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Assessing the performance of various sorbents in micro-solid phase extraction cartridges for pesticide residue analysis in feed†

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Newly designed micro-solid phase extraction cartridges are now available, reflecting the increasing shift towards laboratory automation, especially in the clean-up step for the analysis of pesticide residues in food and feed. In the present study, the introduction of different sorbents on the newly designed PAL μSPE CTC cartridges was investigated for the removal of matrix interferents and the recovery of pesticides. Eight cartridges containing different sorbent combinations and different amounts were used including EMR-lipid (not activated), Z-sep, chitin, C18, PSA, and GCB. The evaluation of co-extractive removal for each cartridge showed that the optimal choice for removing fatty acids was the cartridges containing PSA and Z-sep as clean-up sorbents. However, the presence of C18 and EMR-lipid was still required for the removal of sterols and tocopherols. Two grams of sample, fish feed (FF) and rapeseed cake (RSC) were extracted using QuEChERS citrate buffer, followed by a freeze-out step. The recoveries and repeatability of QuEChERS using μ-SPE clean-up were evaluated for 216 pesticide residues (112 compounds analyzed by GC-MS/MS and 143 compounds by LC-MS/MS, from which 39 compounds were analyzed using both techniques). The best results, with recovery between 70 and 120% and RSD <20%, were achieved when FF samples were cleaned-up with 15 mg EMR-lipid and 20 mg $MgSO_4$. This was achieved for 94% of GC-amenable compounds and 86% of LC-amenable compounds. In the case of RSC, the best results were seen when samples were cleaned-up with the cartridge containing only 20 mg Z-sep and 20 mg $MgSO_4$. This was achieved for 88% of GC-amenable compounds and 90% of LC-amenable compounds. Although these cartridges yielded optimal results in terms of recovery, their use could require more instrument maintenance, especially for GC-MS/MS, due to the lower removal of co-extractives.

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1. Introduction

Ensuring food and feed safety is a universal priority. The demand for international trade increases the necessity for high throughput multiresidue analysis of pesticides in monitoring laboratories all over the world. Many monitoring laboratories do not only face a shortage of resources for instruments and consumables but also often experience limited human resources. Besides, feed and feed ingredients cover a wide range of commodities with various origins and chemical compositions. Due to the considerably more diverse chemical composition of feed compared to food, analyzing pesticide residues and controlling Maximum Residue Levels (MRLs) to comply with EU Regulation 396/2005 [1] and Directive 2002/32 [2] present significant challenges.

Anastassiades *et al.* in 2003 [3] introduced the "quick, easy, cheap, effective, rugged and safe" (QuEChERS) method for sample preparation and determination of pesticide residues. Different modified versions of QuEChERS are used worldwide for residue analysis including not only pesticides but also environmental contaminants,[4–7] veterinary drugs,[8–11] and natural toxin.[12] The QuEChERS method is based on two main steps, sample extraction with acetonitrile and phase separation, followed by dispersive solid phase extraction (d-SPE) clean-up using PSA and/or C18 as a sorbent for pesticide residue analysis in fruits and vegetables. Although it produces reliable results for fruits and vegetables, when it is used in other more complex and difficult matrices, other sorbents (alone or in combination) give better results in the removal of co-extractive compounds. Various sorbents, including Z-sep and EMR-lipid, were used in different applications for the analysis of pesticides and veterinary drugs in complex food matrices.[13–17]

Despite the advantages that the QuEChERS method offers, there are still some disadvantages such as insufficient clean-up and difficulty automating. To reduce labor and improve precision, laboratory automation has been implemented through the utilization of robotic sample preparation tools in sample clean-up.[18] The micro-solid-phase-extraction (μSPE) clean-up method is a clean-up process, where the sample extract is delivered *via*

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a syringe at the desired volume and flow rate. The unwanted matrix components are retained on the cartridge, while the compounds of interest are eluted from the column.[19] The method was introduced by Morris and Schriner in 2015.[20] Later, Lehotay *et al.*[21] applied this technique for the determination of residues in different food matrices. In the following years, the use of μSPE clean-up was demonstrated to be effective for the analysis of pesticide residues in different commodities such as cereals, fish, lamb, hemp, tea, and spice.[6,18,22–29]

A current drawback of μSPE cartridges is a lack of different sorbent packings.

There are two types of μSPE cartridges mainly used in pesticide analyses, known as ITSP (Instrument Top Sample Preparation) μSPE cartridges. A total sorbent amount of 35 mg containing 8 mg of Z-sep, 23 mg of C18, and 1 mg of CarbonX is suggested for LC analysis. Another cartridge, comprising a combination of PSA (12 mg)/C18 (12 mg)/CarbonX (1 mg) and anhydrous $MgSO_4$ (20 mg) sorbents, is intended for GC analysis[19] The main limitation of the ITSP μSPE cartridges is related to the amount of sorbent that can be packed (up to 45 mg) and their low flow rate (2 μL s^{-1}). These limitations were overcome by a new product, PAL μSPE cartridges, introduced by CTC Analytics (Zwingen, Basel-Landschaft; Switzerland) in 2022, which can accommodate up to 150 mg of sorbent and up to a 10 μL s^{-1} flow rate. The PAL μSPE cartridges are septumless and composed of two pieces of polypropylene pressed very tightly together, which significantly lowers the risk of leakage that has been observed in the ITPS μSPE cartridges at flow rates greater than 2 μL s^{-1}. The new μSPE cartridge design allows the application of a higher flow rate.[30]

The aim of the present study was to assess the effect of the introduction of different sorbents on the new PAL μSPE CTC cartridges in terms of sample clean-up efficiency and acceptable levels of pesticide recoveries and reproducibility at 0.01 mg kg^{-1}. Various sorbent (EMR-lipid, Z-sep, PSA, C18, chitin and graphitized carbon black) combinations and amounts were selected, matching the typical combinations in conventional d-SPE methods used in feed analysis. Recoveries and repeatability were evaluated for the customized cartridges for 216 pesticide residues in two fatty feed matrices, fish feed (FF), and rapeseed cake (RSC). The results were further evaluated for matrix removal. FF contains 38% proteins, 34% crude fats, and additives such as astaxanthin.[31] The RSC is rich in crude protein (~30%), crude fiber (~11%), and crude fat (approximately 17%).[32]

2. Materials and methods

2.1. Chemicals and reagents

Pure standards (purity > 96%) of pesticides were purchased from Sigma-Aldrich and LGC Standards. Stock solutions were prepared at a concentration of 1 mg mL^{-1} for each compound and stored at −20 °C. The solvent used for the solution preparation was either toluene or methanol depending on analyte solubility and stability. The stock solutions were combined in a mixture at a concentration of 10 mg L^{-1}. A full list of the compounds investigated in this study and their chemical properties is given in Table S1.†

Acetonitrile and methanol of HPLC-grade were purchased from Merck. Deionized water of 18.2 MΩ cm was obtained using an E-Pure system from Barnstead/Thermolyne Premade. A mixture of salts containing 6.5 grams of $MgSO_4$, NaCl, $C_6H_9Na_3O_9$, and $C_6H_9NaO_8$ (at a ratio of 4/1/1/0.5) in 15 mL polypropylene (PP) tubes was purchased from Merck (Sigma Aldrich, Germany).

Eight different customized μSPE cartridges were obtained from CTC Analytics (Zwingen, Basel-Landschaft; Switzerland). The cartridge sorbent and amounts used in this study are given in Table 1. The sorbents were: EMR-Lipid (EMR), Z-sep, Chitin, C18, PSA, and GCB. The EMR was used in two different amounts in the cartridges, referred to as EMR-low for the sorbent combination containing 15 mg EMR and 20 mg $MgSO_4$, and EMR-high for 30 mg EMR and the same amount of $MgSO_4$. The same approach was taken with chitin; two cartridges were utilized, namely chitin-low for the sorbent combination containing 15 mg chitin and 20 mg $MgSO_4$, and chitin-high for 30 mg chitin with the same amount of $MgSO_4$. The cartridge containing 20 mg Z-sep and 20 mg $MgSO_4$ is referred to as Z-sep. The cartridges containing a mixture similar to ISTP μSPE (12 mg PSA/12 mg C18/1 mg GCB/20 mg $MgSO_4$ and the one containing 8 mg of Z-sep, 23 mg of C18, and 1 mg of GCB) are referred to as μSPE-GC and μSPE-LC cartridges. The cartridge containing a combination of 15 mg C18 and 20 mg $MgSO_4$ is referred to as C18 in the text. It is important to note that these names are used solely for the purposes of this study.

2.2. Sample preparation and extraction

The RSC blank sample was provided by the European reference laboratory for cereals and feeding stuff (EURL-CF), where it was grown in connection with the 15th European Commission's Proficiency Test on Cereals and Feed, EUPT-CF15.[33,34] The FF samples were salmon feed (EFICO) produced by BioMar, Denmark.

The samples were homogenized using an Ultra Centrifugal Mill ZM 200. Two grams of homogenized blank samples were spiked with 100 μL of 0.2 mg L^{-1} pesticide mix solution to yield a concentration of 0.01 mg kg^{-1}. Additionally, 100 μL of 0.2 mg L^{-1} procedural standard consisting of azoxystrobin-d_4, dichlorvos-d_6 and etofenprox-d_5 were added. Blank samples were prepared for quality control measures.

The samples were extracted using the QuEChERS citrate-buffered method. Initially 10 mL of water was added to the sample and mixed. Then, 10 mL of acetonitrile was added for the extraction. The samples were shaken for 1 minute at 750 rpm using a Geno Grinder 2010. For phase separation, a mixture of 6.5 gram of salts, containing $MgSO_4$, NaCl, $C_6H_9Na_3O_9$, and $C_6H_9NaO_8$ (at a ratio of 4/1/1/0.5), was added to the extracts and shaken for another minute, followed by 10 min centrifugation at 4500 with a Thermo Multifuge X3FR. Eight milliliters of supernatant were transferred to a 15 mL polypropylene tube and stored in a freezer at −80 °C for at least 1 hour. After freezing-out, the extract was thawed and centrifuged for another 10 min at 4500 rpm at 5 °C.

Table 1 μSPE cartridge composition

Name	Sorbent composition	Sorbent amount in mg	Total amount in mg
EMR-low	EMR lipid/$MgSO_4$	15/20	35
EMR-high	EMR lipid/$MgSO_4$	30/20	50
Z-sep	Z-sep/$MgSO_4$	20/20	40
Chitin-low	Chitin/$MgSO_4$	15/20	35
Chitin-high	Chitin/$MgSO_4$	30/20	50
C18	C18/$MgSO_4$	15/20	35
μSPE-GC	C18/PSA/GCB/$MgSO_4$	12/12/1/20	45
μSPE-LC	C18/Z-sep/GCB	21/8/1	30

2.3. Automatic sample cleanup

A customized Thermo Scientific™ TriPlus™ RSH™ (based on a PAl3_RTC autosampler from CTC Analytics) controlled with Chromeleon software was used for clean-up. The system contains two independent tray holders dedicated to μSPE in parallel, one for ITSP μSPE and the other for PAL μSPE. A third tray intended to be used for sample dilution and calibration curve preparation is also included in the configuration. The system is shown in Fig. S1.†

The μSPE clean-up workflow, previously described by Hakme & Poulsen,[29] was extended with additional sample preparation, namely, sample dilution, and automatic addition of internal standards.

The clean-up procedure was performed with a 250 μL aliquot of extract. The extract was eluted from the cartridges at 2 μL s^{-1}. The extract volume and flow rate used were recommended at the time of the experiment from the PAL μSPE producer. To align with the matrix amount in the calibration standard, the cleaned extract was diluted with acetonitrile (100 μL extract + 100 μL acetonitrile) and automatically transferred into a clean sample vial. After the dilution, a 20 μL quality standard mix was added and the extract was thoroughly mixed. In Table S2† are given the detailed steps of the updated workflow.

2.4. Assessment of co-extractive removal

Blank sample extracts (for both matrices) obtained with QuEChERS without clean-up, along with the cleaned extracts obtained using various μ-SPE cartridges as previously described, were injected into a GC-MS. A comparison between the total ion chromatograms (TICs) of the sample extract before and after μSPE clean-up was made using the following formula: $[(\text{area}_{\text{raw extract}} - \text{area}_{\text{cleaned extract}})/\text{area}_{\text{raw extract}}] \times 100$.

2.5. Assessment of pesticide recovery

For the evaluation of sorbent effects on the analyte loss, uncleaned spiked extracts were combined after the centrifugation step and were mixed thoroughly in order to make a uniformed extract. Finally, at least 1 mL was transferred to a 2 mL glass vial and placed on the sample tray on a μSPE sample tray holder for clean-up. Five portions for each type of μ-SPE cartridge were used. For quantification, matrix-matched calibration standards were prepared by using a blank sample extract cleaned through the same sorbent. The extracts were analyzed by GC-MS/MS and LC-MS/MS. Recovery in percentage and repeatability expressed as relative standard deviation (RSD) were calculated.

2.6. Analytical instrument

For gas chromatographic separation, a Thermo Scientific™ Trace™ 1310 Gas Chromatograph coupled to a Thermo Scientific™ TriPlus™ RSH autosampler was used. The injection volume was 1 μL and a programmable temperature vaporizer (PTV) large volume mode was used with a PTV baffle liner 2 × 2.75 × 120 mm from Thermo Scientific™. The injection temperature was 70 °C and the split flow rate was set to 15 mL min^{-1} for 1 min at 70 kPa during the injection phase. Afterward, the split vent was closed, and the inlet was heated up to 210 °C at 5 °C s^{-1} and held for 2 min. To remove any high boiling residue inside the inlet, the inlet temperature was finally ramped to 330 °C and a split vent flow rate of 75 mL min^{-1} was set for 10 min. Ultrahigh purity helium was used as the carrier gas at a flow rate of 1.2 mL min^{-1}. A capillary column TG-5SILMS W/5m Safeguard, 30 m length, 0.25 mm internal diameter and 0.25 μm film thickness, was used. The program oven temperature started at 60 °C for 1.5 min, and then ramped up to 25 °C min^{-1} at 90 °C for 1.5 min, up to 180 °C at 25 °C min^{-1}, and then up to 280 °C at 5 °C min^{-1} and finally up to 300 °C at 10 °C min^{-1} for 12 min. For the mass spectrometric analysis, a Thermo Scientific™ TSQTM 8000 Evo was used. The MS has been upgraded with an advanced electron ionization source (AEI) operated with an electron energy of 50 eV. The transfer line was set at 280 °C and the ion source temperature was set at 300 °C. The analyses were performed in multiple reaction monitoring mode (MRM).

For liquid chromatographic separation, an LC system Thermo Ultimate 3000 and a mass spectrometer Bruker EVOQ were used. The analytes were separated on a Waters Accuity UPLC BEH C18 1.7 μm × 2.1 × 100 mm reversed-phase column. The injection volume was 1 μL. The eluents consisted of Milli-Q water with 0.1% formic acid and 5 mM ammonia solution (A eluent) and methanol (B eluent). A flow rate of 0.4 mL min^{-1} was applied. The analytes were separated using a gradient elution program. Before every injection the column was equilibrated with 2% B eluent. After the injection, eluent B increases up to 35% within 0.1 min and then up to 98% in seven min. For three more minutes, the eluent remains still and 98% of B

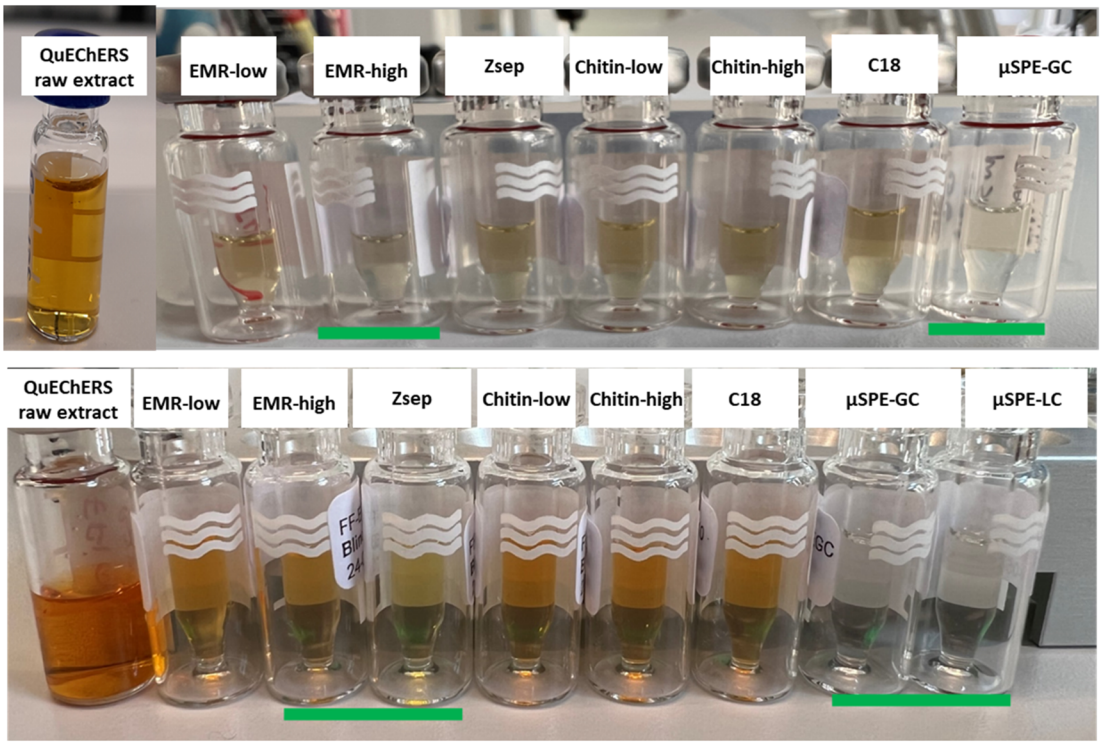

Fig. 1 Vials containing cleaned extracts of RSC (above) and FF (below), including the raw extracts and the cleaned ones with different types of cartridges.

eluent is then maintained for 3 min. In the last step, the eluent goes back to 2% for only 0.1 min. The mass spectrometer was operated in MRM mode and using both positive and negative electrospray ionization (ESI).

The MS/MS conditions for the GC and LC analytes are given in Tables S3 and S4.†

3. Results and discussion

3.1. Co-extractive removal

A visual comparison of the transparency and color of the extracts obtained with QuEChERS without clean-up and the cleaned extracts obtained with the different µ-SPE cartridges are shown in

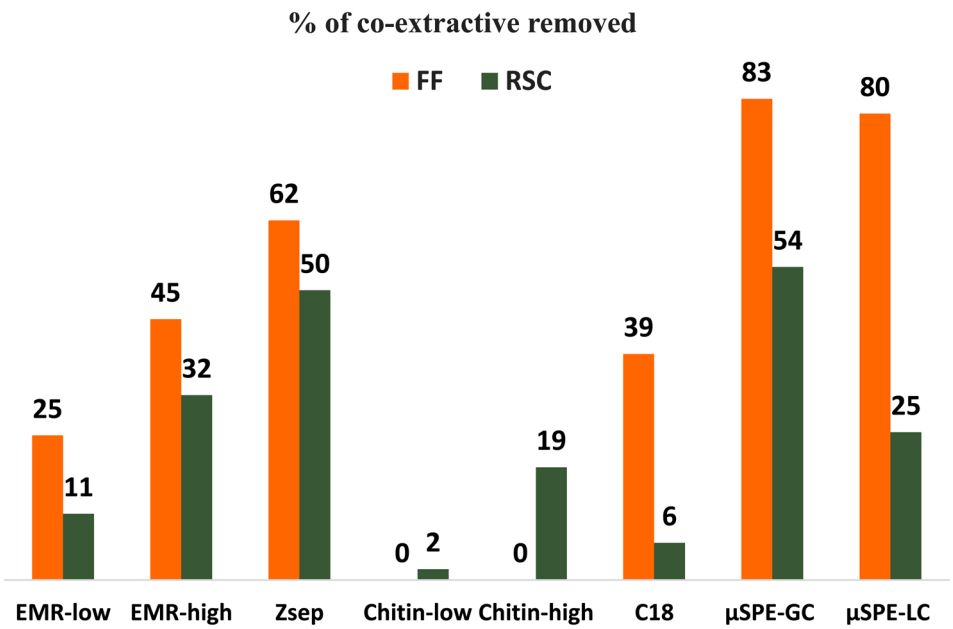

Fig. 2 Percentage of co-extractive compounds removed from FF and RSC by comparing the TICs before and after the clean-up for each matrix and cartridge.

Fig. 1. In both cases, the color intensity (the green in RSC and red in FF) decreased significantly when GCB was used (cartridges μSPE-GC and μSPE-LC). In the RSC, the extract became colorless when cleaned with the cartridges containing 30 mg of EMR. The removal of color for both sorbents has been previously shown in different studies using dispersive clean-up.[16,35,36]

To further explore the clean-up effect of different sorbent compositions, an evaluation of the co-extractive efficiency removal was made in terms of the chromatographic background by comparing the TICs of the sample extract before and after μSPE clean-up using the formula in paragraph 2.4. The TICs obtained from GC-MS scan are shown in Fig. S2–S10.† Fig. 2 shows the percentage of co-extractive removed from FF and RSC using each of the cartridges.

For the RSC, the lowest removal efficiency was observed with the Chitin-low cartridge, where there was approximately a 2% difference between the TIC areas of the cleaned and uncleaned extracts, followed by ~6% for the C18 cartridge, ~11% for EMR-low and ~20% for chitin-high. Improved clean-up was observed with μSPE-LC, EMR-high, Z-sep, and μSPE-GC cartridges, where the co-extractive removal was assessed to be ~25, 32, 50, and 54% respectively.

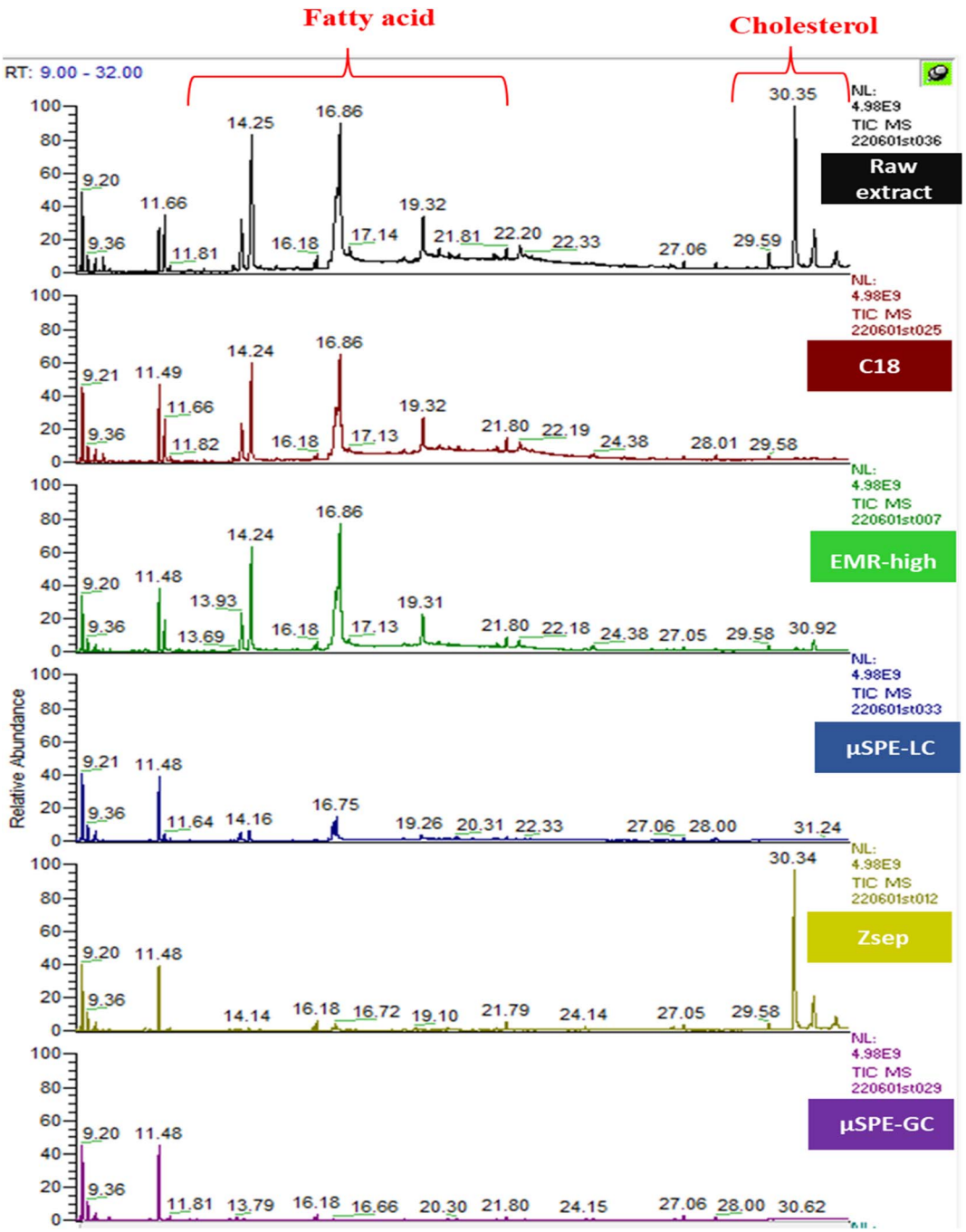

Fig. 3 Total ion chromatogram of the FF extract before clean-up and after μSPE clean-up with C18, EMR-high, μSPE-LC, Z-sep and μSPE-GC.

Table 2 Average recoveries (%) and RSDs (%); ($n = 5$) for spiked extracts of FF and RSC at 0.01 mg kg^{-1}. Recoveries <70% and >120% and RSDs greater than 20% are shown in bold. EMR-low (15 mg EMR-lipid/20 mg $MgSO_4$); EMR-high containing 30 mg EMR-lipid/20 mg $MgSO_4$; Z-sep (20 mg Z-sep/20 mg $MgSO_4$); μSPE-GC (12 mg C18/12 mg PSA/1 mg GCB/20 mg $MgSO_4$); μSPE-LC (21 mg C18/8 mg Z-sep/1 mg GCB)

			EMR-low		EMR-high		Z-sep		μSPE-GC		μSPE-LC	
Nr	Analytes	Tool	FF	RSC	FF	RSC	FF	RSC	FF	RSC	FF	RSC
1	2-Phenylphenol	GC	96 (8)	105 (8)	**128** (6)	118 (8)	**130** (15)	116 (5)	104 (6)	115 (13)	**127** (10)	112 (11)
2	3-Hydroxycarbofuran	LC	83 (14)	**135** (7)	94 (6)	117 (4)	94 (9)	113 (12)	87 (9)	119 (9)	93 (6)	—
3	Acephate	LC	85 (8)	104 (8)	82 (5)	96 (10)	74 (10)	89 (15)	**69** (16)	93 (13)	84 (8)	94 (12)
4	Acetamiprid	LC	89 (5)	**47** (**24**)	92 (4)	**47** (**26**)	99 (8)	105 (5)	91 (5)	107 (1)	87 (4)	93 (6)
5	Acrinathrin	GC	97 (4)	78 (**28**)	113 (3)	96 (**54**)	112 (9)	100 (**26**)	100 (16)	—	101 (8)	—
6	Aldicarb	LC	82 (11)	104 (**34**)	91 (**24**)	86 (20)	92 (20)	**68** (**28**)	99 (13)	**145** (13)	91 (10)	99 (14)
7	Aldicarb-sulfone	LC	94 (17)	—	105 (12)	—	99 (11)	-	95 (9)	—	87 (8)	—
8	Aldicarb-sulfoxide	LC	**68** (7)	89 (15)	75 (8)	82 (4)	**64** (11)	86 (18)	78 (11)	93 (14)	—	82 (**26**)
9	Aldrin	GC	**65** (14)	**62** (9)	**66** (8)	**51** (17)	**69** (16)	**60** (9)	**61** (12)	**61** (71)	**51** (9)	**128** (86)
10	Atrazine	LC	101 (8)	105 (5)	**123** (3)	96 (3)	90 (2)	110 (3)	94 (2)	109 (5)	82 (6)	—
11	Azinphos-ethyl	LC	79 (13)	118 (13)	98 (6)	107 (14)	108 (8)	112 (10)	101 (20)	101 (17)	83 (7)	91 (10)
12	Azinphos-methyl	LC	85 (6)	105 (8)	98 (5)	112 (6)	98 (10)	105 (4)	90 (8)	102 (9)	76 (7)	94 (4)
13	Azoxystrobin	GC	95 (3)	114 (4)	111 (5)	102 (8)	**128** (10)	107 (3)	104 (6)	111 (18)	111 (8)	88 (17)
	Azoxystrobin	LC	89 (4)	112 (4)	104 (4)	103 (3)	97 (9)	111 (7)	94 (5)	108 (2)	88 (4)	104 (5)
14	Bifenthrin	GC	91 (11)	**60** (17)	88 (5)	**47** (9)	99 (9)	71 (18)	115 (8)	78 (8)	104 (10)	**51** (14)
	Bifenthrin	LC	75 (4)	**59** (9)	82 (12)	**64** (12)	84 (20)	**64** (7)	72 (17)	**43** (14)	**61** (15)	**39** (6)
15	Bitertanol	GC	91 (5)	92 (12)	108 (2)	**42** (**22**)	109 (8)	**121** (15)	88 (3)	—	—	—
	Bitertanol	LC	84 (8)	115 (7)	98 (12)	95 (17)	92 (10)	103 (6)	94 (3)	102 (4)	82 (13)	94 (7)
16	Boscalid	GC	93 (3)	105 (4)	108 (2)	101 (5)	117 (9)	113 (6)	94 (6)	**144** (**34**)	99 (10)	—
	Boscalid	LC	92 (10)	109 (10)	90 (5)	110 (6)	92 (3)	101 (6)	84 (7)	—	**65** (5)	—
17	Bromophos-ethyl	GC	79 (5)	71 (10)	89 (5)	63 (7)	106 (13)	77 (3)	77 (13)	**66** (8)	**64** (7)	**56** (10)
18	Bromopropylate	GC	87 (7)	77 (4)	103 (5)	78 (4)	109 (8)	95 (3)	98 (8)	84 (3)	94 (10)	74 (7)
19	Bromoxynil	LC	100 (10)	**121** (11)	92 (**25**)	104 (3)	—	87 (5)	**69** (**25**)	94 (16)	**45** (17)	83 (**26**)
20	Bromuconazole	GC	93 (9)	103 (14)	92 (7)	101 (11)	116 (10)	106 (10)	99 (4)	113 (18)	84 (14)	89 (5)
	Bromuconazole	LC	—	**121** (9)	—	103 (15)	—	103 (12)	-	108 (19)	—	91 (18)
21	Bupirimate	GC	99 (4)	104 (10)	103 (5)	105 (8)	118 (10)	118 (4)	105 (9)	116 (11)	103 (6)	99 (7)
22	Buprofezin	LC	83 (5)	85 (3)	88 (5)	78 (5)	92 (4)	91 (3)	82 (5)	84 (5)	72 (2)	**67** (6)
23	Cadusafos	GC	97 (4)	104 (6)	106 (3)	98 (4)	118 (11)	115 (5)	99 (7)	113 (12)	95 (9)	93 (9)
	Cadusafos	LC	86 (4)	104 (2)	96 (3)	98 (3)	96 (4)	103 (2)	90 (4)	100 (4)	75 (4)	84 (4)
24	Carbaryl	LC	86 (4)	107 (1)	100 (5)	101 (10)	98 (8)	106 (6)	93 (2)	**123** (4)	90 (2)	107 (6)
25	Carbendazim	LC	84 (5)	**62** (11)	85 (7)	**51** (12)	89 (3)	81 (5)	77 (3)	82 (5)	**44** (3)	—
26	Carbofuran	LC	82 (4)	**140** (4)	95 (3)	**133** (5)	91 (4)	**124** (6)	87 (2)	**150** (4)	79 (2)	107 (5)
27	Carboxin	GC	101 (6)	90 (4)	116 (5)	92 (7)	117 (10)	107 (6)	105 (6)	116 (10)	118 (12)	100 (3)
	Carboxin	LC	87 (5)	91 (6)	102 (5)	93 (8)	99 (5)	100 (5)	93 (6)	104 (5)	88 (5)	93 (7)
28	Chlorfenapyr	GC	111 (16)	79 (**39**)	113 (5)	109 (16)	96 (19)	93 (16)	113 (18)	117 (36)	114 (10)	111 (7)
29	Chlorfenson	GC	91 (4)	102 (5)	106 (3)	86 (8)	111 (8)	104 (4)	95 (4)	82 (14)	95 (6)	94 (12)
30	Chlorfenvinphos	GC	100 (2)	110 (12)	109 (4)	106 (7)	118 (7)	120 (6)	105 (5)	**123** (**8**)	100 (8)	114 (16)
31	Chlormephos	GC	118 (**28**)	97 (12)	**138** (**25**)	101 (12)	81 (10)	98 (5)	91 (5)	103 (11)	88 (11)	96 (5)
32	Chlorobenzilate	GC	90 (4)	97 (3)	105 (2)	94 (5)	113 (11)	103 (3)	99 (3)	102 (4)	96 (8)	88 (2)
33	Chlorpropham	GC	105 (10)	94 (13)	**123** (7)	88 (14)	**122** (**23**)	115 (3)	89 (14)	113 (6)	96 (13)	98 (2)
34	Chlorpyrifos	GC	85 (6)	93 (11)	102 (6)	82 (10)	109 (14)	97 (7)	94 (8)	86 (18)	81 (15)	76 (26)
	Chlorpyrifos	LC	82 (7)	86 (4)	102 (4)	85 (9)	90 (6)	82 (2)	78 (3)	75 (6)	**66** (2)	**62** (15)
35	Chlorpyrifos-methyl	GC	99 (13)	97 (10)	120 (6)	104 (8)	**141** (18)	104 (7)	99 (19)	106 (6)	113 (15)	104 (18)
36	Clethodim	LC	—	100 (8)	—	112 (8)	—	99 (7)	—	—	—	99 (16)
37	Clofentezine	GC	94 (6)	82 (16)	112 (14)	100 (15)	103 (**22**)	**68** (10)	—	—	80 (12)	**67** (19)
38	Clomazone	GC	101 (5)	104 (5)	113 (1)	102 (4)	120 (10)	**121** (5)	103 (9)	118 (4)	104 (8)	108 (6)
39	Clothianidin	LC	90 (5)	**40** (**36**)	94 (6)	107 (11)	96 (4)	115 (11)	—	107 (14)	83 (7)	103 (7)
40	Cyazofamid	LC	88 (6)	114 (2)	98 (5)	101 (2)	98 (10)	112 (6)	94 (5)	111 (4)	89 (8)	99 (5)
41	Cyfluthrin	GC	93 (3)	84 (6)	109 (4)	80 (7)	**68** (10)	94 (8)	114 (**27**)	88 (9)	99 (9)	95 (24)
42	Cyhalothrin-lambda	GC	95 (8)	96 (9)	114 (3)	87 (10)	113 (10)	**28** (49)	115 (20)	75 (8)	103 (10)	**55** (20)
43	Cypermethrin	LC	77 (6)	**59** (13)	103 (18)	90 (9)	85 (10)	72 (9)	70 (**26**)	75 (8)	**64** (11)	83 (**38**)
44	Cyproconazole	GC	—	—	—	—	102 (10)	112 (10)	101 (6)	**121** (6)	98 (5)	102 (7)
45	Cyprodinil	GC	84 (5)	83 (6)	96 (9)	86 (9)	108 (9)	102 (10)	86 (14)	92 (7)	**38** (17)	86 (**42**)
46	Deltamethrin_cis	GC	102 (7)	90 (11)	115 (2)	83 (13)	89 (21)	82 (7)	94 (18)	72 (40)	105 (12)	**69** (**36**)
	Deltamethrin_cis	LC	**69** (8)	—	93 (7)	—	99 (4)	72 (7)	85 (18)	76 (9)	81 (8)	81 (**39**)
47	Demeton-*S*-methyl	GC	107 (7)	112 (8)	111 (7)	114 (15)	119 (5)	104 (5)	112 (14)	**125** (8)	119 (14)	**219** (48)
	Demeton-*S*-methyl	LC	—	113 (5)	—	112 (5)	98 (6)	105 (6)	88 (7)	107 (8)	92 (8)	92 (5)
48	Demeton-*S*-methylsulfone	LC	85 (13)	103 (14)	**132** (**24**)	93 (15)	**136** (**35**)	114 (6)	76 (**54**)	115 (9)	86 (**44**)	123 (6)
49	Diazinon	GC	101 (6)	109 (6)	112 (7)	101 (8)	114 (12)	118 (4)	101 (4)	102 (5)	92 (10)	97 (11)

Table 2 (*Contd.*)

			EMR-low		EMR-high		Z-sep		μSPE-GC		μSPE-LC	
Nr	Analytes	Tool	FF	RSC	FF	RSC	FF	RSC	FF	RSC	FF	RSC
	Diazinon	LC	84 (4)	99 (8)	94 (8)	97 (7)	97 (6)	102 (4)	83 (8)	97 (5)	78 (3)	90 (8)
50	Dichlorprop	LC	95 (**27**)	**64** (**44**)	—	—	—	—	—	—	—	—
51	Dichlorvos	GC	85 (10)	**66** (11)	81 (2)	**67** (17)	**67** (8)	73 (7)	87 (7)	98 (13)	86 (8)	97 (14)
	Dichlorvos	LC	**69** (10)	**67** (4)	73 (4)	**42** (14)	**51** (10)	71 (5)	74 (5)	99 (6)	70 (7)	**60** (10)
52	Dicloran	GC	86 (11)	90 (5)	103 (9)	91 (10)	111 (19)	98 (2)	83 (5)	108 (12)	89 (16)	82 (7)
53	Dicofol-pp	GC	104 (12)	107 (7)	**122** (3)	109 (4)	113 (9)	112 (4)	100 (6)	116 (7)	105 (6)	104 (13)
54	Dieldrin	GC	92 (10)	80 (16)	—	—	100 (7)	87 (19)	**66** (18)	**45** (85)	82 (**37**)	—
55	Difenoconazole	GC	93 (4)	109 (4)	103 (4)	95 (3)	110 (11)	107 (3)	96 (7)	114 (3)	84 (12)	93 (4)
	Difenoconazole	LC	85 (3)	96 (2)	88 (4)	99 (4)	90 (8)	104 (2)	86 (3)	99 (7)	**67** (7)	85 (8)
56	Diflubenzuron	LC	95 (10)	108 (3)	86 (2)	113 (6)	99 (11)	101 (7)	86 (5)	95 (5)	75 (4)	83 (5)
57	Dimethoate	LC	88 (3)	112 (5)	99 (2)	—	97 (8)	117 (4)	98 (3)	**124** (3)	88 (3)	111 (3)
58	Dimethomorph	GC	102 (4)	110 (5)	111 (11)	100 (6)	114 (9)	112 (10)	109 (4)	116 (3)	112 (10)	107 (3)
59	Dinoterb	LC	98 (15)	102 (**28**)	—	97 (16)	89 (16)	91 (9)	70 (**40**)	95 (19)	81 (**22**)	**64** (14)
60	Diphenylamine	GC	93 (6)	87 (6)	109 (7)	97 (5)	117 (9)	101 (4)	96 (10)	99 (3)	**123** (12)	94 (10)
61	Disulfoton	GC	84 (14)	93 (12)	109 (5)	87 (**66**)	109 (14)	118 (11)	98 (8)	110 (12)	112 (11)	**66** (**26**)
	Disulfoton	LC	81 (12)	107 (9)	96 (16)	90 (5)	87 (4)	91 (7)	77 (13)	82 (7)	88 (10)	81 (12)
62	Ditalimphos	LC	91 (4)	111 (4)	101 (3)	96 (5)	95 (4)	111 (4)	**54** (8)	93 (4)	88 (6)	96 (4)
63	DMF	LC	85 (5)	108 (4)	97 (3)	100 (6)	91 (6)	109 (5)	87 (5)	108 (3)	90 (2)	95 (3)
64	DMST	LC	75 (5)	118 (8)	89 (5)	112 (6)	87 (7)	115 (7)	91 (5)	109 (6)	82 (4)	101 (6)
65	Endosulfan-alpha	GC	89 (13)	95 (14)	93 (10)	**53** (12)	100 (5)	91 (17)	86 (17)	92 (13)	72 (10)	**68** (14)
66	Endosulfan-beta	GC	86 (18)	93 (10)	100 (20)	**58** (30)	119 (21)	99 (8)	89 (13)	85 (7)	90 (17)	79 (11)
67	Endosulfan-sulfate	GC	96 (8)	100 (5)	107 (12)	90 (12)	**125** (8)	99 (12)	99 (7)	—	99 (6)	80 (18)
68	Endrin	GC	89 (**35**)	76 (**26**)	96 (**26**)	75 (18)	115 (17)	—	82 (11)	—	**64** (18)	—
69	EPN	GC	93 (7)	99 (2)	108 (5)	87 (11)	120 (8)	104 (5)	98 (9)	101 (7)	97 (14)	88 (8)
70	Epoxiconazole	GC	95 (4)	116 (6)	109 (2)	99 (7)	113 (10)	116 (4)	103 (3)	**226** (**92**)	96 (7)	**141** (**72**)
	Epoxiconazole	LC	80 (6)	114 (8)	90 (9)	108 (6)	98 (10)	114 (5)	86 (7)	**247** (**77**)	87 (8)	**139** (**73**)
71	Ethiofencarb	LC	89 (5)	86 (14)	101 (6)	93 (7)	99 (7)	108 (6)	90 (7)	104 (7)	91 (9)	96 (5)
72	Ethion	GC	109 (6)	94 (3)	109 (5)	89 (8)	117 (7)	100 (3)	112 (5)	100 (7)	109 (10)	84 (11)
	Ethion	LC	99 (6)	95 (4)	97 (4)	90 (3)	95 (4)	91 (2)	96 (4)	83 (7)	87 (2)	79 (6)
73	Ethoprophos	GC	98 (5)	108 (6)	109 (4)	113 (7)	121 (8)	116 (2)	102 (8)	110 (5)	101 (7)	103 (13)
	Ethoprophos	LC	84 (8)	120 (6)	93 (11)	93 (5)	97 (10)	109 (11)	79 (3)	103 (7)	89 (7)	92 (8)
74	Ethoxyquin	LC	—	75 (8)	—	83 (13)	—	88 (8)	—	90 (20)	—	74 (17)
75	Etofenprox	GC	82 (5)	**51** (5)	92 (3)	**64** (6)	102 (7)	76 (19)	78 (8)	**63** (2)	**69** (8)	**54** (5)
	Etofenprox	LC	72 (9)	**50** (8)	76 (12)	**42** (**29**)	83 (5)	**66** (3)	72 (6)	**53** (10)	**54** (10)	**43** (4)
76	Fenamiphos	LC	90 (3)	112 (5)	89 (4)	100 (4)	97 (6)	115 (5)	90 (6)	104 (5)	87 (4)	95 (6)
77	Fenamiphos-sulfone	LC	92 (6)	111 (4)	96 (11)	104 (7)	97 (10)	102 (9)	93 (6)	107 (9)	86 (7)	100 (5)
78	Fenarimol	GC	92 (6)	106 (3)	110 (4)	92 (6)	108 (8)	106 (3)	97 (2)	111 (2)	94 (8)	97 (7)
79	Fenazaquin	LC	**68** (4)	71 (4)	**65** (2)	**60** (4)	78 (5)	77 (4)	**53** (8)	**54** (5)	**28** (5)	**31** (5)
80	Fenbuconazole	GC	100 (3)	110 (2)	110 (3)	110 (3)	117 (9)	113 (7)	101 (6)	118 (2)	101 (8)	106 (4)
	Fenbuconazole	LC	89 (21)	**131** (9)	90 (**23**)	92 (10)	97 (19)	108 (11)	94 (18)	102 (11)	86 (14)	101 (10)
81	Fenitrothion	GC	100 (5)	97 (8)	**122** (5)	109 (11)	**123** (9)	113 (8)	105 (7)	109 (12)	104 (11)	116 (17)
82	Fenoxycarb	GC	97 (5)	102 (16)	114 (5)	108 (8)	110 (16)	99 (13)	89 (12)	—	108 (13)	96 (15)
	Fenoxycarb	LC	87 (6)	112 (5)	101 (3)	105 (3)	95 (5)	106 (3)	89 (4)	106 (3)	87 (4)	99 (6)
83	Fenpropathrin	GC	99 (18)	101 (6)	106 (**23**)	**122** (13)	102 (13)	—	94 (18)	—	100 (**69**)	—
84	Fenpropidin	LC	61 (7)	93 (8)	—	71 (11)	**65** (14)	104 (5)	**26** (10)	—	79 (6)	90 (8)
85	Fenpropimorph	GC	71 (2)	99 (4)	**50** (3)	83 (5)	75 (7)	101 (6)	88 (5)	83 (3)	98 (7)	104 (13)
86	Fenson	GC	95 (5)	105 (5)	111 (4)	106 (10)	115 (8)	110 (6)	**149** (**78**)	109 (5)	97 (9)	100 (4)
87	Fenthion	GC	99 (2)	109 (10)	107 (5)	101 (2)	116 (9)	106 (7)	100 (11)	110 (8)	104 (7)	99 (15)
	Fenthion	LC	85 (10)	83 (17)	94 (7)	92 (14)	100 (10)	94 (12)	102 (9)	97 (11)	87 (16)	82 (14)
88	Fenthion-oxon	LC	**20** (**78**)	99 (9)	91 (**25**)	107 (6)	86 (**21**)	109 (3)	95 (16)	106 (1)	97 (19)	100 (2)
89	Fenthion-oxon-sulfone	LC	85 (7)	**121** (12)	96 (5)	115 (10)	92 (8)	118 (7)	87 (6)	119 (9)	83 (6)	111 (5)
90	Fenthion-oxon-sulfoxide	LC	82 (4)	102 (5)	82 (2)	92 (5)	**67** (6)	97 (6)	87 (3)	100 (2)	81 (3)	99 (3)
91	Fenthion-sulfone	LC	85 (13)	93 (15)	107 (8)	**133** (7)	104 (6)	113 (10)	91 (8)	117 (19)	96 (3)	94 (19)
92	Fenthion-sulfoxide	LC	93 (6)	108 (9)	98 (7)	101 (10)	94 (3)	110 (12)	91 (3)	114 (3)	85 (7)	102 (5)
93	Fenvalerate	GC	92 (3)	75 (4)	105 (4)	72 (10)	112 (9)	89 (8)	88 (11)	83 (14)	92 (8)	83 (24)
94	Fipronil	LC	90 (17)	**123** (13)	86 (18)	100 (**21**)	100 (15)	109 (**22**)	116 (19)	**143** (11)	**55** (4)	104 (16)
95	Fluazifop-*p*-butyl	GC	98 (6)	98 (9)	109 (6)	93 (7)	118 (14)	96 (6)	100 (5)	107 (3)	99 (8)	89 (5)
	Fluazifop-*p*-butyl	LC	92 (5)	98 (3)	103 (5)	93 (6)	98 (6)	102 (2)	91 (7)	96 (7)	80 (4)	84 (8)
96	Fludioxonil	GC	96 (6)	105 (6)	110 (6)	99 (13)	118 (10)	113 (12)	111 (3)	123 (3)	100 (12)	109 (7)
97	Flufenoxuron	GC	93 (10)	**123** (**23**)	**126** (13)	100 (13)	**122** (8)	119 (**37**)	**48** (17)	—	—	80 (**52**)
98	Fluoxastrobin	LC	91 (1)	115 (4)	102 (4)	112 (3)	101 (4)	109 (4)	94 (5)	110 (4)	88 (2)	108 (8)

Table 2 (*Contd.*)

			EMR-low		EMR-high		Z-sep		μSPE-GC		μSPE-LC	
Nr	Analytes	Tool	FF	RSC	FF	RSC	FF	RSC	FF	RSC	FF	RSC
99	Fluquinconazole	GC	95 (4)	110 (9)	109 (4)	101 (7)	118 (9)	109 (6)	103 (3)	**124** (4)	100 (8)	102 (5)
100	Flusilazole	LC	88 (3)	114 (6)	92 (2)	**121** (17)	109 (7)	112 (2)	97 (5)	107 (6)	86 (4)	99 (3)
101	Flutriafol	GC	101 (9)	113 (4)	115 (2)	111 (5)	92 (10)	108 (6)	104 (4)	**127** (3)	103 (9)	108 (7)
102	Fluvalinate-tau	GC	99 (**24**)	**26** (**134**)	124 (7)	96 (14)	**134** (9)	88 (12)	99 (15)	—	96 (7)	—
103	Fosthiazate	LC	87 (4)	110 (6)	101 (3)	103 (4)	99 (4)	112 (4)	94 (2)	114 (4)	90 (7)	100 (6)
104	HCH-alpha	GC	85 (6)	78 (13)	108 (4)	100 (8)	105 (6)	101 (7)	95 (6)	89 (14)	95 (11)	95 (14)
105	HCH-beta	GC	95 (6)	80 (**24**)	88 (**56**)	85 (14)	**124** (8)	117 (19)	102 (4)	89 (21)	106 (6)	96 (22)
106	Heptenophos	GC	99 (4)	112 (5)	115 (3)	112 (8)	119 (8)	114 (6)	105 (6)	113 (4)	110 (7)	114 (20)
	Heptenophos	LC	87 (7)	109 (4)	98 (3)	106 (3)	95 (7)	110 (2)	94 (6)	112 (2)	84 (2)	103 (4)
107	Hexaconazole	LC	93 (6)	100 (7)	83 (6)	87 (15)	76 (9)	103 (11)	93 (7)	93 (10)	75 (11)	73 (6)
108	Hexythiazox	GC	81 (11)	85 (14)	100 (3)	**60** (**37**)	100 (2)	92 (12)	95 (5)	87 (12)	87 (12)	**53** (11)
	Hexythiazox	LC	81 (3)	79 (6)	88 (4)	83 (3)	86 (5)	82 (3)	78 (4)	82 (3)	**69** (3)	**64** (2)
109	Imazalil	LC	75 (8)	**67** (15)	**66** (**21**)	**65** (14)	**57** (7)	90 (8)	77 (6)	88 (7)	75 (7)	78 (13)
110	Imidacloprid	LC	92 (4)	107 (12)	90 (2)	114 (3)	94 (5)	99 (13)	93 (6)	96 (12)	86 (5)	98 (7)
111	Indoxacarb	LC	96 (9)	96 (16)	108 (9)	113 (9)	112 (7)	108 (6)	91 (**24**)	116 (6)	73 (12)	96 (**23**)
112	Iodosulfuron-methyl-sodium	LC	80 (17)	97 (18)	94 (12)	100 (8)	89 (15)	101 (6)	—	85 (12)	**58** (18)	102 (13)
113	Iprodione	GC	93 (12)	78 (**65**)	108 (6)	120 (14)	97 (15)	**130** (18)	105 (**34**)	—	101 (13)	**154** (**30**)
114	Iprovalicarb	LC	88 (3)	112 (4)	99 (2)	108 (3)	96 (4)	110 (3)	92 (3)	106 (3)	88 (3)	105 (3)
115	Isofenphos-methyl	GC	100 (5)	111 (4)	114 (1)	107 (6)	**122** (9)	111 (6)	107 (4)	120 (3)	107 (10)	107 (5)
116	Isoprothiolane	GC	95 (7)	120 (2)	105 (4)	114 (10)	119 (8)	112 (9)	93 (7)	119 (3)	103 (9)	110 (6)
	Isoprothiolane	LC	87 (3)	110 (4)	98 (2)	105 (3)	100 (6)	108 (3)	91 (5)	105 (3)	85 (2)	101 (5)
117	Isoproturon	LC	86 (5)	105 (5)	89 (3)	103 (3)	93 (7)	109 (3)	94 (2)	107 (5)	80 (7)	101 (9)
118	Jodofenfos	GC	82 (3)	80 (7)	97 (3)	75 (17)	108 (11)	91 (10)	80 (4)	75 (9)	70 (8)	**62** (18)
119	Kresoxim-methyl	GC	101 (9)	116 (7)	115 (5)	110 (4)	**131** (7)	116 (8)	112 (8)	114 (5)	110 (10)	108 (5)
120	Lindane	GC	96 (6)	**46** (**90**)	107 (5)	77 (**25**)	104 (6)	**40** (**96**)	94 (4)	—	108 (3)	105 (**22**)
121	Linuron	LC	101 (17)	109 (**28**)	93 (15)	105 (14)	99 (8)	**103** (**30**)	—	96 (12)	—	88 (13)
122	Malaoxon	LC	92 (3)	115 (5)	103 (6)	108 (5)	99 (7)	108 (8)	92 (3)	119 (4)	95 (3)	103 (5)
123	Malathion	LC	94 (4)	116 (2)	101 (8)	104 (5)	99 (6)	107 (6)	92 (5)	115 (7)	93 (7)	102 (4)
124	Mecarbam	LC	94 (2)	111 (3)	102 (3)	102 (9)	97 (5)	108 (4)	93 (4)	107 (5)	87 (4)	101 (8)
125	Mepanipyrim	LC	93 (9)	109 (16)	78 (16)	**54** (**12**)	102 (15)	96 (11)	75 (5)	72 (19)	**45** (15)	78 (18)
126	Metaflumizone	LC	88 (4)	102 (5)	103 (2)	75 (**38**)	94 (7)	95 (5)	71 (11)	81 (6)	**57** (9)	78 (9)
127	Metalaxyl	LC	84 (4)	107 (5)	95 (5)	98 (3)	100 (6)	108 (3)	95 (3)	108 (4)	85 (6)	103 (8)
128	Metconazole	LC	81 (14)	97 (8)	81 (10)	95 (9)	84 (12)	101 (8)	83 (13)	94 (10)	74 (7)	74 (10)
129	Methamidophos	LC	71 (4)	81 (4)	77 (3)	74 (4)	**46** (4)	72 (3)	75 (8)	87 (2)	**67** (3)	83 (5)
130	Methidathion	GC	98 (2)	119 (6)	113 (2)	**121** (8)	119 (9)	116 (8)	99 (6)	118 (6)	108 (8)	120 (14)
131	Methiocarb	LC	87 (7)	111 (9)	102 (6)	105 (9)	100 (10)	114 (6)	92 (16)	121 (13)	84 (11)	109 (10)
132	Methiocarb-sulfone	LC	88 (5)	**122** (3)	104 (3)	118 (7)	97 (6)	119 (4)	—	—	95 (9)	118 (4)
133	Methiocarb-sulfoxide	LC	86 (5)	103 (4)	90 (4)	94 (3)	74 (9)	101 (6)	103 (11)	—	81 (6)	96 (5)
134	Methomyl	LC	**123** (**14**)	**171** (17)	**139** (13)	**195** (10)	102 (13)	**204** (19)	116 (11)	116 (14)	99 (18)	**148** (17)
135	Methoxychlor	GC	**305** (**24**)	88 (8)	**201** (**15**)	92 (7)	111 (10)	100 (8)	97 (7)	95 (3)	102 (13)	85 (12)
136	Methoxyfenozide	LC	93 (6)	113 (5)	102 (6)	110 (14)	98 (1)	110 (9)	88 (7)	116 (17)	84 (4)	102 (6)
137	Metribuzin	GC	101 (9)	**160** (7)	112 (2)	**132** (9)	121 (7)	**135** (18)	108 (3)	**122** (8)	111 (6)	110 (4)
138	Metsulfuron-methyl	LC	92 (5)	99 (4)	96 (3)	105 (4)	99 (6)	102 (6)	**23** (**40**)	81 (3)	86 (3)	92 (8)
139	Mevinphos	LC	87 (5)	101 (4)	98 (5)	99 (3)	95 (5)	112 (5)	93 (6)	109 (2)	88 (3)	98 (8)
140	Monocrotophos	LC	84 (3)	101 (9)	87 (6)	97 (4)	86 (3)	101 (6)	91 (5)	106 (6)	84 (6)	105 (6)
141	Monolinuron	LC	88 (4)	102 (7)	98 (8)	99 (10)	100 (5)	114 (6)	96 (6)	115 (6)	88 (4)	98 (2)
142	Myclobutanil	GC	94 (3)	**123** (9)	105 (2)	100 (14)	117 (13)	109 (15)	107 (4)	**123** (17)	102 (5)	117 (10)
143	Nuarimol	GC	92 (4)	113 (4)	102 (3)	105 (3)	112 (8)	113 (8)	106 (5)	120 (6)	103 (7)	101 (5)
144	Ofurace	LC	88 (7)	102 (7)	104 (5)	105 (11)	103 (7)	115 (9)	92 (9)	115 (5)	87 (5)	105 (7)
145	Omethoate	LC	78 (3)	98 (16)	81 (6)	95 (8)	**67** (6)	112 (9)	77 (6)	85 (5)	84 (3)	86 (**22**)
146	Oxadixyl	GC	100 (3)	**129** (18)	114 (4)	101 (10)	121 (12)	119 (11)	103 (3)	104 (3)	110 (8)	101 (4)
147	Oxamyl	LC	87 (4)	113 (4)	97 (4)	104 (5)	94 (3)	108 (3)	85 (5)	108 (5)	81 (7)	103 (3)
148	Oxycarboxin	LC	91 (1)	110 (4)	99 (3)	109 (8)	98 (7)	110 (4)	89 (4)	108 (6)	91 (2)	107 (6)
149	Oxydemeton-methyl	LC	74 (3)	95 (4)	**60** (5)	80 (3)	**15** (14)	94 (5)	85 (5)	97 (7)	**66** (2)	105 (7)
150	Paclobutrazol	GC	104 (**77**)	112 (6)	111 (4)	109 (3)	108 (12)	116 (8)	104 (5)	**122** (1)	102 (12)	107 (5)
151	Paraoxon-methyl	LC	95 (20)	**50** (**78**)	119 (**78**)	86 (5)	79 (**50**)	103 (**22**)	**69** (**61**)	81 (15)	**63** (**33**)	70 (**55**)
152	Parathion	GC	84 (10)	118 (9)	117 (5)	101 (6)	121 (12)	107 (11)	100 (6)	112 (16)	107 (16)	93 (18)
153	Parathion-methyl	GC	105 (5)	115 (12)	118 (9)	**122** (8)	**127** (7)	115 (7)	112 (3)	104 (11)	107 (13)	110 (13)
154	Penconazole	GC	98 (5)	106 (3)	92 (4)	99 (6)	110 (10)	108 (5)	99 (8)	118 (4)	93 (7)	85 (2)
	Penconazole	LC	84 (12)	109 (8)	80 (5)	92 (9)	95 (6)	106 (7)	89 (6)	101 (6)	72 (4)	89 (8)
155	Pencycuron	GC	93 (10)	116 (7)	75 (11)	108 (7)	101 (7)	99 (10)	96 (9)	106 (11)	103 (7)	104 (20)

Table 2 (*Contd.*)

			EMR-low		EMR-high		Z-sep		μSPE-GC		μSPE-LC	
Nr	Analytes	Tool	FF	RSC	FF	RSC	FF	RSC	FF	RSC	FF	RSC
	Pencycuron	LC	81 (6)	91 (3)	94 (2)	84 (4)	94 (7)	91 (5)	85 (4)	86 (4)	76 (3)	77 (6)
156	Pendimethalin	GC	86 (6)	84 (2)	106 (13)	77 (8)	112 (12)	87 (13)	90 (10)	86 (3)	83 (8)	71 (8)
	Pendimethalin	LC	81 (6)	77 (7)	91 (5)	71 (5)	91 (4)	82 (2)	77 (4)	75 (4)	**68** (4)	**62** (2)
157	Phenthoate	GC	107 (3)	104 (11)	119 (5)	101 (4)	**157** (10)	109 (4)	105 (8)	111 (7)	117 (11)	122 (20)
158	Phosalone	GC	85 (6)	—	118 (2)	**51** (**28**)	103 (**23**)	73 (**23**)	86 (14)	—	97 (9)	—
159	Phosmet	LC	92 (5)	114 (10)	96 (8)	113 (7)	103 (10)	104 (9)	93 (11)	97 (10)	79 (11)	99 (10)
160	Phosmet-oxon	LC	92 (3)	111 (5)	102 (4)	102 (4)	95 (6)	108 (2)	91 (2)	99 (2)	87 (3)	102 (4)
161	Phosphamidon	LC	90 (7)	**128** (10)	107 (5)	109 (8)	88 (5)	109 (4)	90 (3)	109 (9)	91 (8)	98 (12)
162	Phoxim	LC	87 (6)	98 (11)	101 (9)	97 (4)	101 (7)	103 (6)	88 (3)	99 (6)	79 (6)	88 (5)
163	Pirimicarb	GC	94 (5)	106 (6)	108 (6)	98 (11)	120 (7)	105 (6)	101 (2)	110 (4)	97 (8)	109 (9)
	Pirimicarb	LC	85 (4)	105 (2)	95 (3)	96 (3)	91 (5)	100 (5)	86 (5)	102 (4)	83 (3)	91 (5)
164	Pirimiphos-methyl	GC	109 (9)	93 (7)	**125** (2)	95 (9)	**143** (16)	108 (4)	103 (12)	104 (7)	118 (12)	100 (15)
	Pirimiphos-methyl	LC	89 (12)	101 (7)	101 (4)	80 (5)	104 (11)	96 (4)	75 (11)	95 (2)	79 (6)	82 (8)
165	Prochloraz	LC	82 (5)	105 (2)	82 (5)	93 (5)	87 (8)	100 (5)	85 (2)	97 (4)	**62** (3)	80 (5)
166	Procymidone	GC	101 (4)	120 (2)	116 (5)	102 (7)	121 (3)	113 (7)	99 (8)	108 (8)	101 (5)	108 (4)
167	Profenofos	GC	90 (8)	97 (8)	101 (4)	105 (17)	115 (12)	113 (7)	97 (17)	99 (12)	83 (6)	110 (21)
168	Propamocarb	LC	**36** (**6**)	**54** (13)	—	**14** (19)	**25** (10)	**47** (6)	**50** (**46**)	**35** (6)	116 (4)	**69** (7)
169	Propargite	LC	78 (10)	89 (3)	86 (5)	87 (3)	86 (20)	107 (**21**)	**65** (**29**)	84 (4)	78 (19)	80 (6)
170	Propiconazole	GC	95 (5)	91 (13)	97 (3)	92 (7)	115 (7)	107 (5)	100 (3)	112 (5)	93 (8)	94 (9)
	Propiconazole	LC	—	96 (6)	—	92 (9)	97 (7)	106 (12)	71 (4)	98 (9)	**62** (10)	73 (7)
171	Propoxur	LC	85 (6)	112 (4)	101 (4)	97 (8)	102 (5)	113 (7)	92 (8)	111 (6)	92 (3)	100 (5)
172	Propyzamide	GC	74 (16)	97 (9)	**131** (6)	117 (9)	**135** (12)	111 (16)	119 (15)	108 (18)	86 (**33**)	109 (15)
	Propyzamide	LC	88 (5)	94 (9)	99 (5)	93 (9)	97 (9)	106 (3)	90 (8)	103 (6)	85 (3)	92 (4)
173	Prosulfocarb	LC	84 (3)	78 (4)	92 (3)	79 (4)	92 (6)	85 (6)	84 (4)	82 (5)	75 (3)	72 (9)
174	Prosulfuron	LC	90 (9)	113 (3)	100 (3)	117 (6)	101 (3)	99 (12)	—	95 (9)	85 (12)	97 (9)
175	Prothioconazole-desthio	LC	95 (11)	108 (5)	72 (**27**)	97 (15)	87 (12)	93 (7)	**58** (**93**)	103 (7)	**67** (12)	92 (17)
176	Prothiofos	GC	78 (9)	53 (11)	89 (7)	62 (7)	106 (15)	78 (18)	77 (4)	**66** (**21**)	69 (9)	**51** (**16**)
177	Pymetrozine	LC	**40** (**14**)	**29** (6)	**20** (**11**)	**19** (19)	**22** (7)	**35** (7)	**58** (10)	**40** (9)	**30** (7)	**34** (9)
178	Pyraclostrobin	LC	92 (3)	106 (6)	97 (2)	100 (4)	95 (7)	101 (5)	78 (6)	**242** (**84**)	**61** (5)	**134** (**83**)
179	Pyrazophos	GC	103 (5)	—	113 (5)	99 (16)	**123** (8)	91 (10)	89 (7)	—	81 (9)	**137** (**143**)
180	Pyridaben	GC	92 (4)	72 (6)	100 (3)	71 (4)	107 (11)	71 (**25**)	84 (7)	76 (3)	83 (10)	**60** (5)
181	Pyridaphenthion	GC	98 (3)	123 (13)	109 (2)	118 (9)	119 (7)	**128** (14)	104 (6)	107 (21)	105 (12)	**134** (18)
182	Pyridate	LC	—	**46** (**25**)	—	**38** (5)	—	76 (7)	—	—	—	**45** (2)
183	Pyrimethanil	GC	87 (6)	97 (9)	99 (2)	93 (12)	104 (17)	112 (9)	83 (8)	108 (6)	**49** (10)	86 (7)
	Pyrimethanil	LC	98 (11)	90 (8)	83 (7)	85 (13)	95 (9)	101 (7)	85 (8)	88 (10)	**44** (17)	82 (15)
184	Pyriproxyfen	GC	88 (4)	76 (4)	100 (2)	83 (6)	109 (10)	87 (10)	86 (8)	79 (4)	82 (7)	70 (6)
	Pyriproxyfen	LC	83 (3)	79 (4)	86 (5)	78 (4)	88 (8)	82 (4)	79 (2)	73 (5)	**69** (4)	**65** (6)
185	Quinoxyfen	GC	76 (4)	72 (5)	82 (4)	70 (2)	96 (9)	84 (12)	**66** (4)	**63** (4)	**46** (10)	**48** (5)
	Quinoxyfen	LC	**66** (5)	71 (6)	76 (5)	**69** (9)	73 (6)	75 (5)	**58** (8)	57 (7)	**37** (5)	**45** (12)
186	Simazine	LC	82 (8)	—	94 (9)	—	93 (16)	—	84 (10)	—	78 (10)	—
187	Spinosad	LC	**26** (12)	77 (17)	—	—	**29** (13)	85 (18)	71 (11)	76 (14)	**69** (14)	75 (11)
188	Spirodiclofen	LC	85 (7)	82 (7)	92 (7)	70 (4)	94 (10)	84 (13)	80 (12)	67 (12)	74 (4)	**66** (9)
189	Spiroxamine	LC	**48** (6)	84 (4)	—	**52** (14)	**56** (9)	96 (4)	**27** (5)	8 (18)	78 (7)	89 (5)
190	Tebuconazole	GC	92 (8)	99 (4)	105 (6)	100 (7)	104 (6)	110 (11)	100 (7)	112 (6)	96 (8)	98 (4)
	Tebuconazole	LC	85 (11)	96 (8)	82 (10)	93 (13)	90 (10)	92 (9)	**37** (**137**)	93 (14)	79 (12)	82 (5)
191	Tebufenozide	LC	90 (11)	**133** (10)	103 (13)	117 (5)	122 (11)	113 (15)	104 (6)	106 (6)	95 (12)	101 (14)
192	Tebufenpyrad	GC	91 (4)	98 (10)	102 (2)	90 (3)	106 (8)	95 (6)	93 (5)	100 (4)	87 (10)	79 (7)
	Tebufenpyrad	LC	90 (5)	90 (4)	70 (5)	84 (5)	92 (6)	91 (5)	81 (8)	88 (5)	75 (5)	71 (8)
193	Tecnazene	GC	87 (7)	89 (10)	94 (9)	74 (5)	95 (10)	96 (6)	86 (14)	80 (6)	80 (11)	**68** (12)
194	Teflubenzuron	LC	90 (**22**)	97 (21)	108 (16)	**66** (**25**)	87 (19)	110 (4)	79 (17)	88 (12)	**47** (14)	85 (**29**)
195	Tefluthrin	GC	94 (3)	78 (11)	104 (1)	70 (12)	115 (10)	89 (10)	97 (4)	78 (14)	88 (7)	64 (8)
196	Tetraconazole	GC	95 (4)	**121** (2)	111 (5)	103 (11)	**122** (8)	112 (6)	95 (**46**)	114 (7)	90 (**54**)	112 (9)
197	Tetradifon	GC	78 (8)	70 (9)	94 (10)	81 (7)	112 (14)	91 (8)	85 (7)	81 (6)	75 (6)	74 (6)
198	Thiabendazole	LC	72 (5)	108 (11)	**68** (6)	101 (7)	**49** (9)	79 (8)	72 (7)	70 (12)	**37** (5)	**66** (9)
199	Thiacloprid	LC	89 (4)	115 (4)	96 (4)	102 (3)	101 (8)	103 (3)	89 (5)	113 (6)	90 (6)	104 (6)
200	Thiamethoxam	LC	88 (6)	**155** (11)	91 (13)	100 (13)	83 (5)	112 (11)	79 (10)	108 (9)	79 (5)	114 (10)
201	Thiodicarb	LC	74 (5)	—	83 (4)	—	81 (8)	—	77 (5)	—	71 (4)	—
202	Thiometon	LC	—	82 (**29**)	**52** (**83**)	89 (**23**)	99 (9)	105 (4)	—	108 (**23**)	82 (**25**)	118 (14)
203	Tolclofos-methyl	GC	95 (4)	97 (6)	109 (2)	101 (12)	121 (9)	104 (3)	95 (4)	95 (5)	94 (9)	94 (14)
204	Triadimefon	GC	94 (4)	**124** (7)	108 (9)	111 (4)	118 (13)	**121** (11)	102 (6)	116 (8)	107 (9)	106 (12)
205	Triadimenol	LC	89 (4)	108 (5)	92 (7)	104 (5)	94 (5)	106 (5)	88 (6)	103 (5)	84 (6)	93 (7)

Table 2 (*Contd.*)

			EMR-low		EMR-high		Z-sep		μSPE-GC		μSPE-LC	
Nr	Analytes	Tool	FF	RSC	FF	RSC	FF	RSC	FF	RSC	FF	RSC
206	Triallate	LC	72 (17)	70 (3)	81 (10)	76 (9)	91 (9)	76 (8)	75 (10)	67 (3)	**60** (19)	**53** (5)
207	Triazophos	GC	103 (4)	91 (16)	117 (5)	111 (5)	118 (13)	117 (11)	103 (6)	104 (6)	103 (9)	112 (16)
	Triazophos	LC	91 (2)	110 (3)	100 (3)	103 (3)	100 (4)	109 (3)	94 (5)	108 (3)	84 (4)	99 (4)
208	Trichlorfon	GC	77 (8)	**67** (11)	81 (3)	**67** (18)	**67** (7)	79 (17)	87 (6)	98 (13)	88 (8)	97 (13)
209	Tricyclazole	GC	98 (11)	120 (8)	115 (8)	110 (9)	121 (8)	118 (9)	105 (9)	115 (6)	101 (2)	101 (9)
	Tricyclazole	LC	76 (4)	98 (5)	77 (3)	90 (3)	**18** (16)	**51** (7)	78 (5)	94 (4)	**47** (5)	**56** (6)
210	Trifloxystrobin	LC	94 (5)	104 (5)	102 (3)	102 (4)	101 (6)	111 (2)	92 (4)	106 (3)	86 (3)	94 (5)
211	Triflumuron	LC	88 (4)	105 (4)	93 (5)	104 (2)	100 (5)	107 (3)	89 (5)	101 (4)	74 (6)	93 (7)
212	Trifluralin	GC	96 (4)	82 (7)	106 (3)	86 (12)	116 (13)	93 (7)	97 (5)	86 (6)	100 (11)	76 (13)
213	Triticonazole	LC	85 (6)	111 (7)	91 (9)	102 (6)	73 (12)	108 (6)	81 (4)	109 (5)	82 (3)	91 (6)
214	Vamidothion	LC	87 (2)	100 (11)	90 (5)	95 (5)	83 (7)	101 (4)	92 (4)	112 (9)	84 (9)	104 (14)
215	Vinclozolin	GC	96 (8)	108 (5)	112 (5)	108 (9)	**125** (11)	109 (9)	103 (8)	105 (3)	113 (10)	103 (8)
216	Zoxamide	LC	88 (10)	99 (9)	96 (4)	92 (7)	96 (4)	104 (3)	94 (3)	101 (7)	85 (8)	85 (6)

For the FF, the clean-up removal efficiency was approximately ~25% for the EMR-low cartridges, followed by ~39% for C18, ~45% for EMR-high, ~62% for Z-sep, ~80% for μSPE-LC and ~83% for μSPE-GC. For both cartridges containing chitin, there was no significant difference between the TICs, before and after the clean-up, suggesting that chitin did not have any effect on matrix removal.

3.1.1. Fatty acid removal. The fatty acids, *n*-hexadecanoic acid (Rt. 14.2 min) and oleic acid (Rt. 16.8 min), present in both FF and RSC, as well as canolol, which is the main fatty acid in the RSC, were removed with cartridges containing Z-sep (Z-sep and μSPE-LC) and PSA (μSPE-GC). In the RSC extract, canolol was reduced by ~41% in the Z-sep cartridge and by ~52% in the cartridge μSPE-GC. The removal of canolol in the other cartridges varied from ~5% using C18, ~17% using EMR-high and ~18% with μSPE-LC. The same was observed in the removal of *n*-hexadecanoic acid and oleic acid in FF. No effect on fatty acid removal by C18 has earlier been reported by Herrmann & Poulsen.[37] The best cartridges for removing those two fatty acids, achieving more than 90% removal, were those containing Z-sep and PSA (Z-sep, μSPE-GC and μSPE-LC). Only 17 or 25% of co-extractive compounds were removed when clean-up was performed with EMR-high and C18 cartridges.

3.1.2. Sterol removal. Sterols such as cholesterol (Rt. 30.2 min) and tocopherol (Rt. 30.8 min), which are the main compounds found in FF, were almost completely removed after the clean-up throughout the C18 and EMR-high cartridges.

In RSC extracts, the main detected compounds were phytosterols stigmasterol (Rt. 30.3 min) and campesterol (Rt. 31.3 min). Again, EMR-high and C18 cartridges seem to play a major role in the removal of these compounds. The sample clean-up through these two cartridges completely removed stigmasterol and lowered the area of campesterol by approximately 94% and 97%, respectively. The removal efficiency of sterol is in line with other studies done on SPE or d-SPE clean-up.[5,38,39]

The total ion chromatogram of a FF raw extract and cleaned extract in different cartridges (C18, EMR-high, μSPE-LC, Z-sep and μSPE-GC) showing the effect of different cartridges on fatty acids and sterols region is given in Fig. 3.

As a conclusion, in terms of the clean-up efficiency, the cartridges containing EMR (EMR-high) and C18 did not play any significant role in fatty acid removal, but they removed up to 100% of sterols in both matrices. Although these compounds are eluting at the end of the chromatogram, their removal is important to extend the life of the GC column.

The best removal efficiency for the fatty acid was achieved with the cartridges containing PSA (μSPE-GC) and Z-sep (Z-sep and μSPE-LC), but Z-sep did not have a similar effect on the sterol's region. The presence of GCB had a positive visual effect on the FF, most probably due to the removal of carotenoid. EMR and C18 have almost the same clean-up efficiency for sterols and phytosterols, but EMR seems to have a positive effect on color removal especially due to the removal of chlorophyll in the RSC extract compared to C18. Increasing the amount of the sorbent Z-sep improved the removal efficiency of fatty acids. A comparison between the two cartridges containing the same total amount of sorbents, 35 mg each, EMR-low and C18, showed differences in the total area removal of co-extractives.

Considering the overall removal efficiency, the best cartridge was the one containing PSA (μSPE-GC) and Z-sep. It is also important to note that EMR requires the addition of water prior to clean-up in order for it to work well.[16,35] During our study, this step was not performed due to the way in which the sorbent was combined in the cartridges containing EMR. Both cartridges, EMR-low and EMR-high, contained 20 mg $MgSO_4$ in their sorbent combination mix.

3.2. Recovery study

To further investigate the effect of different sorbents used in the PAL μSPE cartridges, recovery experiments were performed. The five sorbent combinations that demonstrate the highest efficiency in removing matrix components, EMR-low, EMR-high, Z-sep, μSPE-GC and μSPE-LC, were selected for the recovery study.

Recoveries were calculated for 216 pesticides in the two matrices. Of those, 112 compounds were analysed by GC-MS/MS

and 143 compounds by LC-MS/MS. Thirty-nine compounds were analyzed by both GC-MS/MS and LC-MS/MS. The 255 average recoveries (%) and RSDs of spiked samples at 0.01 mg kg^{-1} ($n = 5$) of FF and RSC are given in Table 2.

For the FF, the cartridges that resulted in the highest percentage of compounds with recoveries between 70 and 120% were EMR-low with 105 (94%) compounds and μSPE-GC with 103 (92%), followed by μSPE-LC 96 (86%), EMR-high 95 (85%) and Z-sep 88 (79%).

For RSC, the best performance was obtained with the cartridges containing Z-sep for 98 compounds (88%), EMR-high for 93 (83%), and EMR-low for 90 (80%). When both cartridges containing GCB (μSPE-GC and μSPE-LC) were used, recoveries between 70 and 120% could only be achieved for 81 (72%) and 75 (67%) compounds, respectively.

Poor results were obtained when the extract was cleaned with the μSPE-LC cartridge. This cartridge does not contain $MgSO_4$; therefore the water content in the extract was not removed and this could have affected the column, and thus this cartridge is not recommended for GC-MS/MS analysis.

In the LC-MS/MS, FF sample extracts were analyzed for 143 pesticides and metabolites. The results showed that 123 (86%) compounds for the EMR-low cartridge had recoveries between 70 and 120%, followed by EMR-high, Z-sep, μSPE-GC and μSPE-LC with 119 (83%), 120 (84%), 115 (80%) and 103 (72%), respectively.

A comparison of recoveries in the RSC spiked samples showed the largest number of compounds with recoveries between 70 and 120% when the extract was cleaned throughout Z-sep with 128 (90%), followed by EMR-low, EMR-high, μSPE-

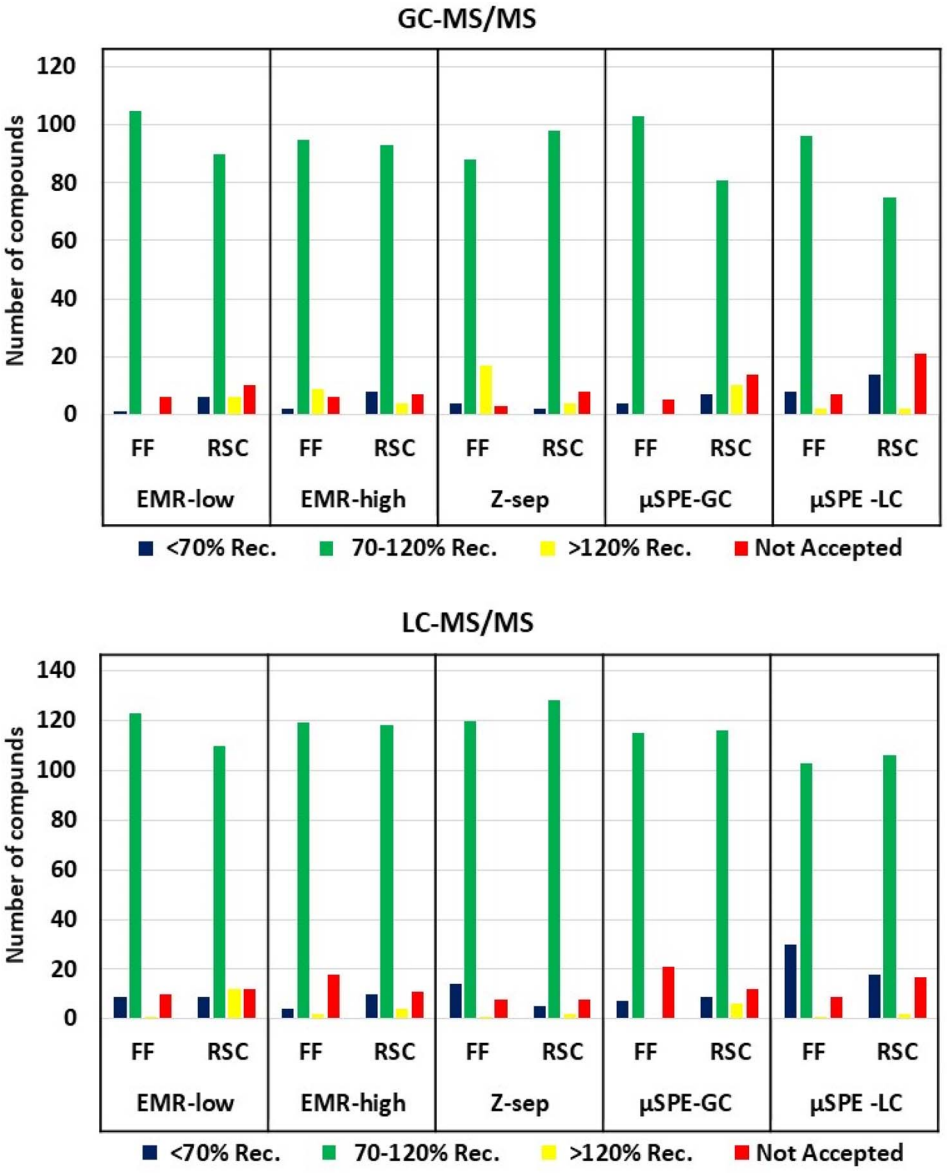

Fig. 4 Number of compounds within different ranges of recoveries at a spiking level of 0.01 mg kg^{-1} ($n = 5$) in both matrices, FF and RSC. The number of compounds analyzed is 123 by GC and 143 by LC. Not accepted are all the compounds that either could not be detected or whose RSD was higher than 20%.

GC and μSPE-LC with 110 (77%), 118 (83%), 116 (81%) and 106 (74%).

The number of compounds within different ranges of recoveries analyzed by GC-MS/MS and LC-MS/MS, in FF and RSC, is shown in Fig. 4.

Compounds with a planar structure have been previously shown to be affected by GCB. The same was observed in our study. Planar compounds such as quinoxyfen gave poor recovery in both matrices and both instruments, between 37 and 45% with μSPE-GC and μSPE-LC cartridges. To overcome this issue, an isotopically labeled standard can be used to normalize potential losses[30] when still using GCB or removal or replacement with other sorbents may be considered. For instance, good recoveries were obtained for quinoxyfen with cartridges containing EMR and Z-sep sorbents (76% and 73%, respectively).

Acid compounds, fenpropidin, iodosulfuron-methyl-sodium, and metsulfuron-methyl resulted in low recoveries or unacceptable RSD (>20%) when the extract was cleaned-up using the μSPE-GC cartridge, due to their interaction with PSA.

Increasing the amount of sorbent in the case of EMR did not significantly affect compound recoveries but it improved the sample clean-up, as reflected by the reduced TIC background. The lack of EMR "activation" during the clean-up may have affected the recoveries for some compounds.

4. Conclusions

The study investigated the performance of different sorbents and amounts in μSPE cartridges using an automatic clean-up and sample preparation workflow. Eight different sorbent combinations, including EMR, Z-sep, chitin, C18, PSA, and GCB, were tested in terms of clean-up efficiency. The cartridges containing only EMR and C18 did not play any significant role in fatty acid removal, but they removed up to 100% of sterols in both FF and RSC matrices. The best removal efficiency for fatty acids was achieved with the cartridges containing PSA (μSPE-GC) and Z-sep (Z-sep and μSPE-LC). However, the Z-sep cartridge, without C18, did not have a similar effect on the removal of sterols. The presence of GCB had a positive visual effect on the FF extract, most probably due to the removal of carotenoid. For RSC, GCB and EMR had the same effect on color removal proving once again that the role of GCB could be reconsidered in the cartridge's composition, by replacing or lowering its amount. Increasing the amount of Z-sep improved the removal efficiency of fatty acids. Overall, the clean-up with the different sorbents introduced into the new μSPE cartridges showed similar clean-up efficiency to conventional d-SPE proving that the automatic clean-up has equal performance.

In terms of recovery and precision, five cartridges were investigated. The best results with recovery between 70 and 120% and RSD<20% were achieved when FF samples were cleaned-up with EMR-low (94% for the compound analysis by GC-MS/MS and 86% for the ones analyzed by LC-MS/MS). In the case of RSC, the optimal results were obtained when samples were cleaned-up with the cartridge containing only Z-sep (98% by GC-MS/MS and 88% by LC-MS/MS). Although these cartridges give the best results in terms of recovery, their use could require more instrument maintenance, especially for GC-MS/MS, due to the lower removal of co-extractives. To avoid this potential challenge, a novel sorbent combination, which includes Z-sep and EMR, can be introduced into the new type of cartridge and further investigated for pesticide residue analyses.

Conflicts of interest

The authors report no conflicts of interest.

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