Utilizing a Rapid Multi-Plug Filtration Cleanup Method Determination of 72 Pesticides in Grape Wines by Gas Chromatography Tandem Mass Spectrometry

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Abstract:A convenient and fast multi-residue method had been established for the qualitative and quantitative analysis of 72 pesticides pertaining to different chemical classes in red and white grape wines. The analysis was carried out by gas chromatography tandem quadrupole mass spectrometric determination (GC–MS/MS). An optimization strategy including the screening of MWCNTs amount and cleanup procedure cycle times for m-PFC was performed to achieve ideal recoveries and reduce sample matrix compounds in the ultimate extraction. At three spiking levels of 0.01, 0.05 and 0.2 mg/kg, the optimized procedure obtained consistent recoveries between 70.2 and 108.8% (70.2% and 108.8% for white wine, 72.3% and 106.0% for red wine) , with relative standard deviations (RSDs) generally below 8.3% . Using the pesticide standards prepared in pure solvent and presence of matrix for analysis, linearity in the range of 0.005 - 0.2 mg/kg was acceptable for all pesticides, with coefficients of determination (R^2) above 0.985. Matrix matched calibration curves were used for calculating the quantification results to improve accuracy. Finally, the method was used successfully in detecting pesticide residues in commercial gape wines.

Key words: pesticide residue /GC- MS/MS/m-PFC/Wine

1 Introduction

As one of the most commonly consumed alcoholic beverages, Grape wine is popular worldwide. Besides its distinctive flavor, wine consumed moderately is correlated with reducing risk for both mortality and morbidity of human cardiovascular disease [1]and oxidative damage[2]. The worldwide consumption of wine is increasing steadily and has reached up to 240 Mhl per year according to the record collected during the recent years (*http://www.oiv.int/oiv/info/enpublicationsstatistiques*).

Grape wine is produced from grapes. During the grape cultivation period, it is common practice in vineyards to use pesticides, such as fungicides,insecticides and herbicides to obtain high production. Grapes received multiple doses of pesticides which may transfer into wine partly[3-7].A ccording to previous market surveillance studies[8-12], metalaxyl, tebuconazol, cyprodinil, procymidone, fenhexamid, iprodione azoxystrobin and more were detected in commercial grape wines, with the first three being the most frequently detected pesticides. The risk of residues of these pesticides in wines will imply a health hazard. For this reason, their maximum residue limits (MRLs) should be set by the current regulations[13]. Up to now and with regard to the grapevine products, MRLs are only set for grapes, taking into account the transfer in the wine. MRLs for wine are still scarcely established[14,15]. Consequently, it is significant to establish rapid, simple, sensitive and environmentally friendly analytical methods for the trace analysis of pesticides residues in wine samples to assess their safety and possible risk to human health.

Sample preparation is considered as one of the most important steps in any pesticide residue analytical procedure. The determination of pesticide residues in wine is challenging due to the complexity of the matrix, which consists of alcohol, organic acids, sugars, and polyphenols (e.g. anthocyanins, flavonols, and tannins). Many sample preparation methods for wine has been successfully reported.Include liquid-liquid extraction (LLE) with different organic solvents[10,16-18], solid-phase extraction (SPE) with reversed-phase C18 or polymeric sorbents[19-25] , solid-phase microextraction (SPME)[20,26,27], and ultrasound-assisted emulsification microextraction (USAEME) [26,28], single drop liquid liquid microextraction (SDME) [29-32], Membrance-assisted solvent extraction [3] and dispersive liquid–liquid microextraction (DLLME) [33-35]

Recently, the QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) is a sample preparation technique that was first reported in 2003 by Anastassiades et al [36].The QuEChERS cleanup technique belongs to dispersive-solid phase extraction (dispersive-SPE) [37]. To the present, there have been many reports on the QuEChERS-based method for the determination of pesticides in wines [38-44].

According to the Iijiama in 1991[45], Carbon nanotubes (CNTs) is a type of novel and interesting class of carbonaceous materials. Based on the principle of carbon atom layers in the wall of nanotubes [46-47], These materials were classified into single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). Resently, MWCNTs have been repoterd as effective SPE materials in extraction of

pesticides[48-51].

In pesticide multi-residue analysis with QuEChERS method, MWCNTs were used as a type of alternative reversed-dispersive solid phase extraction materials , as our previous studied [52-54]. And these materials were also blended with other sorbents, such as PSA, GCB and C18, for dispersive cleanup of acetonitrile extracts from complex matrices like tea[53], scallion, ginger and garlic[55-56]. During the new multi-plug filtration cleanup(m-PFC, see Section “2.4 m-PFC procedures”) procedure developed by our group, the mixture of MWCNTs, anhydrous magnesiumsulfate and other sorbents were used as solid-phase sorbents, which packed in a short syringle cartridge. With the syringe needle kept under the surface of the extract, the syringe piston was pushed and pulled for several timeswhich intended to adsorb the interfering substances in the matrix and removed water. The m-PFC method only took just about tens seconds to perform,which was so rapid that none of solvent evaporated[57-59] .

The main objective of the work was to devopment a rapid, sensentive and reliable analytical method by m-PFC cleanup. In this work, 72 pesticides with different chemical structure in wine determinated using GC-MS/MS. This method was successfully applied in market survey samples.

2 Materials and meththods

2.1 Chemicals and materials

Initial sample preparation was identical to that used for QuEChERS method,the standard compounds were offered by the Institute of the Control of Agrochemicals, Ministry of Agriculture, P. R.China. The purities of the standard pesticides were from

95 to 99%. 10 mg/L Stock solutions of mixture pesticides were prepared in acetonitrile stored at -20℃. The working solutions were prepared daily. HPLC-grade acetonitrile was obtained from Fisher Chemicals (Fair Lawn, NJ, USA). Analytical reagentgrade anhydrous sodium chloride (NaCl) and magnesium sulfate (MgSO4) were obtained from Sinopharm Chemical Reagent (Beijing, China). Tianjin Bonna-Agela Technologies (China) provided MWCNTs with different average external diameters and PSA. MWCNTs were dried for 2 h at 120℃ to remove the absorbed water and then kept in desiccators for storage.

2.2 Apparatus and conditions

Centrifugation was carried in two different instruments:Anke TDL-40B centrifugewith a bucket rotor (4×100 mL) (Shanghai, China) and SIGMA 3K15 microcentrifuge with angular rotor (24×2.0 mL)(BMH Instruments, China).

Samples were preparing by QL-901 Vortex (Kylin-bell Lab Instruments, Jiangsu, China). And The temperature of samples was controled by Meiling BCD-245W refrigerator freezer (Beijing, China).

The determinations were conducted using an Agilent 7000A triple-quadrupole mass spectrometer with an Agilent 7890A GC. The GC separation was performed using an Agilent Technologies capillary column, HP-5MS analytical column (30 m × 250 μm × 0.25 μm film thickness) with helium (99.9999%) as carrier gas at a flow rate of 1.2 mL /min. The column temperature was initially at 50 ℃ (hold for 1 min), ramped up to 130 ℃(hold for 1 min) at 30 ℃/min and then to 250 ℃ at 5 ℃/min, and finally to 290 ℃ at 10 ℃/ min, holding for 5 min. The temperature of the injector port was 250 ℃,

and the injection volume in the non-split mode was 1 μL. The total running time was 38 min.

The mass spectrometer was processed in electron ionization mode (70 eV). All MS/MS experiments used the default settings of the instrument, i.e. collision gas flow rate of 1.5 mL/min of N2 and 2.25 mL/min of He, and quadrupole temperature of 150 °C. The detector voltage was determined automatically by the instrument after automated MS/MS tuning and was typically 1250 V. Prior to each sequence, the mass spectrometer was fully autotuned using the instrument's default parameters.. Agilent MassHunter was used for instrument control,data acquisition and processing. For the final multiple reaction monitoring (MRM) acquisition method, two ion transitions were monitored at the experimentally optimized collision energy (CE) for each analyte. Both pairs of the MRM transitions were used for confirmation analysis and the more sensitive transitions were selected for quantification analysis in order to obtain more effiency separation. the optimized MS/MS conditions for the individual analytes and their typical retention times (RT) were shown in Table 1.

2.3 Sample preparation

A QuEChERS-based approach was adapted to isolate the 72 analytes in wine samples. The samples obtained from a local supermarket homogenized with a blender for 1 min at room temperature. The homogenized samples (10.0 ± 0.1 g) spiked at two concentration levels of 10, 50,100 μg/kg left for 30 min before extraction, which was used to determinate recovery of 72 pesticides. 10.0 ± 0.1 gof wine samples were weighed into a 50 mL centrifuge tube, adding to 10 mL of acetonitrile. After vortexing

for min, 1 g of sodium chloride and 4 g of anhydrous magnesium sulfate were added. Then the tube was cooled immediately to room temperature with ice-water bath. To prevent salt agglomeration, the centrifuge tube was shaken vigorously for 1 min before centrifugation at 3800 rpm for 5 min. At last, 1ml supernatant was used for further m-PFC.

2.4 m-PFC procedures

For m-PFC procedure, 1 mL of the supernatant was introduced into a 2.0 mL centrifuge tube. The sorbents (including 150 mg anhydrous $MgSO_4$) in column were adopted from optimized d-SPE sorbents. As shown in Figure 1, with the syringe needle placed under the surface of the extract, the syringe piston was pulled and pushed to enable the extracts to pass through the sorbents for purification. Finally, the layer was filtered with 0.22 μm filter membrane, then placed into an GC vial for the chromatographic analysis.

2.5. Method performances

Validation of the analytical method was carried out as followed parameters: linearity, limit of quantification(LOQ), limit of detection(LOD), precision and accuracy. Linearity research used matrix-matchedcalibration by analyzing samples of red wine and white wine. The precision and accuracy experiments were carried out in five replicates each at two fortification levels (10 and 100 μ g kg-1) for sample matrix. The LODs were determined as the concentration of analyte with signal-to-noise ratio (S/N) of 3 for the target ion; LOQs were decided by the concentration of analyte with a signal-to-noise ratio (S/N) of 10 for the target ion.

3 Results and discussion

3.1 Amount of the MWCNTs

After extraction of the analytes with 10 mL acetonitrile, the analyte molecules were partitioned in the organic solvent in the presence of the salt mixture (salting effect), then 1 ml of acetonitrile phase was further cleaned up by m-PFC. Zhao et al. [58] found that there were significant influences on the purification and recoveries of the pesticide extracts with different amounts of MWCNTs sorbents. To evaluate the effect of this parameter, different amounts of MWCNTs(5, 10, 15, 20 mg progressively) were investigated in the same procedure. The experiment was performed using 1 mL of the acetonitrile extract at the spiked level of 0.1 mg/kg and then cleaned up by m-PFC of containing different amounts of MWCNTs. With increased amount of MWCNTs, most recoveries of the analytes were acceptable, ranging from 70 to 120%[60]in matrix of red wine. As shown in figure 3. With increasing the amount of MWCNTs from 5 mg to 10 mg, the recoveries for epoxiconazole, Profenofos, Azoxystrobin, Bifenthrin remained at the acceptable level (70–103%). However, the amount of MWCNTs incresed to 15 mg and 20 mg, resulting in the recoveries of 33-69%. In addition, although better recoveries were achieved with 5 mg MWCNTs materials, the purification performance was not as good as 10 mg MWCNTs materials,which had acceptable recoveries with less chromatography. Therefore, 10 mg (1 mL extract) was used as the optimum amount for m-PFC due to its acceptable recoveries and good cleanup performances.

3.2 Optimization of the m-PFC procedure cycle times

The cycles of pulling and pushing during m-PFC procedure were optimized to improved recoveries and purification performance. Recoveries were accepted with 1 and 2 times of pulling and pushing, but the cleanup performance was not as good as 3 times due to more chromatography interferences observed. 4 times were also tested, but there was no significant difference preparing with the cleanup performance of 3 times. As a result, 3 times of pulling and pushing were chosen as the optimized m-PFC procedure, and the purification effects of different cleanup times were shown in figure 4 shows.

3.3 Validation of method

3.3.1 Linearity and matrix effects

The linearity of all pesticides in the range 0.002–0.1 mg/L with five calibration levels (0.002, 0.005, 0.01, 0.02, 0.05 and 0.1mg/L) was investigated by matrix-matched standard calibration in blank extracts of red and white wine. Linear calibration graphs were constructed by plotting the analyte concentrations versus relative peak area of the calibration standards. Linearity values calculated from the matrix-matched calibration (m-PFC cleanup) plotsfor each pesticide were coefficients of determination(R^2), as shown in Table 3. The quantitative results of detection method depend to a large extent on its calibration. Both pure solvent-based as well as matrix-matched gave R^2 values better than 0.985. Considering the complexity of the matrices, the matrix effects(ME) were evaluated in terms of slope ratios 100×(1-slope acetonitrile/slope matrix)[56].

The matrix effects include enhancement or suppression effects,so the obtained concentration rusuits can be erroneously depending on the solvent calibration curves[18].

Matrix-matched standards was compared with that in solvent standards to examine the matrix effects. Table 2 summarized the results. In our work, it was considered that, if the value was in the range of -10%–10%, the matrix effect could be ignored; if the value was lower than -10% or higher than 10%, it could show matrix suppression or enhancement effect responsively[57]. The results showed in red and white wine 45 and 25 of pesticides presented enhancement effect(ME>0),and the anthers 27 and 47 of pesticides shows suppression effect (ME<0),44 and 34 of pesticides expressed matrix suppression and enhancement effect distinctly. Consequently, to obtain more accurate results, pesticide residue concentrations in non-compliance samples and validation experiments were calculated using matrix-matched calibration standards, as suggested in EU guidelines[55], excluding any influence produced by matrix effects. In order to overcome the adverse impact of matrix effects on the quantified results,We calibrated samples results with matrix-matched standards to guarantee correct quantification of pesticides concentrations in real samples.

3.3.2 Recovery and precision

Recovery and repeatability of the method were established to assess the method performance. The repeatability and the trueness of the method were investigated by performing five consecutive extractions (n=5) of spiked matrices at three concentration levels (0.01, 0.05 and 0.1 mg/kg). All the recoveries of 72 pesticides were determined by using matrix-matched calibration standards, as stated in Section 3.3.1. As shown in Table 3, The recoveries of all pesticides were in the range 70.2–108.8% (between 70.2% and 108.8% for white wine, 72.3% and 106.0% for red wine), with Relative standard

deviations (RSDs) below 8.3%. All the recoveries and RSDs are in the acceptance range of the SANCO/10684/2009 of the European Quality Control guidelines[60]

3.3.3 Limitation of quantitation and detection

The developed method was examined for simultaneous extractionand determination of 72 analytes in wine matrices with varying levels of LOD and LOQ. Due to the matrix dependence of LODs and LOQs, it is suggested to performmatrix-matched calibration for quantitative analysis of unknown complex samples. Table 3 showed the LOD and LOQ values for the pesticides studied in wine. The LODs ranged from 0.002 to 0.01 mg/kg ,while the LOQs were in range of 0.01 to 0.05 mg/kg.

At a result, the validation data for all analytes conformed to the EU guidelines[55] for pesticide residue analysis, reflecting acceptable performance in the developed method.

3.5 Method application

The developed QuEChERS method with m-PFC cleanup step was applied to real samples. Seventy referred samples (including 50 red wine and 20 white wine) from supermarket in Beijing were treated and analyzed by GC-MS/MS. Due to the lack of MRLs in wine, It is accepted that MRLs for wine are the same as the wine grapes according to European Regulation 396/2005/EC. Pesticide residues were detected in 6 samples (10%), such as Difenoconazole(2.9%), Pyridaben (4.3%), Carbosulfan (2.9%), Pyrimethanil(1.4%),Propyzamide(1.4%), Simazine(4.3%) and Atrazine(4.3%), which were the most frequently detected pesticides with corresponding average values 0.015, 0.014, 0.040, 0.031, 0.035, 0.023 mg/kg. All selected wine samples were not exceed

the maximum permitted residue levels set by EU 396/2005/EC.

4 Concluding

An efficient and effective m-PFC multiresidue method has been developed for the determination of 72 pesticides in wine by GC–MS/MS. The m-PFC method shows a simplified rapid and cleanup method without any solvent evaporation, vortex or centrifugation procedure. The method achieves high quality of results (good repeatabilities, recovery, and wide analytical scope) and practical benefits (low cost, little labour, high sample throughput, hardly any waste and few labware and spacedemands). The method was found to be very sensitive and gave LOQ<0.05 mg/kg for all analytes. Above all, the m-PFC could be used as a feasibility of convenient, rapid and high-throughput cleanup method on analysis of analytes in wine.

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Table 1 MRM parameters of 72 pesticides in wine by GC-MS/MS.

No.	Pesticide	RT(min)	quantification transition[a]	confirmation transition[a]
1	Dichlorvos	5.22	109→79(5)	185→93(10)
2	O-Phenylphenol	10.21	170→169(10)	169→141(10)
3	Sulfotep-ethyl	13.31	322→146(25)	322→65(40)
4	Phorate	13.41	121→65 (10)	260→75 (5)
5	Simazine	14.32	201→172 (10)	186→68 (25)
6	Thiabendazole	14.33	201→130 (25)	201→174 (15)
7	Carbofuran	14.51	164→149 (10)	164→131 (20)
8	Indoxacarb	14.51	218→203 (15)	264→176 (15)
9	Atrazine	14.52	171.9→69 (15)	172→43 (30)
10	Acephate	14.52	136→94 (10)	136→42 (10)
11	Clomazone	14.60	124.9→89 (20)	204→107 (20)
12	Terbufos	15.01	231→129(25)	231→175 (10)
13	Pyrimethanil	15.33	198→118 (25)	198→156 (25)
14	Acetochlor	17.18	223→132 (20)	146→118 (10)
15	Methyl parathion	17.23	263→109 (15)	263→79 (30)
16	Dimethoate	17.36	125→79 (5)	125→93 (10)
17	Tolclofos-methyl	17.36	265→250 (15)	265→93 (25)
18	Iprovalicard- Ⅰ	17.88	158→98 (10)	158→116 (10)
19	Fenitrothion	18.29	277→260 (5)	277→109 (20)
20	Ethofumesate	18.44	286→207 (5)	286→179 (15)
21	Carbosulfan	18.74	160→104 (10)	160→57 (15)
22	Malathion	18.76	173→99 (15)	173→117 (15)
23	Metolachlor	18.87	162→133 (15)	162.2→132 (25)
24	Fenthion	18.99	278→109 (10)	278→125 (15)
25	Diethofencarb	19.01	267→225 (5)	196→168 (5)
26	Chlorpyrifos	19.06	314→258 (15)	314→286 (15)
27	Triadimefon	19.26	208→181 (10)	208→111 (15)
28	Isocarbophos	19.34	136→108 (14)	230→212 (8)
29	Cyprodinil	19.977	225→224 (10)	224→208 (20)
30	Metazachlor	20.18	209→132 (20)	133→117 (25)
31	Pendimethalin	20.25	252→162 (10)	252→161 (20)
32	Chlorfenvinphos	20.68	267→159 (20)	267→81 (40)
33	Fipronil	20.78	367→213 (30)	367→228 (30)
34	Procymidone	20.90	283→96 (10)	283→255 (10)
35	Vinclozolin	20.90	212→145 (15)	212→172 (25)
36	Methidathion	21.18	145→85 (5)	145→58 (15)
37	Butachlor	21.76	237→160 (5)	188.1→160 (10)
38	Flutriafol	21.94	164→109 (20)	219→123 (15)
39	Carbaryl	22.04	144→116 (15)	144→114 (30)
40	Napropamide	22.04	128→72 (10)	271→128 (5)
41	Hexaconazole	22.14	213.9→172 (20)	214→159 (20)

42	Profenofos	22.40	208→63 (35)	208→98 (25)
43	Oxadiazon	22.72	175→112 (15)	302→175 (13)
44	Iprovalicard-Ⅱ	22.73	158→98 (10)	158→116 (10)
45	Carboxin	22.76	235→143 (5)	144→87 (5)
46	Oxyfluorfen	22.97	252→252 (5)	252→196 (20)
47	Flusilazole	23.05	233→152 (20)	233→165 (20)
48	Kresoxim-methyl	23.13	206→116 (5)	206→131 (10)
49	Metalaxyl	23.13	206→132 (5)	206→162 (20)
50	Diniconazole	24.11	268→232 (15)	270→234 (15)
51	Triazophos	24.72	161→134 (5)	257→162 (5)
52	Propiconazole-Ⅰ	25.27	259→173 (15)	261→175 (15)
53	Propiconazole-Ⅱ	25.46	259→69 (12)	259→191 (5)
54	Propyzamide	25.47	173→145 (20)	175→147 (20)
55	Diclofop methyl	25.96	253→162 (15)	340→253 (15)
56	Epoxiconazole	26.55	192→138 (10)	192→157 (5)
57	Iprodione	26.85	314→245 (10)	314→271 (20)
58	Cypermethrin-Ⅰ	27.33	181→152 (30)	181→127 (35)
59	Bifenthrin	27.33	181→165 (25)	181→166 (25)
60	Bifenox	27.77	311→279 (10)	311→216 (20)
61	Pyriproxyfen	28.61	136→78 (25)	-
62	Cypermethrin-Ⅱ	28.91	181→152 (30)	181→127 (35)
63	Beta-cypermethrin	28.92	181→152 (30)	181→127 (35)
64	Cypermethrin-Ⅲ	29.26	181→152 (30)	181→127 (35)
65	Permethrin-Ⅰ	30.58	183→153 (20)	183→168 (20)
66	Pyridaben	30.52	147→117 (20)	147→132 (10)
67	Permethrin-Ⅱ	30.37	183→115 (25)	183→77 (30)
68	Cypermethrin-Ⅳ	30.58	181→152 (30)	181→127 (35)
69	Difenoconazole	33.61	323→265 (10)	265→139 (25)
70	Azoxystrobin	34.40	344→329 (15)	253→172 (20)
71	Deltamethrin-Ⅰ	33.62	181→152 (25)	253→172 (10)
72	Deltamethrin-Ⅱ	33.92	181→152 (25)	253→172 (10)

[a]Collision energy (eV) is given in parentheses.

Table 2 Linearity parameters(rang,slope,R2)obtained by using standards in acetonitrile and matched as well as matrix effects measured as 100×(1-slope acetonitrile/slope matrix)

Pesticide	Linearity range (mg/kg)	Acetonitrile		Red wine			White wine		
		Slope	R^2	Slope	R^2	Matrix effect,%	Slope	R^2	Matrix effect,%
Dichlorvos	0.002-0.1	9.6E-04	0.9924	1.1E-05	0.9977	9.4	9.5E-04	0.9999	-1.7
O-Phenylphenol	0.002-0.1	6.8E-05	0.9989	8.5E-05	0.9912	19.5	7.0E-05	0.9958	2.2
Sulfotep-ethyl	0.002-0.1	3.3E-05	0.9916	3.6E-05	0.9982	8.5	3.4E-05	0.9920	3.6
Phorate	0.002-0.1	2.2E-05	0.9897	2.3E-05	0.9899	6.1	2.3E-05	0.9957	5.9
Simazine	0.002-0.1	3.4E-04	0.9878	3.9E-04	0.9985	12.5	3.1E-04	0.9990	-7.4
Thiabendazole	0.005-0.1	6.8E-03	0.9855	5.9E-03	0.9959	-14.9	6.6E-03	0.9956	-3.8
Carbofuran	0.002-0.1	3.1E-05	0.9968	3.3E-05	0.9986	8.1	3.2E-05	0.9921	4.5
Indoxacarb	0.005-0.1	3.0E-03	0.9997	2.8E-03	0.9922	-5.9	2.5E-03	0.9894	-17.0
Atrazine	0.002-0.1	1.7E-04	0.9989	2.0E-04	0.9954	11.1	1.5E-04	0.9853	-15.3
Acephate	0.005-0.1	3.3E-03	0.9991	3.8E-03	0.9858	13.6	3.4E-03	0.9887	2.6
Clomazone	0.002-0.1	3.1E-05	0.9926	3.7E-05	0.9495	14.8	3.2E-05	0.9885	3.2
Terbufos	0.002-0.1	2.1E-04	0.9917	2.5E-04	0.9916	17.4	2.5E-04	0.9977	17.1
Pyrimethanil	0.002-0.1	1.7E-05	0.9957	1.5E-05	0.9987	-10.1	1.6E-05	0.9986	-6.9
Acetochlor	0.002-0.1	8.8E-04	0.9935	1.2E-05	0.9984	24.1	9.5E-04	0.9910	6.9
Methyl parathion	0.002-0.1	3.8E-05	0.9996	4.1E-05	0.9941	7.2	3.7E-05	0.9915	-2.1
Dimethoate	0.002-0.1	1.0E-06	0.9919	9.3E-05	0.9896	-7.2	8.9E-05	0.9994	-12.9

Tolclofos-methyl	0.002-0.1	5.0E-06	0.9928	6.0E-06	0.9959	16.7	5.4E-06	0.9995	7.4
Iprovalicard- I	0.002-0.1	5.5E-03	0.9937	6.8E-03	0.9866	18.7	4.9E-03	0.9956	-12.8
Fenitrothion	0.002-0.1	8.4E-04	0.9930	9.5E-04	0.9859	12.3	8.5E-04	0.9943	1.9
Ethofumesate	0.002-0.1	2.1E-05	0.9954	2.2E-05	0.9973	5.8	1.9E-05	0.9899	-11.2
Carbosulfan	0.005-0.1	9.2E-02	0.9919	1.1E-03	0.9928	15.4	1.1E-03	0.9945	15.6
Malathion	0.002-0.1	2.8E-05	0.9966	3.1E-05	0.9959	10.4	2.5E-05	0.9948	-11.9
Metolachlor	0.002-0.1	4.5E-05	0.9987	5.5E-05	0.9866	18.2	4.5E-05	0.9942	-0.4
Fenthion	0.002-0.1	1.4E-05	0.9934	1.6E-05	0.9967	7.5	1.4E-05	0.9984	-3.5
Diethofencarb	0.002-0.1	3.7E-05	0.9997	4.0E-05	0.9819	6.5	3.9E-05	0.9894	5.6
Chlorpyrifos	0.002-0.1	1.9E-05	0.9942	2.2E-05	0.9925	15.7	1.9E-05	0.9948	1.3
Triadimefon	0.002-0.1	1.2E-05	0.9998	9.7E-04	0.9937	-24.1	1.1E-05	0.9951	-9.3
Isocarbophos	0.002-0.1	3.3E-05	0.9929	3.5E-05	0.9958	5.8	3.4E-05	0.9935	4.2
Cyprodinil	0.002-0.1	9.5E-05	0.9999	8.6E-05	0.9863	-10.4	7.7E-05	0.9864	-23.1
Metazachlor	0.002-0.1	1.5E-05	0.9991	1.4E-05	0.9988	-9.2	1.8E-05	0.9987	14.0
Pendimethalin	0.002-0.1	1.0E-05	0.9894	1.0E-05	0.9979	2.2	1.2E-05	0.9839	15.1
Chlorfenvinphos	0.002-0.1	1.0E-05	0.9931	1.2E-05	0.9890	12.6	8.9E-04	0.9847	-14.9
Fipronil	0.002-0.1	5.2E-04	0.9968	6.5E-04	0.9881	19.0	4.9E-04	0.9850	-6.6
Procymidone	0.002-0.1	2.2E-05	0.9914	2.1E-05	0.9959	-3.2	1.8E-05	0.9854	-23.2
Vinclozolin	0.002-0.1	6.6E-03	0.9934	6.0E-03	0.9948	-10.5	5.9E-03	0.9994	-13.2
Methidathion	0.002-0.1	4.3E-05	0.9895	4.7E-05	0.9939	9.2	3.8E-05	0.9885	-11.3
Butachlor	0.002-0.1	7.5E-04	0.9916	9.1E-04	0.9957	18.0	7.3E-04	0.9887	-1.7
Flutriafol	0.002-0.1	1.3E-05	0.9967	1.4E-05	0.9955	10.7	1.2E-05	0.9916	-8.6
Carbaryl	0.005-0.1	2.7E-04	0.9958	2.4E-04	0.9889	-13.9	2.6E-04	0.9943	-6.9

Napropamide	0.002-0.1	1.7E-05	0.9938	1.7E-05	0.9998	1.5	1.6E-05	0.9979	-6.3
Hexaconazole	0.002-0.1	5.1E-04	0.9996	4.6E-04	0.9964	-12.0	4.8E-04	0.9948	-6.7
Profenofos	0.002-0.1	1.6E-04	0.9949	2.1E-04	0.9962	25.3	1.8E-04	0.9999	12.3
Oxadiazon	0.002-0.1	3.0E-05	0.9925	3.0E-05	0.9969	-0.8	2.5E-05	0.9948	-18.9
Iprovalicard-Ⅱ	0.005-0.1	1.1E-03	0.9939	9.9E-02	0.9928	-5.7	9.3E-02	0.9972	-12.7
Carboxin	0.002-0.1	2.5E-05	0.9916	3.4E-05	0.9896	28.6	2.4E-05	1.0000	-4.2
Oxyfluorfen	0.002-0.1	2.3E-05	0.9984	2.6E-05	0.9927	11.5	2.0E-05	0.9942	-17.5
Flusilazole	0.002-0.1	1.1E-05	0.9956	8.8E-04	0.9990	-24.3	9.5E-04	0.9940	-15.0
Kresoxim-methyl	0.002-0.1	1.9E-05	0.9942	1.6E-05	0.9792	-19.6	1.8E-05	0.9998	-10.1
Metalaxyl	0.002-0.1	1.2E-05	0.9967	9.7E-04	0.9963	-20.1	9.3E-04	0.9965	-25.2
Diniconazole	0.002-0.1	1.5E-05	0.9924	1.3E-05	0.9928	-21.4	1.4E-05	0.9971	-14.1
Triazophos	0.002-0.1	9.2E-04	0.9913	9.2E-04	0.9969	-0.8	9.1E-04	0.9857	-2.0
Propiconazole-Ⅰ	0.002-0.1	9.4E-04	0.9957	9.4E-04	0.9942	-0.8	9.1E-04	0.9920	-3.7
Propiconazole-Ⅱ	0.002-0.1	2.1E-05	0.9962	2.2E-05	0.9967	2.5	1.9E-05	0.9854	-10.3
Propyzamide	0.002-0.1	5.5E-05	0.9938	4.0E-05	0.9966	-37.3	4.9E-05	0.9801	-13.0
Diclofop methyl	0.002-0.1	1.1E-05	0.9989	1.3E-05	0.9894	18.3	1.0E-05	0.9900	-3.9
Epoxiconazole	0.01-0.1	6.0E-04	0.9937	6.4E-04	0.9964	5.5	5.1E-04	0.9977	-17.2
Iprodione	0.002-0.1	5.5E-04	0.9988	7.3E-04	0.9922	24.3	5.6E-04	0.9884	1.9
Cypermethrin-Ⅰ	0.002-0.1	2.2E-04	0.9936	2.4E-04	0.9960	8.4	2.1E-04	0.9978	-4.3
Bifenthrin	0.002-0.1	8.8E-05	0.9942	1.0E-06	0.9920	12.3	8.8E-05	0.9920	0.4

Bifenox	0.002-0.1	4.1E-04	0.9969	4.9E-04	0.9935	16.2	5.6E-04	0.9918	26.8
Pyriproxyfen	0.002-0.1	2.0E-05	0.9960	2.6E-05	0.9919	24.4	2.0E-05	0.9912	3.3
Cypermethrin-Ⅱ	0.005-0.1	5.3E-04	0.9938	4.7E-04	0.9933	-11.8	4.2E-04	0.9924	-25.4
Beta-cypermethrin	0.005-0.1	3.4E-04	0.9962	3.7E-04	0.9957	9.9	3.2E-04	0.9909	-4.4
Cypermethrin-Ⅲ	0.005-0.1	2.8E-04	0.9973	2.8E-04	0.9872	-1.7	2.5E-04	0.9955	-11.7
Permethrin-Ⅰ	0.005-0.1	3.9E-04	0.9959	4.7E-04	0.9868	16.0	5.0E-04	0.9947	21.6
Pyridaben	0.002-0.1	8.0E-05	0.9929	1.0E-06	0.9910	20.0	8.3E-05	0.9948	4.0
Permethrin-Ⅱ	0.005-0.1	2.5E-04	0.9954	2.3E-04	0.9925	-8.1	2.8E-04	0.9944	10.5
Cypermethrin-Ⅳ	0.005-0.1	7.7E-03	0.9966	9.2E-03	0.9890	16.2	9.3E-03	0.9978	17.0
Difenoconazole	0.002-0.1	5.9E-05	0.9919	6.2E-05	0.9887	3.9	4.6E-05	0.9991	-28.4
Azoxystrobin	0.005-0.1	2.0E-04	0.9961	2.4E-04	0.9921	16.2	1.6E-04	0.9958	-26.8
Deltamethrin-Ⅰ	0.002-0.1	3.8E-03	0.9958	3.4E-03	0.9858	-13.1	3.6E-03	0.9957	-6.8
Deltamethrin-Ⅱ	0.002-0.1	5.0E-03	0.9952	4.30E-03	0.9853	-16.1	4.20E-03	0.9875	-18.9

Table 3 Average recoveries,RSDs,LOD and LOQ after application of m-PFC procedure by GC-MS/MS in wine

Pesticide	Red wine					Whit wine				
	Recovery(RSD),%			LOD	LOQ	Recovery(RSD),%			LOD	LOQ
	0.01 mg/kg	0.05mg/kg	0.1mg/kg	(mg/kg)	(mg/kg)	0.01 mg/kg	0.05mg/kg	0.1mg/kg	(mg/kg)	(mg/kg)
Dichlorvos	102.2 (6.2)	99.8 (3.2)	98.4 (8.1)	0.002	0.01	88.8 (2.1)	100.4 (8.0)	103.2 (2.5)	0.002	0.01
O-Phenylphenol	100.5 (5.0)	88.4 (1.0)	83.4 (3.2)	0.002	0.01	81.8 (4.7)	97.1 (4.0)	86.9 (3.4)	0.002	0.01
Sulfotep-ethyl	93.1 (1.4)	87.1 (3.1)	84.2 (2.7)	0.002	0.01	103.8 (4.8)	91.1 (1.1)	91.3 (3.1)	0.002	0.01
Phorate	95.0 (4.9)	86.0 (2.1)	84.0 (2.5)	0.002	0.01	102.9 (4.1)	97.0 (1.2)	93.0 (0.5)	0.002	0.01
Simazine	82.2 (4.4)	86.5 (1.8)	82.8 (1.3)	0.002	0.01	100.7 (2.6)	90.6 (4.4)	83.5 (2.7)	0.002	0.01
Thiabendazole	84.7 (0.9)	99.3 (2.2)	88.1 (2.0)	0.002	0.01	-	91.3 (1.9)	86.9 (2.7)	0.01	0.05
Carbofuran	97.3 (2.9)	89.1 (0.7)	92.5 (4.6)	0.003	0.01	108.4 (1.8)	100.7 (4.1)	100.2 (0.9)	0.003	0.01
Indoxacarb	-	100.5 (2.3)	100.8 (5.9)	0.01	0.05	-	108.3 (0.8)	82.7 (2.1)	0.01	0.05
Atrazine	94.9 (2.5)	86.8 (2.9)	84.8 (3.0)	0.002	0.01	96.0 (2.7)	95.9 (3.2)	91.3 (1.4)	0.002	0.01
Acephate	-	87.6.0 (8.3)	94.5 (4.0)	0.01	0.05	-	90.0 (2.6)	95.3 (1.1)	0.01	0.05
Clomazone	84.5 (5.6)	94.8 (2.5)	97.9 (5.8)	0.002	0.01	96.2 (4.0)	97.2 (3.4)	84.2 (1.1)	0.002	0.01
Terbufos	73.7 (0.7)	83.6 (3.8)	79.4 (2.4)	0.002	0.01	92.4 (4.9)	98.9 (3.4)	89.4 (0.6)	0.002	0.01
Pyrimethanil	99.7 (2.4)	92.7 (2.0)	96.1 (2.4)	0.002	0.01	94.8 (1.4)	90.2 (2.2)	85.1 (0.4)	0.002	0.01
Acetochlor	87.1 (9.2)	92.7 (3.2)	84.1 (4.4)	0.002	0.01	105.3 (3.3)	101.6 (3.4)	90.8 (1.3)	0.002	0.01
Methyl parathion	72.3 (2.8)	81.5 (2.6)	87.7 (6.8)	0.002	0.01	106.1 (3.0)	89.7 (4.4)	97.0 (1.7)	0.002	0.01
Dimethoate	85.1 (3.0)	87.4 (2.9)	82.2 (2.1)	0.002	0.01	89.4 (2.3)	85.6 (2.0)	91 .3(5.9)	0.002	0.01
Tolclofos-methyl	84.6 (3.4)	85.3 (2.4)	82.2 (2.4)	0.002	0.01	93.9 (3.8)	81.2 (3.5)	81.7 (2.0)	0.002	0.01
Iprovalicard- Ⅰ	-	94.2 (6.2)	104.3 (2.4)	0.02	0.05	99.3 (4.1)	96.3 (5.4)	84.2 (1.5)	0.002	0.01

Fenitrothion	80.1 (3.2)	78.4 (3.3)	90.0 (4.4)	0.002	0.01	90.7 (3.7)	90.6 (5.7)	95.7 (1.7)	0.02	0.05
Ethofumesate	94.7 (2.4)	89.4 (4.7)	90.7 (4.7)	0.002	0.01	96.1 (3.1)	100.2 (2.7)	93.4 (2.1)	0.003	0.01
Carbosulfan	-	96.8 (3.2)	92.3 (3.0)	0.002	0.05	-	95.9 (4.8)	73.1 (5.5)	0.002	0.05
Malathion	81.3 (3.9)	86.0 (4.0)	89.0 (6.7)	0.002	0.01	95.2 (4.3)	102.6 (0.3)	100.6 (2.4)	0.002	0.01
Metolachlor	81.9 (5.0)	94.1 (3.1)	82.4 (5.2)	0.002	0.01	102.0 (1.6)	103.1 (3.8)	94.3 (1.4)	0.002	0.01
Fenthion	88.8 (6.5)	92.2 (4.0)	84.6 (4.7)	0.002	0.01	87.5 (0.6)	91.0 (2.8)	84.8 (1.4)	0.002	0.01
Diethofencarb	72.3 (2.1)	90.1 (3.5)	80.2 (6.2)	0.002	0.01	87.9 (3.3)	81.0 (2.3)	77.9 (0.7)	0.002	0.01
Chlorpyrifos	82.9 (5.7)	99.8 (5.3)	85.5 (2.3)	0.002	0.01	78.8 (3.6)	77.9 (3.8)	73.0 (0.3)	0.002	0.01
Triadimefon	99.4 (0.9)	90.5 (3.5)	94.9 (4.2)	0.002	0.01	85.0 (2.4)	109.1 (1.0)	93.4 (1.9)	0.002	0.01
Isocarbophos	73.7 (4.6)	77.5 (4.1)	89.2 (3.2)	0.002	0.01	89.8 (5.5)	98.5 (1.3)	98.6 (0.9)	0.004	0.01
Cyprodinil	104.0 (2.0)	86.9 (3.3)	97.7 (1.5)	0.002	0.01	72.0 (1.5)	73.3 (4.4)	83.2 (1.8)	0.002	0.01
Metazachlor	93.9 (5.2)	91.9 (4.4)	82.2 (6.7)	0.002	0.01	106.0 (2.2)	105.1 (4.5)	87.5 (0.9)	0.002	0.01
Pendimethalin	84.1 (1.9)	80.8 (4.6)	72.8 (3.9)	0.002	0.01	86.8 (8.3)	78.6 (3.6)	74.7 (1.1)	0.002	0.01
Chlorfenvinphos	103.1 (2.0)	81.8 (1.2)	100.0 (2.6)	0.002	0.01	104.2 (3.5)	100.0 (6.5)	108.8 (1.4)	0.002	0.01
Fipronil	95.6 (5.2)	94.6 (7.3)	87.1 (5.2)	0.002	0.01	98.7 (8.2)	87.3 (4.4)	97.4 (0.1)	0.002	0.01
Procymidone	105.1 (2.1)	98.7 (2.3)	86.8 (3.2)	0.002	0.01	92.2 (2.0)	94.1 (4.2)	85.1 (2.1)	0.002	0.01
Vinclozolin	96.2 (1.4)	79.5 (3.7)	82.7 (3.4)	0.002	0.01	85.0 (2.8)	99.9 (3.5)	90.3 (1.2)	0.002	0.01
Methidathion	76.7 (1.6)	108.4 (2.9)	92.8 (4.1)	0.002	0.01	102.5 (5.6)	98.2 (4.9)	104.8 (1.5)	0.002	0.01
Butachlor	89.3 (6.7)	90.8 (1.9)	84.2 (4.7)	0.002	0.01	101.2 (2.4)	99.0 (3.7)	92.7 (0.7)	0.002	0.01
Flutriafol	93.8 (0.9)	85.2 (0.5)	84.2 (2.3)	0.002	0.01	94.0 (2.3)	92.4 (2.1)	94.5 (2.5)	0.002	0.01
Carbaryl	-	80.7 (4.0)	97.4 (4.0)	0.03	0.05	86.6 (2.4)	85.9 (3.9)	70.2 (1.3)	0.005	0.01
Napropamide	92.5 (2.0)	89.9 (1.9)	96.0 (0.9)	0.002	0.01	84.3 (2.1)	98.0 (0.8)	93.6 (0.6)	0.002	0.01
Hexaconazole	95.4 (0.6)	96.0 (2.8)	97.3 (1.7)	0.002	0.01	90.1 (0.9)	90.2 (1.4)	82.7 (1.0)	0.002	0.01

Profenofos	94.1 (2.5)	83.9 (3.0)	100.7 (5.6)	0.002	0.01	100.8 (3.9)	91.7 (1.8)	100.8 (2.5)	0.002	0.01
Oxadiazon	97.2 (3.5)	92.6 (1.8)	84.1 (5.3)	0.002	0.01	96.3 (1.6)	97.3 (3.6)	87.4 (1.0)	0.002	0.01
Iprovalicard-Ⅱ	-	96.2 (4.3)	98.0 (4.1)	0.01	0.05	-	96.4 (1.9)	91.0 (2.5)	0.02	0.05
Carboxin	106.1 (2.7)	90.6 (4.9)	89.5 (1.2)	0.002	0.01	85.8 (3.5)	89.7 (3.8)	93.7 (0.9)	0.002	0.01
Oxyfluorfen	87.0 (0.8)	101.8 (4.8)	84.7 (2.5)	0.002	0.01	83.5 (3.0)	88.4 (7.7)	84.9 (1.4)	0.002	0.01
Flusilazole	-	92.4 (5.3)	90.9 (4.2)	0.01	0.05	86.8 (1.6)	85.1 (1.0)	85.3 (3.1)	0.002	0.01
Kresoxim-methyl	83.6 (2.9)	84.9 (0.8)	81.4 (4.2)	0.002	0.01	101.0 (1.4)	95.5 (2.3)	88.4 (1.7)	0.002	0.01
Metalaxyl	79.8 (2.3)	78.0 (2.2)	84.8 (4.3)	0.002	0.01	92.0 (6.3)	90.5 (3.4)	88.8 (0.8)	0.002	0.01
Diniconazole	105.4 (2.4)	106.0 (0.8)	99.0 (5.5)	0.002	0.01	96.4 (1.8)	94.7 (2.8)	92.7 (1.7)	0.002	0.01
Triazophos	-	86.0 (1.8)	95.5 (3.2)	0.01	0.05	100.8 (5.6)	93.8 (2.4)	94.5 (2.4)	0.002	0.01
Propiconazole-Ⅰ	95.0 (5.1)	89.8 (0.5)	99.4 (4.5)	0.002	0.01	97.0 (2.1)	90.0 (1.1)	94.2 (2.7)	0.002	0.01
Propiconazole-Ⅱ	96.5 (2.5)	92.1 (1.3)	97.1 (0.2)	0.002	0.01	91.7 (4.0)	89.6 (2.1)	94.9 (3.0)	0.002	0.01
Propyzamide	92.8 (3.4)	85.6 (2.3)	101.9 (2.6)	0.002	0.01	98.3 (2.1)	91.3 (2.2)	94.2 (2.9)	0.002	0.01
Diclofop methyl	99.2 (2.3)	89.6 (3.1)	96.1 (4.5)	0.002	0.01	93.3 (4.6)	92.6 (5.3)	81.2 (1.3)	0.002	0.01
Epoxiconazole	-	72.4 (3.7)	76.9 (2.8)	0.02	0.05	-	75.7 (6.0)	77.1 (0.4)	0.02	0.05
Iprodione	83.4 (4.2)	93.8 (2.1)	103.8 (7.5)	0.002	0.01	104.1 (1.9)	77.8 (3.5)	79.9 (2.2)	0.002	0.01
Cypermethrin-Ⅰ	87.1 (0.8)	89.6 (2.3)	78.6 (4.0)	0.002	0.01	94.7 (5.0)	102.5 (3.4)	93.3 (0.8)	0.002	0.01
Bifenthrin	85.0 (3.1)	89.9 (4.5)	85.7 (1.6)	0.002	0.01	98.9 (3.4)	85.6 (2.3)	84.9 (1.0)	0.002	0.01
Bifenox	102.6 (2.3)	90.7 (6.8)	87.9 (4.5)	0.002	0.01	97.7 (1.6)	104.3 (1.2)	103.4 (3.8)	0.002	0.01
Pyriproxyfen	83.5 (0.7)	85.1 (4.2)	83.0 (3.0)	0.002	0.01	86.3 (0.6)	79.0 (2.2)	73.9 (0.4)	0.002	0.01

Cypermethrin-Ⅱ	-	91.7 (2.9)	93.4 (1.6)	0.01	0.05	91.0 (2.8)	100.6 (2.0)	83.7 (0.8)	0.002	0.01
Beta-cypermethrin	-	91.7 (2.9)	93.4 (1.6)	0.01	0.05	91.0 (2.8)	100.6 (2.0)	83.7 (0.8)	0.002	0.01
Cypermethrin-Ⅲ	-	103.6 (4.5)	94.2 (3.9)	0.01	0.05	98.5 (5.5)	105.8 (2.5)	105.4 (1.9)	0.002	0.01
Permethrin-Ⅰ	-	94.7 (2.3)	97.2 (3.2)	0.01	0.05	-	104.2 (0.8)	104.9 (2.5)	0.02	0.05
Pyridaben	98.4 (5.5)	97.9 (2.2)	96.5 (4.9)	0.002	0.01	103.4 (2.9)	83.3 (1.3)	97.2 (0.8)	0.002	0.01
Permethrin-Ⅱ	83.7 (1.7)	83.9 (2.1)	98.1 (4.6)	0.003	0.01	95.7 (2.0)	93.2 (1.5)	96.0 (2.7)	0.002	0.01
Cypermethrin-Ⅳ	-	94.7 (3.0)	95.7 (2.3)	0.01	0.05	-	101.7 (1.1)	92.9 (1.9)	0.01	0.05
Difenoconazole	94.2 (4.3)	93.7 (2.6)	95.1 (3.5)	0.002	0.01	94.6 (2.8)	89.9 (1.0)	93.1 (2.2)	0.002	0.01
Azoxystrobin	-	98.2 (6.1)	95.2 (1.7)	0.01	0.05	-	91.2.0 (4.1)	103.6 (1.3)	0.01	0.05
Deltamethrin-Ⅰ	-	95.8 (3.3)	91.6 (4.6)	0.01	0.05	96.4 (3.2)	101.3 (0.7)	98.8 (1.8)	0.002	0.01
Deltamethrin-Ⅱ	-	96.1 (2.7)	95.2 (3.5)	0.01	0.05	98.3 (1.1)	97.9 (3.6)	84.8 (2.1)	0.002	0.01

Figure 1. Schematic diagram of an m-PFC tip

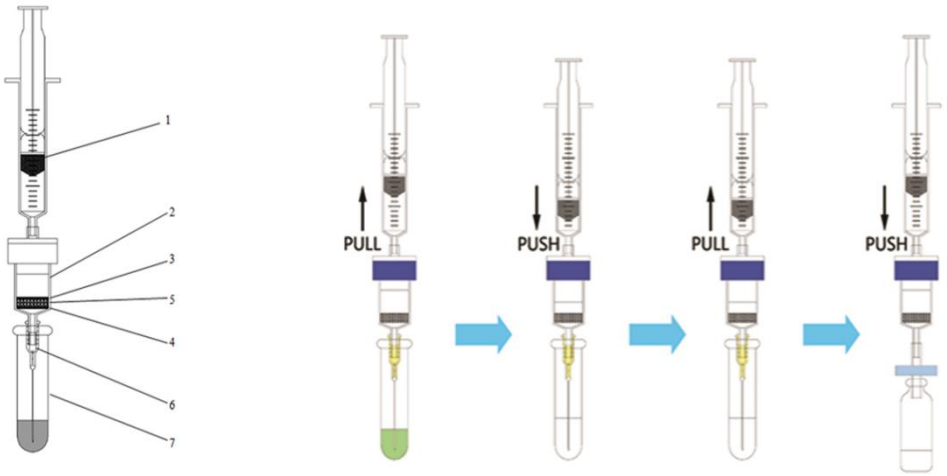
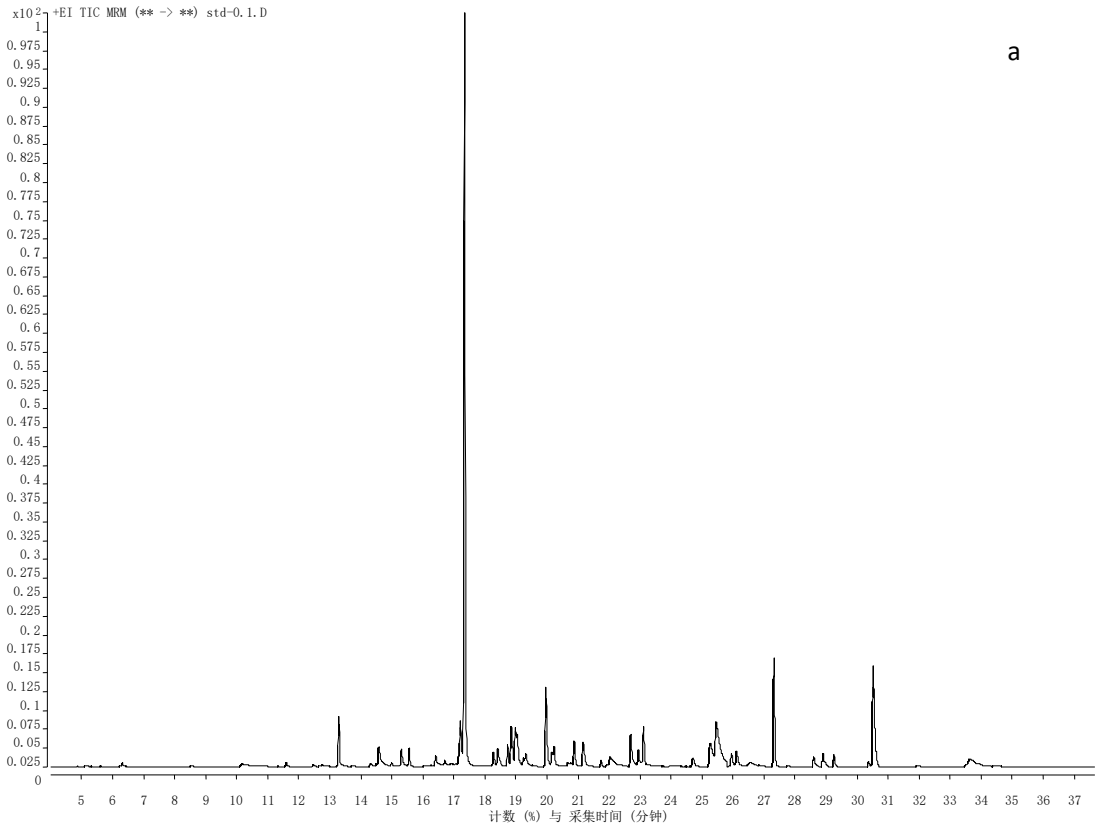
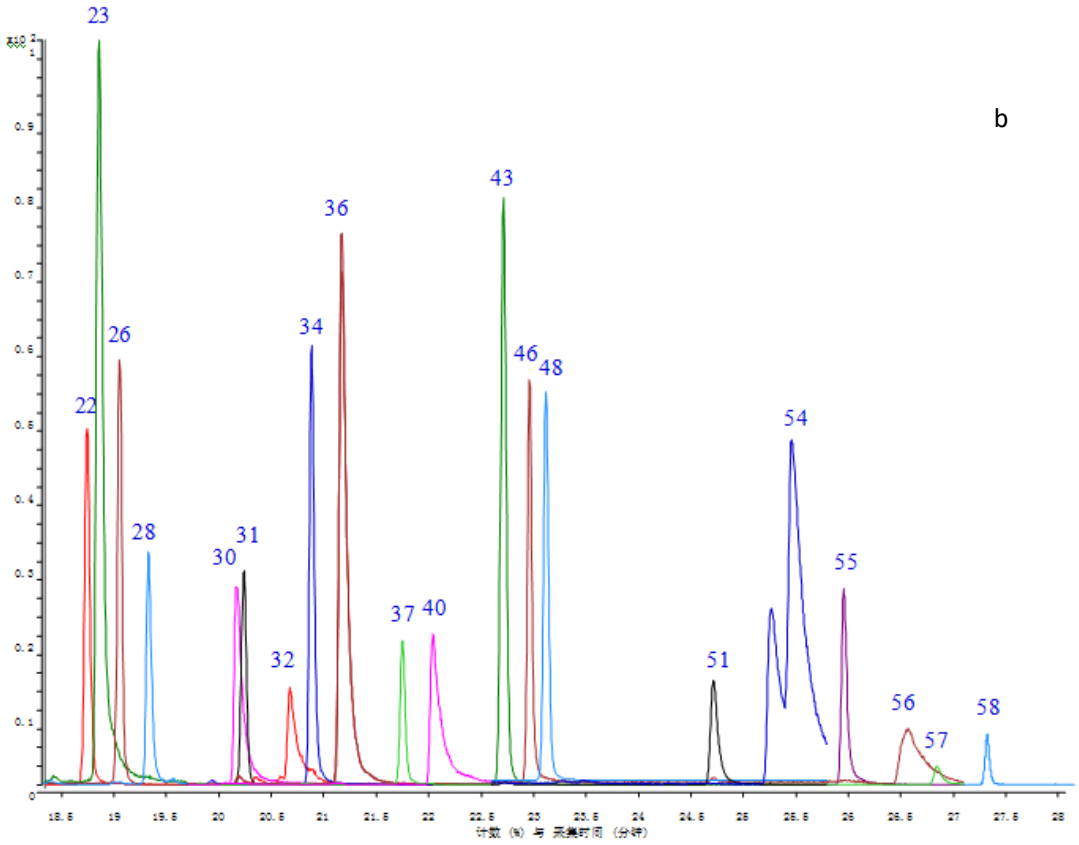
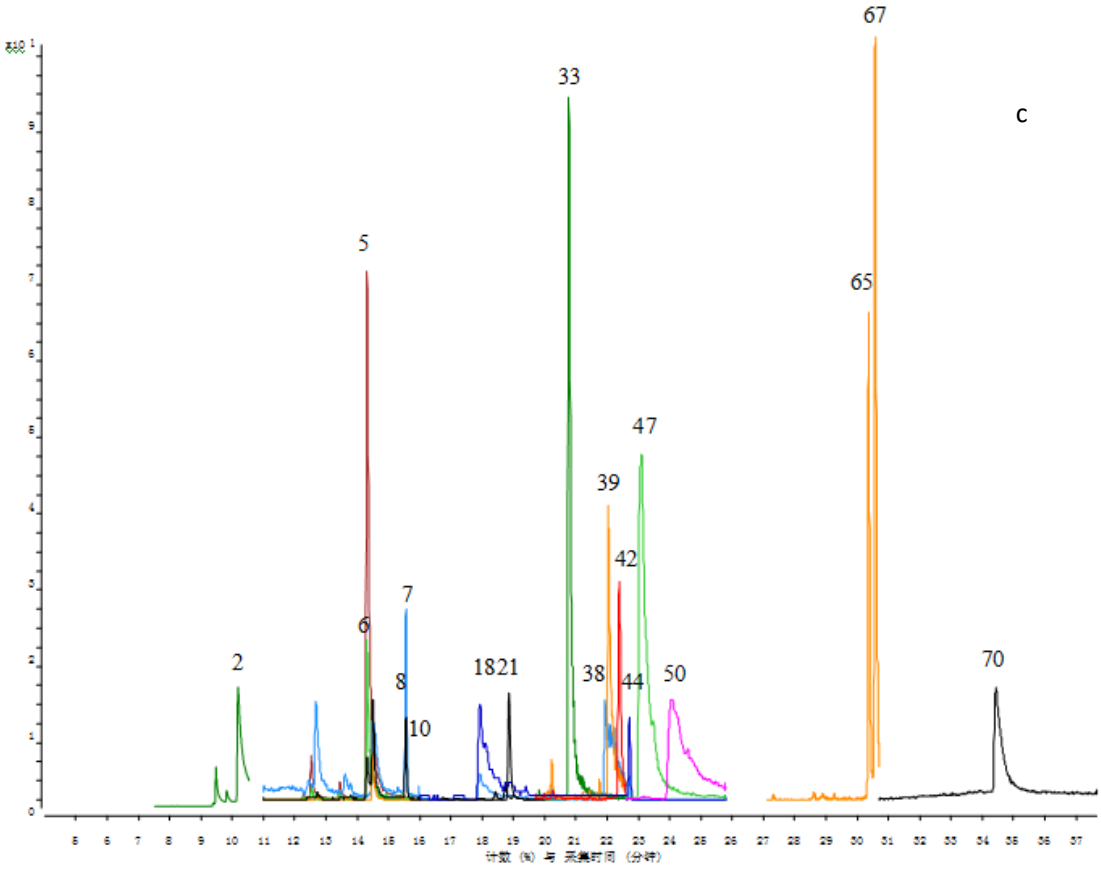


Figure 1. Schematic diagram of an m-PFC tip(Original drawing from Zhao et al.[53])
1, syringe; 2, column; 3,PE frits (upper); 4, PE frits (low); 5, MWCMNs (10 mg) and anhydrous magnesium sulfate (150 mg); 6, syringe needle; 7, 2.0 mL microcentrifuge tube.

Figure 2. The TIC chromatogram of o.1 mg/kg Mixed standard solution and Quantitative ion chromatograms by GC-MS/MS .







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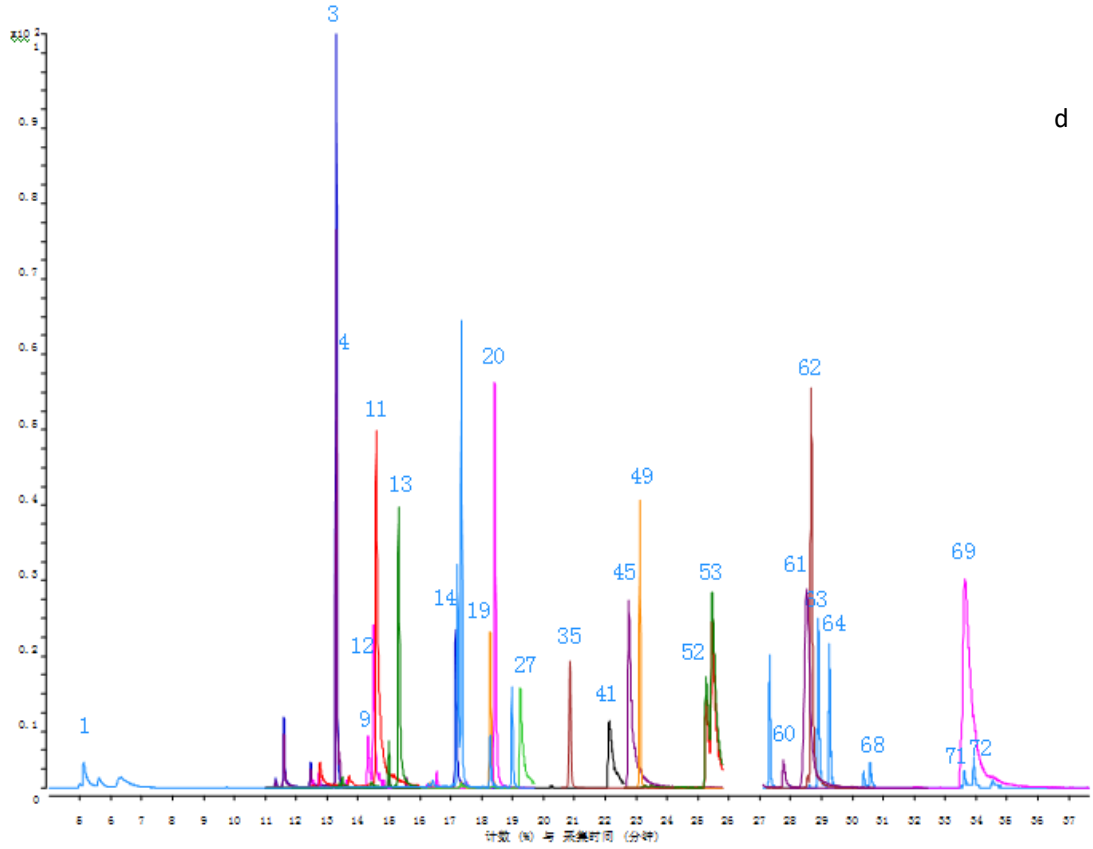

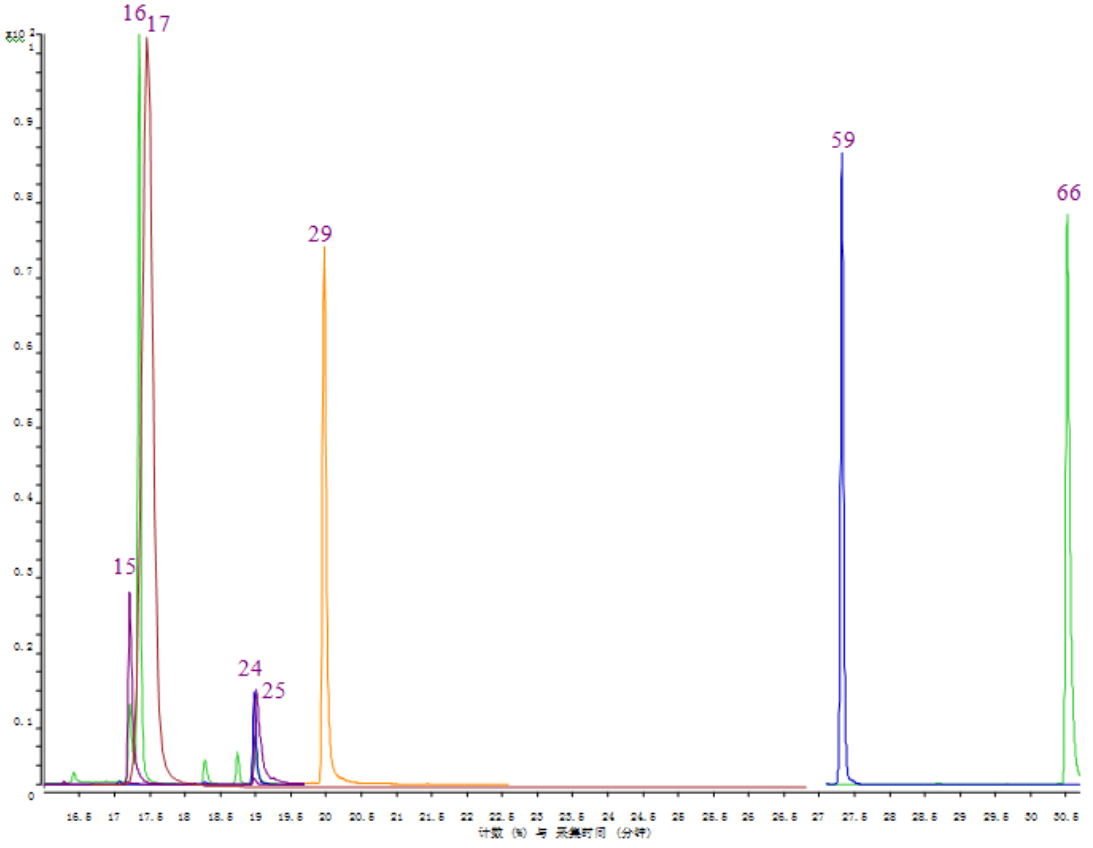

Figure 2 The TIC chromatogram of 0.1 mg/kg Mixed standard solution (a) and Quantitative ion chromatograms by GC-MS/MS (b,c,d) (The Number of peak in accordance with Table 1)

Figure 3 Effects of amount of MWCNTs on method recoveries

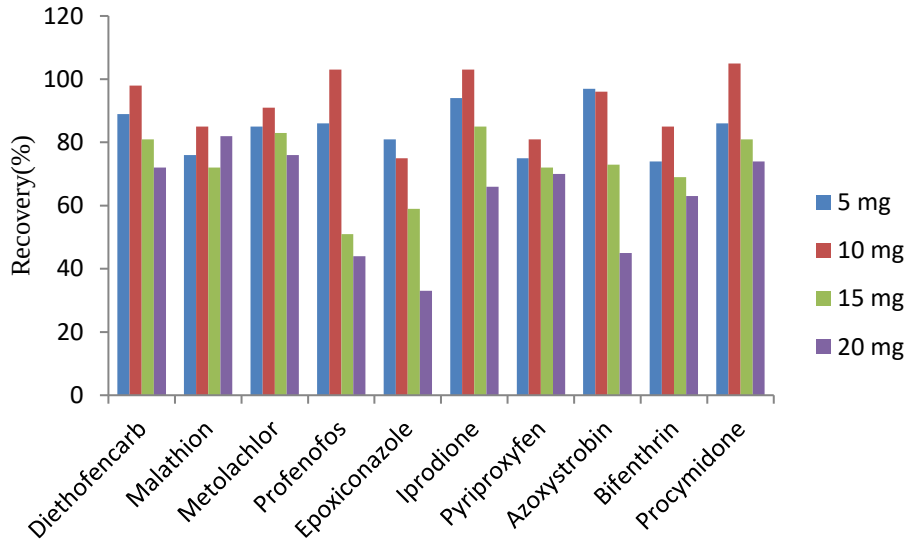

Figure 3 Effects of amount of MWCNTs on method recoveries

Figure 4 the optimization of m-PFC procedure cycle times by pulling and pushing to red wine blank sample

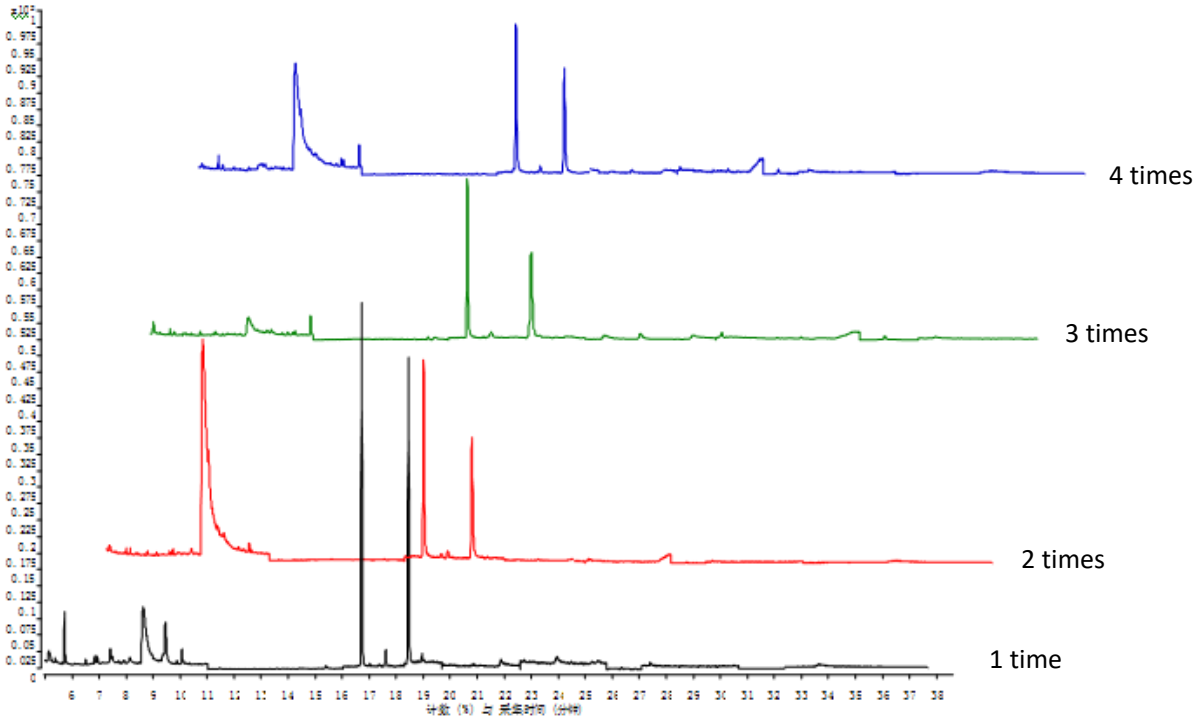

Figure 4 the optimization of m-PFC procedure cycle times by pulling and pushing to red wine blank sample