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Liquid chromatography–electrospray mass spectrometry multi-residue determination of pesticides in apples and pears

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Abstract

This paper describes a rapid, specific and sensitive multi-residue method for the routine quantitative analysis of pesticides of several classes used for the treatment of apples and pears, down to their respective maximum residue limits (MRLs). It involves a rapid extraction procedure and liquid chromatography coupled to electrospray mass selective detection. Seven pesticides were extracted at pH 4.5 with a mixture of acetone–dichloromethane–hexane (50:20:30, v/v/v). Ionization was performed at atmospheric pressure in an electrospray-type source and detection was carried out using the selected ion monitoring (SIM) mode. Extraction recoveries were between 55 and 98% except for methylthiophanate (<20%). Limits of detection (LODs) and limits of quantitation (LOQs) ranged, respectively, from 0.01 to 0.02 mg/kg and from 0.02 to 0.05 mg/kg, with relative standard deviation (R.S.D.) less than 19%. An excellent linearity was observed for LOQs up to 5 mg/kg. Intermediate (''inter-assay'') precision and accuracy were satisfactory. The method was applied to many fruit samples intended for commercialisation.

Keywords: Maximum residue limits; Pesticides

1. Introduction

The monitoring of pesticide residues in food became a priority in pesticide research and health care. It presents a real interest for the protection of environment and for the evaluation of food quality. Pesticides are usually minimal in fruits, but one must be certain that they are below the maximum residue limits (MRLs), which are the MRLs accepted by the European Union [1–3].

Since our laboratory became involved in the control of apples and pears intended for commercialisation, we had to develop efficient and specific routine methods for the determination of the pesticides most frequently used by fruit growers. Gas chromatography (GC) has been the most common technique used for analysing fruits for pesticides [4]. As most polar and thermolabile pesticides are not suitable for GC [5,6], we developed a specific liquid chromatography–mass spectrometry (LC–MS) procedure for carbendazim, thiabendazole, dimethoate, pyrimicarb, methylthiophanate, phosmet, phenoxycarb.

High-performance liquid chromatographic (HPLC) methods for pesticide analysis in fruits occasionally used fluorescence [7], electron-capture and electrochemical detection methods [8,9] that

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present low selectivity. On the other hand, diode array UV–Vis and MS detectors [10,11] were frequently used and provided a selective detection. Among the different LC–MS interfaces, particle beam [12], electrospray (ES) [13] and atmospheric pressure chemical ionization (APCI) sources [14] have been seldom used, while thermospray has often been [15,16]. Now, the more recent ES and APCI interfaces seem to be the ideal systems for polar compounds. Recently, some authors used LC–ES-MS or tandem mass spectrometry (LC–ES-MS–MS) and demonstrated the suitability of these approaches for the sensitive and specific detection of pesticide residues [17–19], but up till now, the routine applications to pesticides in fruits are scarce [20]. The cost of instrumentation is probably a limitation to these methods.

Many of the methods published involved extraction and clean-up procedures, including solvent partitioning [12], solid-phase extraction (SPE) on Florisil [21,22], supercritical fluid extraction (SFE) [23], which are laborious and time consuming [24].

The purpose of the present method was to develop a rapid, specific and sensitive method for the routine analysis of seven thermally labile and polar pesticides in apples and pears. It involves a rapid extraction procedure and LC coupled, via an electrospray ionization source, to mass selective detection, in order to perform quantitative analysis below the pesticides' MRLs and suitable for large numbers of samples.

2. Experimental

2.1. Reagents and materials

Pure standards of all the pesticides were purchased as powders from Cluzeau Info Labo (Libourne, France). Stock standard solutions for each of the seven pesticides (carbendazim, thiabendazole, dimethoate, pyrimicarb, methylthiophanate, phosmet, phenoxycarb) were prepared at 1 g/l in methanol. Dichloromethane (DCM), acetone, hexane, acetonitrile (of pestinorm grade), acetic acid, ammonium acetate were purchased from Prolabo (Fontenay-sous-bois, France). All were of chromatographic purity. Working solutions were prepared by appropriate dilution of stock solutions in a mixture of acetone–dichloromethane–hexane (50:20:30, v/v/v) at the following concentrations: 1, 10 and 50 mg/l. A 50 mg/l solution of parbendazole (internal standard, I.S.) was prepared in the same solvent mixture. All standards and stock solutions were stored at +4°C over a three-month period.

2.2. Samples

Samples of apples and pears were collected from various fruit growers in Haute-Vienne (France). Pesticide-free fruits, controlled by ECOCERT (control office, certified by the European Union) were provided by La Vie Claire Company (Limoges, France) and used as blank matrix to prepare matrix matched standards for calibration.

2.3. Liquid chromatography–mass spectrometry

The HPLC system consisted of a SA 200 autosampler (Perkin-Elmer, Foster City, CA, USA), two Shimadzu LC-10AD pumps, a Nucleosil C_{18} (150×1 mm I.D., 5 μm particle-size) reversed-phase column (LC-packings, Touzart and Matignon, Courtaboeuf, France). A gradient of acetonitrile in 2 m*M* ammonium formate (pH 3) with a constant flow-rate of 40 μl/min was used as mobile phase. The percentage of acetonitrile was set at 25% for 1 min, then raised to 80% in 20 min, held at 80% for 1 min then reset to 25%. All chromatographic solvents were degassed with helium beforehand.

An API-100 Perkin-Elmer–Sciex (Sciex, Toronto, Canada) mass spectrometer, equipped with a pneumatically assisted-electrospray (Ionspray) system was used. It was operated in the positive ion detection mode. High-purity nitrogen was used as nebulization and curtain gas. Calibration of the mass analyzer was performed by infusion (5 μl/min) of a commercial mixture of polypropyleneglycol (Applied Biosystems, Saint Quentin-en-Yvelines, France) using a Harvard Model 11 syringe pump (Harvard Scientific, South Natick, MA, USA) and monitoring eight mass-to-charge ratios (m/z) in the 55 to 2300 u mass range. The main parameters settings of the MS were as follows: nebulization gas flow 0.95 l/min; curtain gas flow 1.16 l/min; orifice voltage 50 V; ionspray voltage 3500 V; electron multiplier voltage

1900 V. The main settings of the mass spectrometer acquisition were as follows: all 17 ions monitored in a single group with a dwell time of 100 ms for each ion at a step size of 0.1 unit. For each analyte, the most abundant and characteristic ion (generally the protonated molecule) was chosen for quantitation and one or two fragment ions selected for confirmation (Table 1). These mass-to-charge ratios were carefully selected to avoid all those belonging to other pesticide residues of the same class.

2.4. Extraction procedure

After homogenization of 1 kg of fruits, 10-g portions were sampled, to which were sequentially added 100 μl of internal standard solution (50 mg/l) and 10 ml of 3 *M* ammonium acetate solution (pH 4.5). The residues were extracted using 25 ml of an acetone–dichloromethane–hexane (50:20:30, v/v/v) mixture, by shaking for 15 min and then centrifuging at 3000 rpm (1600 *g*) for 5 min. The organic phase was evaporated at 50°C under a gentle stream of nitrogen. The dry extract was dissolved in 1 ml mobile phase containing 50% acetonitrile, and 2 μl of this solution were injected in the LC–MS system.

2.5. Validation

All validation procedures were performed using pesticide-free fruits. Calibration standards were prepared by adding appropriate working standard solutions to 10 g of pesticide-free fruit samples prior to extraction, in order to obtain concentrations ranging from 0.02 to 1 or 5 mg/kg. Recovery was determined in triplicate at three concentration levels by comparing the analyte/I.S. peak area ratios obtained after extraction of spiked samples with those of pesticide-free fruit extracts, spiked afterwards.

The intra-assay (repeatability) precision was assessed at 0.05, 0.2 and 0.8 mg/kg by extraction and analysis on the same day of five fortified fruit samples for each level. For the intermediate (''inter-assay'' or reproducibility) precision a set of calibrating samples were analyzed each day for five days. The detection limit (LOD) was determined as the lowest concentration giving a response of three-times the average of the baseline noise defined from three unfortified samples. The limit of quantitation (LOQ) was determined as the lowest concentration of a given pesticide giving a response that could be quantified with an inter-assay R.S.D. (or reproducibility's R.S.D.) of less than 26%.

Calibration graphs of the pesticide-to-internal standard peak-area ratios of the quantitation ions versus expected pesticide concentration were constructed, using a least-square linear regression analysis.

3. Results and discussion

Figs. 1 and 2 show TIC chromatograms of all 17 ions monitored, obtained, respectively, from a 1 mg/kg spiked apple sample and from an unspiked apple sample. The chromatographic resolution was satisfactory, except for pyrimicarb and dimethoate which were poorly resolved; however, they could be

Table 1
Chromatographic relative retention times, quantitation and confirmation ions selected for the LC–MS determination of seven pesticides in fruits

Pesticide	Relative retention time	Quantitation ion *m/z*	First confirmation ion		Second confirmation ion	
			m/z	Relative intensity (%)	m/z	Relative intensity (%)
Carbendazim	0.368	192	160	50	–	–
Thiabendazole	0.438	202	175	2	–	–
Dimethoate	0.605	199	171	41	–	–
Pyrimicarb	0.614	239	182	33	72	30
Parbendazole (I.S.)	1.000	248	–	–	–	–
Methylthiophanate	1.026	343	151	27	–	–
Phosmet	1.579	160	318	60	356	1
Phenoxycarb	1.675	302	256	22	–	–

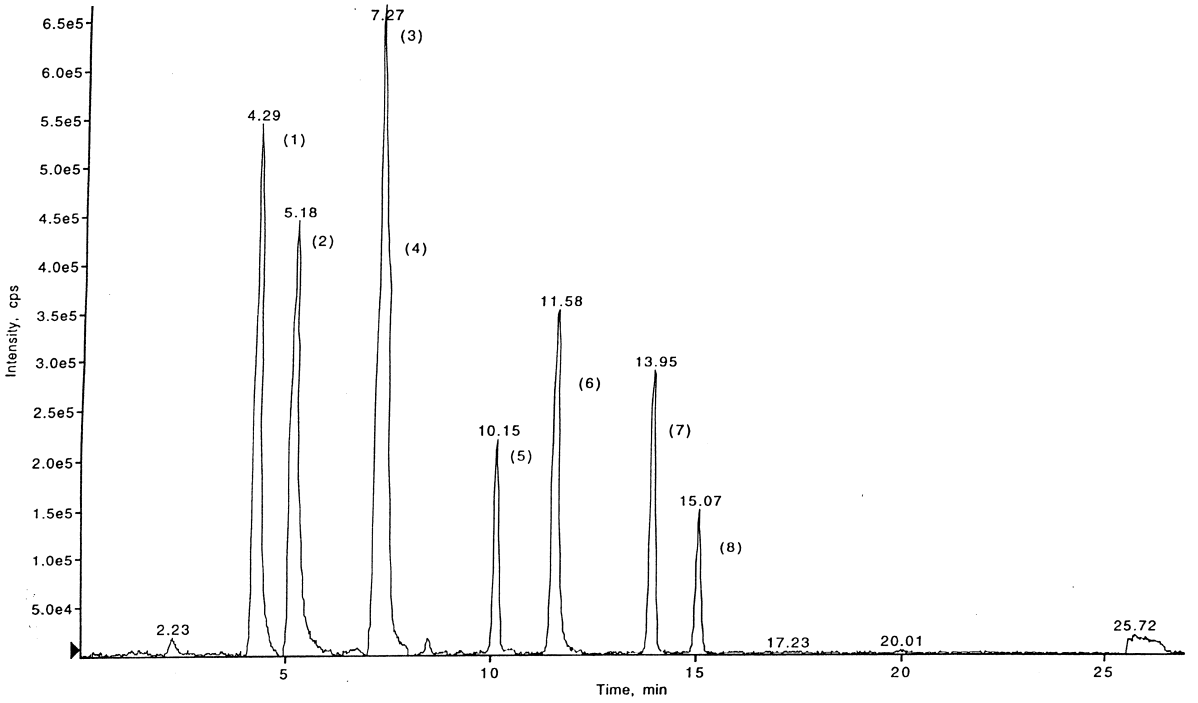

Fig. 1. Total ion current (TIC) chromatogram (17 ions monitored) of an apple sample spiked at 1 ppm of each pesticides mixture. Peaks: 1=Carbendazim, 2=thiabendazole, 3=pyrimicarb, 4=dimethoate, 5=methylthiophanate, 6=I.S.: parbendazole, 7=phosmet, 8=phenoxycarb.

easily identified and quantitated on individual ion chromatograms (in the SIM mode), due to different pseudo-molecular and fragment ions. The background obtained from chromatograms of real samples was very low and thus the extracts did not require further clean-up. Analysis of blank samples revealed no trace of the pesticides studied.

This multi-class/multi-residue extraction method, using only a mixture of acetone–dichloromethane–hexane, is suitable for both polar and slightly apolar pesticides. The combination of acetone–water extraction followed by a hexane–dichloromethane partitioning previously proved effective for a wide range of multi-class pesticide residues [4,25–27]. In addition to its high extraction efficiency in fruit, acetone has the advantages of low cost and relatively low toxicity. Addition of dichloromethane, which is widely used in liquid–liquid extraction procedures, despite its toxicity [28], present the significant advantage of a single partition. We have also tested polar solvents (methanol, acetonitrile) which are very efficient for polar residues and polar coextractives. Contrary to hexane, they revealed inefficient for coextractive partitioning and required a further clean-up to give clean extracts [25]. Instead, the mixture of acetone–dichloromethane–hexane yielded the maximal recoveries together with a low background for the seven compounds. Moreover, owing to the selectivity of the mass detector, no clean-up was necessary and time required was reduced. Average recoveries were in the range of 52.0 to 96.8%, except for methylthiophanate (18.9% at 0.20 mg/kg), with relative standard deviations (R.S.D.s) less than 19% (Table 2). We noticed average recoveries of methylthiophanate in pears are generally higher then those in apples except when methylthiophanate is present at 0.05 mg/kg (34.8%); in this case the R.S.D. is quite high (20%). The poor recovery and the high R.S.D. of methylthiophanate is probably due both to matrix effect and to its partial degradation to carbendazim during fruit processing. Few authors [29] have reported this partial degradation to carben-

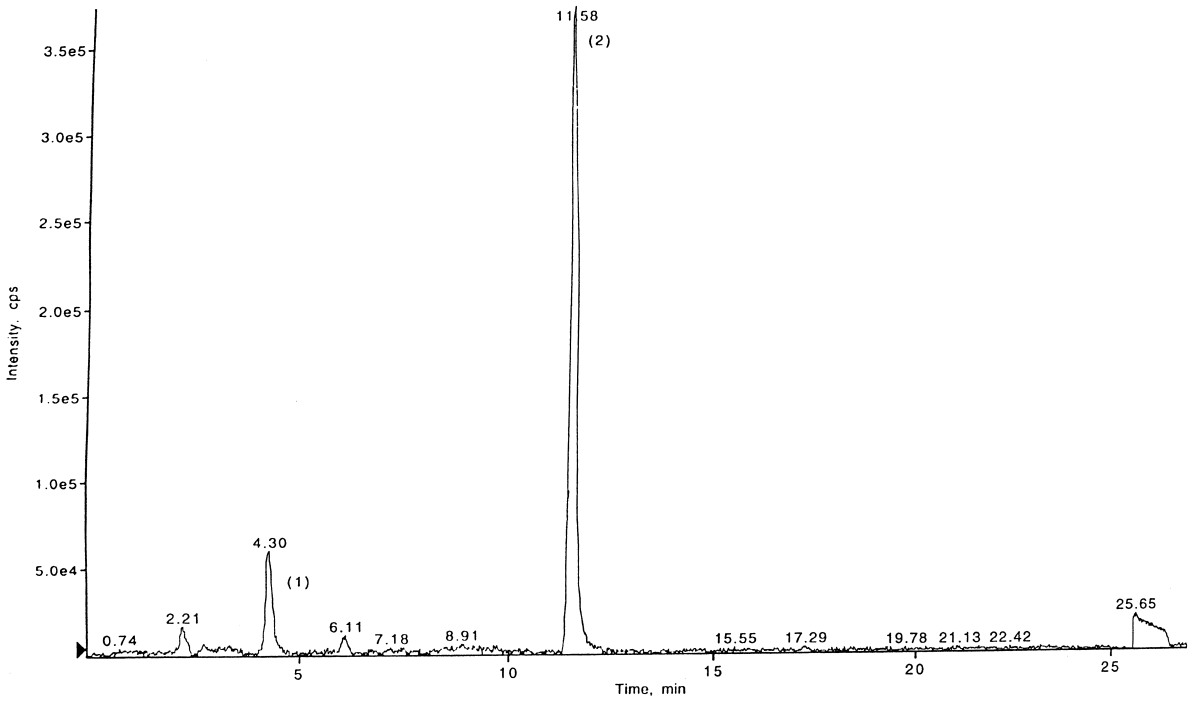

Fig. 2. Example of total ion current (TIC) chromatogram (17 ions monitored) of a positive real apple sample at 0.09 mg/kg. Peaks: 1=Carbendazim, 2=I.S.: parbendazole.

dazim under acidic conditions. Nevertheless, methylthiophanate is also reportedly stable in acidic solutions, but unstable at pH 7 and under alkaline conditions [30]. As, the acidic pH of our procedure of extraction has to be convenient for all the pesticides studied, it could not be set to another value, eventually more favourable to methylthiophanate.

We observed differences between the two matrices: LOQs obtained in apples are slightly higher than those obtained in pears (the same tendency is observed for phosmet and phenoxycarb). We noticed that more than 50% LOQs are over 0.02 mg/kg in apples. On the other hand, only the LOQ of methylthiophanate in pears is over 0.02 mg/kg. Nevertheless, we failed to show any statistical significance difference between LOQs of 0.02 and 0.05 mg/kg for any of these compounds, probably due to the high R.S.D. values.

ES ionization [31–33] is a soft ionization technique that induces a low fragmentation and produces mainly protonated molecular ions $[M+H]^+$. All the analytes displayed simple positive-ion mass spectra with an intense protonated molecule and only a maximum of one fragment ion of relevant abundance (except for pyrimicarb). In the present method, collision induced dissociation in the atmospheric pressure source allowed to obtain at least one ion of confirmation for each analyte of reasonable intensity (Table 1). Fragmentation can thus be induced by varying the orifice voltage; we carefully fixed this parameter, which is also crucial for an efficient transmissions of ions, to obtain the best compromise between sensitivity and fragmentation. Despite its low relative intensity, the reproducibility of m/z 175 in the thiabendazole spectrum is sufficient to use it as confirmation ion. Moreover, the selectivity and specificity of the determination were enhanced by using relative retention times and ratios of confirmation ions to their respective quantitation ion (Table 1).

The results of the validation procedure are summarised in Table 3. LODs of the method ranged from 0.01 to 0.02 mg/kg and LOQs from 0.02 to 0.05 mg/kg (Table 3), i.e., a good similarity of results

Table 2
Results of the validation procedure of the LC–MS analysis of seven pesticides in apples and pears

Concentration (mg/kg)	Recoveries		Repeatability		Reproducibility (n=5)	
	Average (R.S.D., %)		Average (R.S.D., %)		Acurracy (R.S.D., %)	
	Apples	Pears	Apples	Pears	Apples	Pears
Carbendazim						
0.02	–	–	–	–	200 (23.1)	100 (11.4)
0.05	84.6 (56)	79.28 (9.6)	0.07 (17.5)	0.09 (9.2)	140 (17.9)	140 (15.6)
0.10	–	–	–		140 (10.1)	130 (13.5)
0.20	87.1 (3.9)	72.86 (4.0)	0.37 (8.2)	0.31 (11.0)	115 (11.8)	105 (9.6)
0.50	–	–	–	–	112 (12.4)	118 (11.3)
0.80	91.66 (2.3)	93.32 (5.5)	0.97 (2.9)	0.90 (8.6)	101 (4.9)	98.8 (4.8)
1.00	–	–	–	–	94 (4.9)	101 (9.3)
r					0.995 (0.399)	0.991 (0.35)
Thiabendazole						
0.02	–	–	–	–	150 (17.8)	100 (15.5)
0.05	65.86 (4.2)	60.7 (16.4)	0.06 (15.4)	0.08 (11.7)	100 (18.4)	100 (19.9)
0.10	–	–	–	–	110 (10.0)	100 (17.1)
0.20	65.94 (5.4)	65.18 (2.6)	0.32 (6.8)	0.22 (11.6)	95 (3.9)	100 (11.0)
0.50	–	–	–	–	101 (15.7)	108 (4.8)
0.80	74.78 (3.3)	82.38 (3.1)	0.96 (3.9)	0.74 (7.6)	100 (6.5)	97.5 (9.6)
1.00	–	–	–	–	99 (6.4)	102 (6.7)
r					0.996 (0.273)	0.995 (0.27)
Dimethoate						
0.02	–	–	–	–	150 (25.6)	100 (11.8)
0.05	70.16 (5.8)	87.58 (6.8)	0.06 (15.7)	0.09 (6.9)	120 (21.6)	120 (21.5)
0.10	–	–	–	–	120 (15.7)	100 (16.6)
0.20	61.18 (6.5)	56.44 (4.4)	0.32 (10.0)	0.33 (11.0)	110 (9.5)	90 (13.6)
0.50	–	–	–	–	106 (19.2)	116 (3.2)
0.80	75.52 (6.7)	52.94 (5.5)	0.97 (4.3)	0.99 (0.19)	98.5 (8.1)	96.3 (8.0)
1.00	–	–	–	–	98 (9.5)	106 (4.0)
r					0.999 (0.821)	0.995 (3.53)
Pyrimicarb						
0.02	–	–	–	–	150 (17.9)	100 (18.4)
0.05	88.24 (3.8)	85.6 (6.5)	0.05 (19.0)	0.06 (6.6)	120 (14.4)	100 (21.6)
0.10	–	–	–	–	110 (16.8)	110 (21.6)
0.50	76.86 (6.4)	75.92 (4.4)	0.29 (4.1)	0.35 (10.5)	100 (6.0)	90 (18.2)
1.00	–	–	–	–	106 (12.2)	110 (2.8)
2.00	82.56 (3.4)	91.9 (4.2)	0.95 (2.2)	1.08 (11.1)	95 (8.3)	93.8 (6.1)
5.00	–	–	–	–	100 (6.4)	102 (4.2)
r					0.999 (0.307)	0.998 (0.13)
Methylthiophanate						
0.02	–	–	–	–	100 (22.2)	100 (22.7)
0.05	20.18 (3.8)	34.8 (20.0)	0.05 (15.7)	0.05 (14.4)	100 (36.1)	80 (16.7)
0.10	–	–	–	–	110 (26.0)	100 (16.6)
0.20	18.9 (8.7)	59.96 (12.8)	0.31 (8.1)	0.36 (12.8)	90 (14.8)	100 (17.0)
0.50	–	–	–	–	94 (11.0)	98 (8.9)
0.80	23.18 (5.0)	52.94 (4.6)	1.10 (3.9)	1.10 (14.4)	90 (14.4)	105 (8.8)
1.00	–	–	–	–	108 (9.3)	92 (8.0)
r					0.998 (1.051)	0.998 (1.36)

Table 2. Continued

Concentration (mg/kg)	Recoveries		Repeatability		Reproducibility (n=5)	
	Average (R.S.D., %)		Average (R.S.D., %)		Acurracy (R.S.D., %)	
	Apples	Pears	Apples	Pears	Apples	Pears
Phosmet						
0.02	–	–	–	–	150 (17.5)	150 (15.5)
0.05	83.42 (8.3)	90.1 (2.8)	0.07 (11.9)	0.08 (8.7)	120 (12.5)	160 (10.1)
0.10	–	–	–	–	150 (18.8)	140 (16.5)
0.20	77.58 (6.2)	92.9 (8.3)	0.37 (2.4)	0.38 (7.6)	115 (11.5)	130 (17.7)
0.50	–	–	–	–	110 (6.3)	116 (6.9)
0.80	94.5 (1.8)	96.8 (5.9)	1.02 (13.4)	0.93 (13.3)	96.3 (8.2)	94 (4.9)
1.00	–	–	–	–	98 (3.6)	99 (5.8)
r					0.999 (0.186)	0.988 (0.29)
Phenoxycarb						
0.02	–	–	–	–	150 (36.3)	100 (20.6)
0.05	71.66 (5.1)	88.36 (6.9)	0.07 (14.8)	0.04 (10.2)	120 (10.7)	120 (12.1)
0.10	–	–	–	–	120 (17.9)	120 (8.4)
0.20	82.36 (5.4)	88.7 (9.4)	0.20 (7.8)	0.37 (9.5)	100 (22.0)	102 (6.8)
0.50	–	–	–	–	110 (7.9)	112 (3.8)
0.80	83.66 (3.1)	94.04 (4.9)	0.74 (6.9)	1.05 (5.0)	95 (11.3)	100 (4.0)
1.00	–	–	–	–	100 (6.9)	99 (2.7)
r					0.999 (0.374)	0.998 (0.07)

r: Average of coefficients of correlation.
R.S.D.: Relative standard deviation.
Accuracy=100+[(measured value−true value)/true value]·100.

despite the diversity of the pesticides. The poorest LOQs (0.05 mg/kg) correspond to low recoveries (methylthiophanate and dimethoate) and the highest R.S.D.s to a low ionization efficiency (confirmed by tests on pure substances). We also observed differences between the two matrices analyzed with respect to LOQs and recoveries: LOQs obtained for methylthiophanate and dimethoate in apples were slightly higher than those obtained in pears; nevertheless, they were all satisfactory, being 10–100-times lower than MRLs admitted in the European Union for fruits [1], and comparable to those obtained by other authors with LC–ES-MS and LC–ES-MS–MS [18,19]. Moreover, these last methods required additional clean-up steps after analyte extraction.

The intra-assay precision was satisfactory (R.S.D.<19%) for all compounds at the three levels of concentrations tested (Table 2). The intermediate (''inter-assay'') precision was satisfactory for car-

Table 3
Maximum residue limits (MRLs) authorized in France, limits of detection and limits of quantitation of the seven pesticides assayed

Pesticide	MRL (mg/kg)	Limit of quantitation (mg/kg)		Limit of detection (mg/kg)	
		Apples	Pears	Apples	Pears
Carbendazim	2.00	0.05	0.02	0.02	0.01
Thiabendazole	3.00	0.02	0.02	0.01	0.01
Dimethoate	1.00	0.05	0.02	0.02	0.01
Pyrimicarb	0.50	0.02	0.02	0.01	0.01
Methylthiophanate	2.00	0.1	0.05	0.05	0.02
Phosmet	2.00	0.02	0.02	0.01	0.01
Phenoxycarb	0.50	0.05	0.02	0.02	0.01

bendazim, thiabendazole, phosmet and phenoxycarb, but not for methylthiophanate, dimethoate and pyrimicarb which showed R.S.D.s higher than 20%. We noticed variability for the reproducibility of methylthiophanate at low levels of concentration. On the contrary, the intra-assay precision was acceptable. The explanation is the variability of ionization recovery in electrospray source. We observed that there is difference in accuracy between reproducibility and repeatability for a given pesticide and a matrix. Accuracy is defined as the agreement between the measured value and the true value (see Table 2). If accuracy is high, then the difference between the measured value and the average concentration is low.

For all the pesticides, the repeatability and sensitivity of the method were good enough to ensure a reliable determination at levels lower than the respective MRL.

We have conclusively tested the routine efficiency of our method on hundreds of apple and pear samples. Time consuming methods could not allow the routine analysis of so many samples. The LC–MS response during routine analysis was found to be linear for the seven pesticides with r^2 ranging from 0.991 to 0.999 with a maximum R.S.D. of 1.36%. Our results showed that carbendazim was sometimes detected in pear and apple samples at levels lower than the MRL, and that the other pesticides were absent or found at very low levels. Regarding our validation results, and routine experience, we think that LC–MS is a mature technique for the multiresidue pesticide analysis in food.

4. Conclusions

The present method, involving a rapid and nonselective extraction and a LC–MS analytical technique allows the simultaneous determination of seven pesticides in apples and pears. It combines the advantages of LC and MS for the separation and unequivocal identification of pesticides belonging to different classes in real matrices. It showed satisfactory recovery values, repeatability and reproducibility and is highly sensitive and specific.

Moreover, it is rapid and allows the routine analysis of large number of samples. Finally, it is complementary to a GC–MS technique previously developed for the determination of pesticides of good thermal stability and low polarity in fruits [4]. The coupling of these two techniques provided us with an efficient and specific analytical system for this application and can be applied to others fruit matrices (bananas, red fruits, etc.).

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