay of SIM cycle 30 ms for 10 ms dwell time and 1 ion measured. The calculated peak half width is, ca. 0.11 s. Also the maximal number of ions for a given peak width in SIM window can be estimated. For the peak width, e.g. 1.68 s (peak width at the baseline of chlorpyrifos from our measurements) and the minimum number of cycles, e.g. six in order to obtain six data-points per peak with the minimum dwell time 10 ms (25 ms per ion and 5 ms per cycle) approximately 11 ions can be acquired. If three ions per compound are taken, up to four compounds can be simultaneously detected. The maximal number of compounds detectable in one fast GC–MS run is depending on elution times of analytes. Some gap approx. three to five seconds between the peaks groups is necessary for the adequate changing of SIM

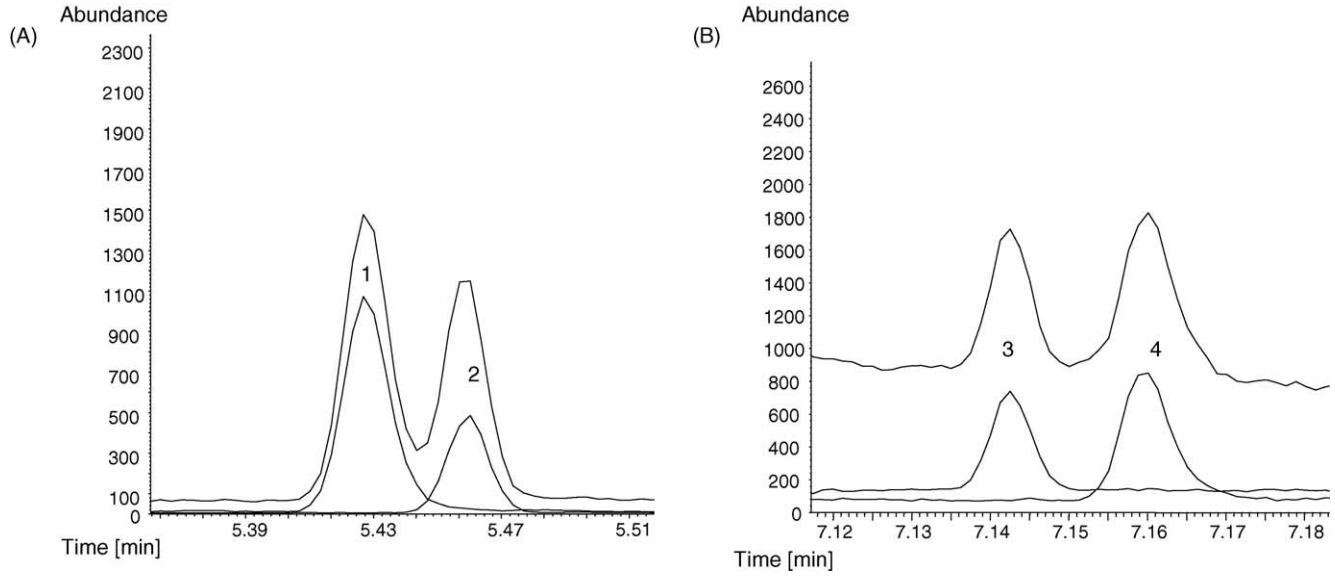

Fig. 6. Overlaid extracted ion chromatograms and TIC in SIM mode of close eluting compounds terbuthylazine (1) *m*/*z* 214 and diazinon, (2) *m*/*z* 304 in the chromatogram A; kresoxim-methyl, (3) *m*/*z* 131 and myclobutanil and (4) *m*/*z* 179 in the chromatogram B, measured with dwell time 10 ms in fortified apple extract (concentration 0.025 ng μl^{-1}, what represents concentration level in the sample 0.01 mg kg^{-1}) prepared according to ref. [16].

groups. To maximize the number of compounds to be analyzed in one fast GC–MS run, they should be selected to obtain the appropriate gaps for changing SIM groups. The proposed fast GC–MS method would be ideal for repetitive measurements of samples to perform quantitative analysis, for samples where the high degree of precision and trueness is needed, e.g. samples potentially exceeding maximal residual limits of pesticides in food. Fig. 6 shows an example of the overlaid ion chromatograms and total ion current (TIC) of co-eluting compounds represented by one ion for each compound (terbuthylazine and diazinon in the chromatogram A, kresoxim-methyl and myclobutanil in the chromatogram B) acquired at the dwell time 10 ms in SIM groups where six ions were simultaneously monitored in the extract of apple prepared according to ref. [15] fortified with pesticide standards at ultra-trace concentration of 0.025 ng μl^{-1} (10 μg/kg in original apples).

Utilization of narrow-bore columns with I.D. 0.15 mm (instead of 0.1 mm) in this study is a compromise between the time of analysis and requirements of quadrupole mass spectrometer and complexity of the analytical sample. It provides the use of MS at faster separation speed than conventional laboratory practice. Analysis time of 10 min is shorter by the factor of 1.7, when compared to conventionally used 0.25 mm I.D. columns when calculated using Method Translation Software [16]. Moreover, the ruggedness of 0.15 mm I.D. columns was shown very good and applicable to a complicated analysis as pesticide residues analysis in plant matrices [15] under criteria (LOQs $\leq$5 $\mu g\,kg^{-1}$) necessary for the analysis of pesticide residues in baby-food [17].

4. Conclusions

Presented results shows possibilities for the utilization of quadrupole MS as a detector in both, full scan and SIM mode for the detection in fast GC employing narrow-bore capillary columns. Good results of spectra quality were obtained for the highest scan rate. Careful selection of the scanned masses together with “samples” set to 0 can provide fast detection with as many as 20 spectra (20 data-points) per peak with 0.7 s width at half height. It is important to notice that sensitivity is significantly decreasing with increased scan rate and should be considered when selection of parameters is performed. When the highest sensitivity for identification is required and the peak shape is not important, the higher number of samples can be advantageously utilized. When the SIM mode is employed, there is a certain loss on S/N ratio with the shorter dwell times observed but the degree of the loss depends on a compound nature. The shortest dwell time 10 ms works comparably to longer ones with regards to peak areas measurements, but there are compound’s dependent differences in peak areas repeatability.

Acknowledgments

The authors gratefully acknowledge the support of a part of this research within the framework of the Slovak Grant Agency (VEGA, project no. 1/2463/05) and NATO project no. SfP 977 983.

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