



Original Research Article

Development of QuEChERS extraction method for the determination of pesticide residues in cereals using DART-ToF-MS and GC-MS techniques. Correlation and quantification study

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ABSTRACT

Cereal crops comprise more than 60 % of agricultural production worldwide. To ensure high production, the extensive use of pesticides is common practice. Analysis of pesticide residues in food and particularly cereals has become an essential requirement for consumers, producers, food inspectors and authorities. However, the determination of pesticides in cereal samples is not an easy task due to the complexity of the matrices and the trace levels of pesticides. In this study, a simple and high-throughput method was validated for the determination of multi-residue pesticide in 30 different types of cereals which are commonly consumed around the world. QuEChERS procedure has been developed, a mixture of primary-secondary amine and C18 proved better performance for the reduction of the interfering substances from the cereal grains than multiwalled carbon nanotubes. For a comprehensive investigation, the pesticide cereals contents were purified following the established cleanup method and detected by DART-ToF-MS and GC-MS. As “soft” and “hard” MS ionization methods, DART-ToF-MS and GC-MS are strong nominated for comprehensive studies of the unknown molecules. The results showed that 19 pesticides were successfully identified by both techniques in all samples, 16 by DART-ToF-MS and 13 using GC-MS. Regarding the correlation between the developed methods, 10 pesticides were detected as a commonality between the two techniques, this indicates that a single MS technique is not sufficient to detect all of the existing pesticides in cereals. The findings exposed that the two MS techniques are complementary, and both can be used for comprehensive identification of the pesticides presented in cereals. Quantitative analysis was performed using GC-MS under the selective ion monitoring mode by external and internal standard methods. Tributyl phosphate has been used as an internal standard. The measured limits of detection ranged between 4 and 9 $\mu\text{g kg}^{-1}$ for all pesticides, while the limit of quantification values was $<34.8 \mu\text{g kg}^{-1}$, which were below the regulatory maximum residue limits. The coefficient of determination was >0.9980 within the calibration linearity range of 15–6250 $\mu\text{g kg}^{-1}$ for the detected pesticides. The recovery of all detected pesticides was in the range 75.28–122.02 % ($n = 3$) with associated RSDs <14 % indicating satisfactory accuracy.

1. Introduction

Cereal crops comprise more than 60 % of agricultural production worldwide. Among cereals, wheat, rice and corn are the three most consumable around the world (He et al., 2015). The extensive use of agrochemicals (pesticides and fertilizers) is common practice to ensure high production (Zhang et al., 2018). The U.S. Environmental Protection Agency (EPA) defines a pesticide as “any substance or mixture of substances

intended for preventing, destroying, repelling, or lessening the damage of any pest” (Tarola et al., 2008). Pesticides have increasingly been used all over the world. They are used to kill and affect weeds (herbicides), fungi (fungicides), insects (insecticides) and other various pests (Aktar et al., 2009). The vapors and residues may drift or volatilize off the treatment site, depending on the type of pesticide applied, thereby contaminating vegetation, air and soil and increasing the potential for human exposure.

The main routes of pesticide exposure are inhalation, ingestion and

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dermal absorption where both acute and chronic poisoning cases with pesticides have been reported. However, exposure of humans to pesticides is mainly from residues in food. The level of exposure depends on both the level of the residues and the quantity of food consumed (Damalas and Koutroubas, 2016). Thus, the concentration levels of pesticides and their metabolites in the environment must be continuously monitored (Chang et al., 2016). The methods used for the analysis of pesticides in cereals often follow the general strategies for pesticide analysis in fruits and vegetables, with a common extraction step and clean-up followed by separation and detection (Raina-Fulton, 2015; Grimalt and Dehouck, 2016). However, the determination of pesticides in food samples including cereals is not an easy task due to the complexity of the matrices and the trace levels of pesticides in samples. Recently, one of the most successful approaches for the extraction and cleanup of pesticides from food samples is the QuEChERS method (Quick, Easy, Cheap, Effective, Rugged and Safe).

Since it was introduced by Anastassiades et al. (Anastassiades et al., 2003) in 2003, the QuEChERS approach has been widely accepted by the scientific community. The QuEChERS procedure is based on a salting-out extraction with a solvent (mainly acetonitrile) followed by a dispersive solid-phase extraction (*d*-SPE) (Paiga et al., 2015). The flexibility of the QuEChERS approach is a powerful feature that is no less important than the other confirmed advantages such as simplicity and efficiency. Most of the analytical procedures used in the determination of pesticides are based on the use of chromatographic techniques (Ravikumar et al., 2013), mainly gas chromatography with a selective detector such as mass spectrometry (MS) detector (Saito-Shida et al., 2020; Jonghwa et al., 2017; Mondal et al., 2018).

Since the first research article introducing direct analysis in real time-mass spectrometry (DART-MS) in 2005 as a new ion source for the analysis of substances in the open air under atmospheric pressure (Cody et al., 2005), this technique has rapidly progressed and the number of corresponding analytical applications increases in various fields (Hajšlova et al., 2011; Vaclavik et al., 2010; Al-Rifai et al., 2017; Gross, 2014; Pavlovich et al., 2018). DART-MS ion source has been used for high-throughput mass measurements because it does not need a vacuum ionization step and a specific sample preparation; therefore, the solid, liquid, and gaseous samples can be analyzed in their native state (Hossain and Nagoor, 2011). Combined with different types of mass spectrometers such as quadrupole, time-of-flight (ToF), or orbitrap, DART was used to detect the residual pesticides in some raw materials and processed food samples (Guo et al., 2017; Yong et al., 2017; Kern et al., 2014; Edison et al., 2011; Gómez-Ríos et al., 2017; Kiguchi et al., 2014; Crawford and Musselman, 2012; Farré et al., 2013; Wang et al., 2012). Consequently, DART ionizes highly nonpolar to moderately polar compounds (Hossain et al., 2011), thus, many pesticide compounds are good candidates to ionize through DART mechanisms and suitable for determination by this ambient ionization technique.

The present research aims to investigate the residues of pesticides in cereals from the Saudi market using DART-ToF-MS and GC-MS. To the best of our knowledge, the DART-ToF-MS technique has not been applied for the identification of pesticide contents in cereals. The soft-ion source DART along with the high-resolution ToF mass analyzer is a strong candidate as an alternative technique for rapid analysis of pesticide residual contents in cereals and other related matrices. Studying the correlation between different MS techniques; DART-ToF-MS as a soft and high-resolution and electron impact MS as a hard and low-resolution can be more effective for a comprehensive investigation of pesticides in cereals, which is a very limited approach in the literature.

2. Experimental

2.1. Chemicals and materials

Pesticide standards; dichlorvos, diazinon, pirimicarb, chlorpyrifos-

methyl, carbaryl, pirimiphos-methyl, malathion, aldrin, ethion, triazofos, tebuconazole, proflenofos, fenprothrin, lambda-cyhalothrin, cypermethrin, deltamethrin, spiromethrin, propham, metalaxyl, prometryn, pyrimethanil and cyprodinil were purchased from Aldrich (Steinheim, Germany) and Fisher Scientific (Leicestershire, UK). Polyethylene glycol with an average relative molecular weight of 600 and tributyl phosphate (TBP) used as internal standard were acquired from Sigma-Aldrich (Steinheim, Germany). Anhydrous magnesium sulfate (reagent grade) and pure sodium chloride were obtained from BDH (Lutterworth, UK). The QuEChERS kits with salt packets containing 900 mg MgSO₄, 300 mg primary-secondary amine (PSA) and 150 mg C18 were purchased from CHROMATific (Heidenrod, Germany). A centrifuge, model 800, Jiangsu Zhenji Instruments Co., Ltd. (Jiangsu, China); and 50 mL centrifuge tubes (Corning Inc., NY, USA) were used during sample preparation. Multiwalled carbon nanotubes (MWCNTs) with 10–50 mm length, about 8 nm outer diameter, about 5 nm inner diameter and 95 % purity were provided from Chengdu Organic Chemicals Co. Ltd. (Chengdu, China).

2.2. Instrumentation and conditions

High-resolution mass spectrometry determinations were carried out using Jeol AccuTOF LC-plus JMS-T100 LP atmospheric pressure ionization ToF-MS (Tokyo, Japan) equipped with a DART ion source, Ion-Sense (Saugus, MA, USA). The mass spectrometer was operated in both positive and negative ion modes to optimize the ionization conditions of pesticides. The ring lens potential was set to 13 V, while the orifice 1 and 2 potentials were set at 20 and 5 V, respectively. Orifice 1 was set to a temperature of 80 °C. The RF ion guide potential was 300 V. The ion source was operated with helium gas at 3.0 L min⁻¹ flow rate. The gas heater was set to 400 °C. The potential on the discharge needle electrode of the DART source was set to 3.0 kV; perforated and grid electrode potentials were at 100 and 250 V, respectively. Data acquisition was monitored in the mass range of 10–550 *m/z* at acquisition rate 10 spectra min⁻¹. To perform mass drift compensation for accurate mass values, a PEG with 200 µg mL⁻¹ solution in methanol was applied just before each sample. The samples were introduced manually using a glass rod. The mass resolution of MS spectra was in the range 3900–5300. The elemental composition has been determined on selected peaks using the MassCenter software, version 1.3.m from Jeol.

After this quick investigation, pesticide standards and cereal samples extracts were submitted to analysis by GC-MS chromatography. Shimadzu GC/MS-Q2010 Ultra (Kyoto, Japan) was used for determination of pesticide residues. The instrument is equipped with Shimadzu AOC-20i autosampler and split/splitless injector at 260 °C. RXISIL 5MS fused silica column, 30 m length × 0.25 mm i.d. × 0.25 µm film thickness sourced from Restek (Bellefonte, USA) was used for separation of the pesticide standards and cereal extracts contents. The column temperature was programmed as follows: the initial temperature was 70 °C (for 1 min) and increased to 160 °C at 20 °C min⁻¹, then ramped to 280 °C at 8 °C min⁻¹, and then it was held for 6 min. The total run time was 38.50 min. The injection volume was 1.0 µL in splitless mode and the split vent was opened after 1 min. Operation condition settings of mass spectrometer components were followed as: The electron impact energy was 70 eV, interface temperature 250 °C, MS ion source temperature 230 °C, MS Quad temperature 150 °C, electron multiplier voltage 1200 V was operated at 250 °C, transfer line temperature 200 °C and analyzer temperature 230 °C. The MS detector was run in both scan mode (from 50 to 600 *m/z*) and SIM mode.

2.3. Preparation of pesticide standard mixtures

Stock standards (1000 mg L⁻¹) and internal standard solutions (500 mg L⁻¹) were prepared in acetonitrile. Of these stock solutions, a stock mixture of pesticides was prepared by mixing 100 µL of each stock standard. The stock mixture was diluted by acetonitrile to different

concentrations with acetonitrile to receive working standards; 0.05, 0.10, 0.20, 0.30, 0.50, 1.00, 2.00, 3.08, and 6.25 mg L⁻¹, which were used to optimize the parameters affecting the QuEChERS procedure as well as a method validation. Stock standards, stock mixtures, working standards and internal standard were stored under refrigeration below 4 °C.

2.4. Sample treatment and preparation

Different types of cereal samples; 30 cereals which are commonly consumed in Saudi Arabia were collected from local markets in Riyadh and Jizan cities in 2019. Table 1 shows the studied samples and their sources. The collected cereals were milled to obtain similar degree of fineness.

The optimal QuEChERS procedure for preparation of cereal samples was as follows: a 10 g portion of each ground cereal sample was weighed into a 50 mL centrifuge tube; 12 mL deionized water, 10 mL acetonitrile, and 20 µL TBP were added to the sample, which was shaken by hand for a few seconds to hydrate the sample. After 30 min of standing at 4 °C, 4.0 g of MgSO₄, and 1.0 g of NaCl were added to the mixture. Then it was shaken vigorously by hand for 1 min to prevent the formation of crystalline agglomerates during MgSO₄ hydration. The mixture was then centrifuged at 8000 rpm for 5 min. The supernatant was transferred to a new centrifuge tube containing 900 mg MgSO₄, 300 mg PSA, and 150 mg C₁₈, vortexed for 1 min, and centrifuged at 6000 rpm for 5 min. Finally, 1 mL of the supernatant was collected and placed directly into the vials for DART-ToF-MS and GC-MS analyses. Schematic diagram for the extraction and cleanup of cereal samples using QuEChERS method demonstrated in Fig. 1.

2.5. Method validation

The proposed GC-MS method was validated in terms of linearity, accuracy, precision, LOD and LOQ based on the quality guidelines of ICH, 2005 (International Conference on Harmonization (ICH), 2005). A calibration curve is determined by the analysis of each pesticide at five calibration levels in both scan and SIM modes. A recovery study was carried out to determine the method accuracy. For this purpose, Jizan brown wheat (sample 6) was chosen. The recovery studies for the pesticide's mixtures in 10 g of test wheat were carried at medium concentration level in triplicate. The pesticide spiked wheat was extracted following the optimum conditions and the resulting volume concentrated to 1 mL. The extracts were then injected into the GC-MS. The recovery percentages of each compound were calculated by comparing the peak area of standard compounds in the sample and in the standard solution. LOD and LOQ were determined based on signal-noise ratio of the quantification and qualification ions selected for each detected pesticide.

3. Results and discussion

3.1. Optimization of the extraction procedure

QuEChERS method was originally developed as a dispersive solid-

phase extraction technique for detection of the pesticide residues in food. However, the application of the QuEChERS method for cereal samples still limited (He et al., 2015; Han et al., 2017; Melo et al., 2020; Cabrera et al., 2016; Guo et al., 2019; Hou et al., 2013). In this work, thirty types of cereals samples including different kinds of wheat, corn, rice, millet, barley, fenugreek, oat, lentils and chickpeas (Table 1) were subjected to modified QuEChERS procedure as described in Fig. 1. Prior to analysis, two sorbents were tested in the *d*-SPE cleanup of cereals matrix; MWCNT and a mixture of PSA and C₁₈. The obtained chromatograms using DART-ToF-MS and GC-MS techniques did not reveal significant peaks for almost all pesticides when 20 g MWCNT was used as a sorbent for this purpose (Fig. 2(A)), however, some polar organic acids and fatty acids were identified in various samples. On the other hand, several pesticides were successfully detected after using a mixture of the two most common sorbents used in the *d*-SPE cleanup of QuEChERS; consists of 300 mg PSA and 150 mg C₁₈ in addition to 900 mg MgSO₄. As an anion exchanger, PSA can remove various polar organic and fatty acids in addition to some sugars, while C₁₈ is a general sorbent for many types of non-polar interferences such as lipids. Based on the identified compounds, the mixture of PSA and C₁₈ was very effective for the reduction of the interfering substances from the cereal grains such as fatty acids and sugars, which can act as interferences during chromatographic analysis.

3.2. Fast profiling of cereals

Mass spectrometry is one of the most powerful techniques for the structural identification of organic substances. DART ion source along with ToF mass analyzer are very strong candidates as powerful techniques for fast screening of several types of samples with high-resolution mass numbers directly in real-time. In this work, the QuEChERS extracts of thirty cereal samples were subjected to the DART-ToF-MS system under different conditions to check the presence of pesticides. As examples, Fig. 3 displays the high-resolution DART-ToF mass spectra of samples no. 11 and 25. DART-ToF mass spectra for all other cereal samples are provided in Supplementary data (Figures S1–S28). The analysis of all cereals shows 16 confirmed pesticides on the type of protonated molecular ions [M+H]⁺. Four of these pesticides; pirimicarb, prothion, pyrimethanil and cyprodinil also demonstrate the formation of ammonium adduct ions [M + NH₄]⁺ under various conditions. Table 2 presents the detected pesticides by the DART-ToF-MS technique along with their chemical classes, experimental and calculated masses, and the samples in which pesticides were found. The unsaturated degree was also used to confirm the chemical structure of the detected pesticides. The difference between the experimental and calculated mass was less than ±9.71 m Da in all cases, which means a high accuracy. It should be noted that the optimum conditions of DART-ToF-MS are not the same for all detected pesticides, and then the same sample should be analyzed at different conditions to detect all of the presented pesticides. In conclusion, the findings prove that DART-ToF-MS is a useful technique for the rapid identification of the main pesticides in cereals.

Table 1

Commercial cereal samples and their sources.

#	Cereal type	Source	#	Cereal type	Source	#	Cereal type	Source
1	Wheat	Australia	11	Millet	India	21	Rice	–
2	Wheat	UAE	12	Corn	Yemen	22	Rice	Bangladesh
3	Wheat	Oman	13	Barley	Qassim*	23	Barley	Yemen
4	Brown wheat	Yemen	14	Fenugreek	Qassim*	24	Millet	Jizan*
5	Brown wheat	Kharamah*	15	Oat	–	25	Red corn	Jizan*
6	Brown wheat	Jizan*	16	Rice	India	26	Rice	Vietnam
7	Brown wheat	Qassim*	17	Rice	Egypt	27	White chickpeas	Turkey
8	Brown wheat	Najran*	18	Rice	USA	28	Black chickpeas	UAE
9	White corn	Jizan*	19	Orange lentils	Syria	29	Cracked wheat	Turkey
10	White corn	India	20	Yellow lentils	Turkey	30	Pope corn	India

* Local cereals; KSA.

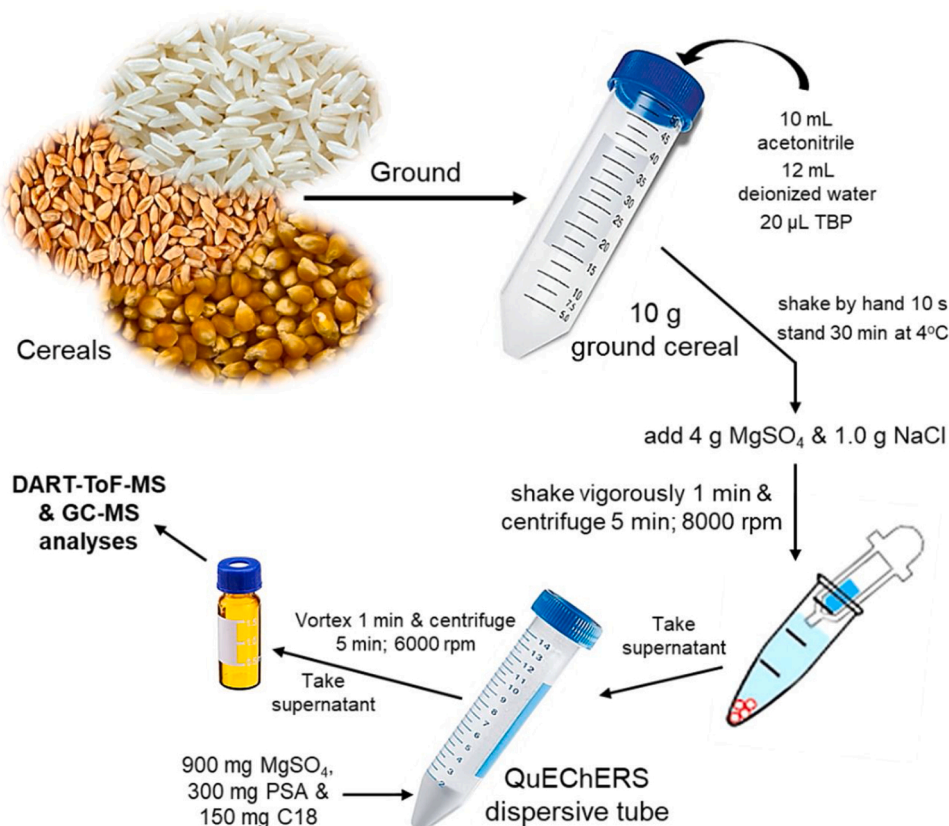


Fig. 1. Schematic procedure of QuEChERS procedure for cereals extraction.

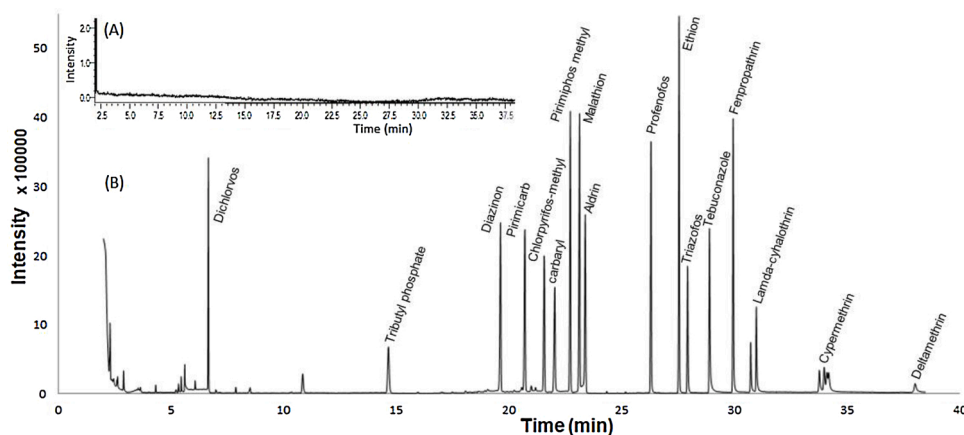


Fig. 2. (A) The chromatogram of standard mixture of pesticides ($0.625 \mu\text{g mL}^{-1}$) when using 20 mg MWCNTs as sorbent in QuEChERS method. (B) Typical separation chromatogram of the pesticide standards ($0.625 \mu\text{g mL}^{-1}$) using SIM mode at optimum conditions.

3.3. GC-MS analysis

In order to confirm the DART-ToF-MS findings, all samples were analyzed using GC-MS in the full scan mode by means of detecting mass fragments (m/z). The identification of pesticides in the full scan mode was performed using the NIST mass spectral library. At optimum separation conditions, 13 pesticides were successfully detected in all samples, two of them; pirimicarb and diazinon have been identified by the previous results. Table 3 presents the detected pesticides by GC-MS technique along with their chemical classes, molecular weights, and m/z ratios of the base peak and the main fragments. The pesticides were arranged by order of elution as observed from the retention time values.

For more verification and to improve the sensitivity of the method, selective ion monitoring (SIM) mode has been used. Under the SIM mode, the mass analyzer monitors few specific ions for each target compound within the retention time range that the target elutes from the GC column, and hence improves the signal to noise ratio. For this purpose, four ions were selected for each pesticide; the highest relative abundant ion was functioned as the quantifier ion while the other ions were used for confirmation as qualifier ions. Under the same separation conditions, the detected pesticides were confirmed, and the detection limits of all compounds were significantly improved. Fig. 2(B) shows the typical chromatogram of $0.625 \mu\text{g mL}^{-1}$ of each pesticide standard using SIM mode at optimum conditions.

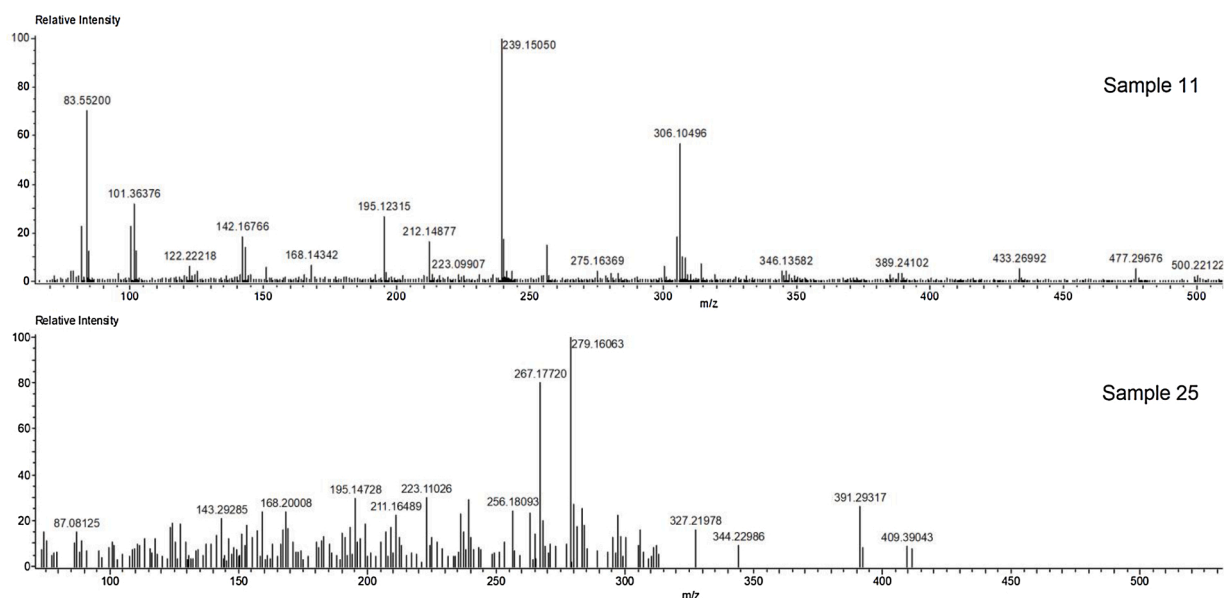


Fig. 3. High-resolution DART-ToF mass spectra of samples no. 11 and 25.

Table 2

The classes, experimental and calculated masses and their difference, unsaturated degrees and the samples in which pesticides were found by DART-ToF-MS.

Pesticide	Chemical Class	Exp. mass (Avg.)	Calc. mass	Mass diff.(mmu)	Ion	Unsat. degree	Samples
Pirimicarb	Carbamate	239.15498	239.15080	$\leq \pm 4.19$	$[M+H]^+$	4.5	1, 5, 6, 8–10, 13, 15, 19, 24, 25, 29
		256.17832	256.17735	$\leq \pm 1.03$	$[M + NH_4]^+$	3.5	
Diazinon	Organophosphate	305.11574	305.10887	$\leq \pm 7.12$	$[M+H]^+$	4.5	1, 11, 16, 25
Dichlorvos	Organophosphate	221.74977	221.75373	$\leq \pm 4.26$	$[M+H]^+$	0.5	8, 10–12, 16–30
Chlorpyrifos-methyl	Organophosphate	323.34227	323.34122	$\leq \pm 1.27$	$[M+H]^+$	3.5	3, 8, 15, 20, 25
Pirimiphos-methyl	Organophosphate	306.09607	306.10412	$\leq \pm 5.08$	$[M+H]^+$	3.5	5, 9, 12, 15, 17–20, 25
Spiroxamine	Spiroketalamine	298.27714	298.27460	$\leq \pm 2.54$	$[M+H]^+$	1.5	15, 25
Metalaxyl	Acylalanine	280.15764	280.15488	$\leq \pm 2.76$	$[M+H]^+$	5.5	1, 6, 22
Malathion	Organophosphate	331.04125	331.04389	$\leq \pm 2.94$	$[M+H]^+$	1.5	8, 15, 25, 27
Propham	Carbamate	180.11416	180.10845	$\leq \pm 5.71$	$[M+H]^+$	4.5	9, 21
		197.12774	197.12900	$\leq \pm 1.26$	$[M + NH_4]^+$	3.5	
Prometryn	Triazine	242.14652	242.14394	$\leq \pm 2.58$	$[M+H]^+$	3.5	14
Ethion	Organophosphorus	345.29490	345.29544	$\leq \pm 0.85$	$[M+H]^+$	-1	8, 11, 13, 20, 25, 26
Triazofos	Organophosphate	214.06956	214.07282	$\leq \pm 3.51$	$[M+H]^+$	6.5	1, 24
Tebuconazole	Triazole	308.14762	308.15296	$\leq \pm 6.22$	$[M+H]^+$	7	3, 6, 11, 12, 16, 17, 22
Fenpropathrin	Pyrethroid	350.17161	350.17562	$\leq \pm 4.04$	$[M+H]^+$	12	8, 13, 15, 16, 19, 20, 25
Pirimethanil	Aminopyrimidine	200.15503	200.14880	$\leq \pm 6.23$	$[M+H]^+$	7.5	10
		217.15503	217.14532	$\leq \pm 9.71$	$[M + NH_4]^+$	6.5	
Cyprodinil	Aminopyrimidine	243.13490	243.13545	$\leq \pm 0.55$	$[M+H]^+$	8.5	10
		260.16121	260.16097	$\leq \pm 0.24$	$[M + NH_4]^+$	7.5	

Table 3

The classes, molecular weights, average retention times, and m/z ratios of the base peak and the main fragments for the detected pesticides by GC-MS method.

Pesticide	Chemical Class	MW ($g\ mol^{-1}$)	t_R (min) \pm RSD%	Base peak (m/z)	Main fragments (m/z)
Dichlorvos	Organophosphate	220.97	6.63 ± 0.51	109	79, 185
Diazinon	Organophosphate	304.34	19.60 ± 0.59	179	137, 152, 29
Pirimicarb	Carbamate	238.29	20.69 ± 0.26	166	72, 238, 24
Chlorpyrifos-methyl	Organophosphate	322.53	21.55 ± 0.21	286	125, 288, 47
Pirimiphos-methyl	Organophosphate	305.33	22.71 ± 0.15	290	276, 305, 125
Malathion	Organophosphate	330.35	23.13 ± 0.13	125	173, 93, 127
Aldrin	Organochlorine	364.90	23.37 ± 0.16	66	263, 265, 261
Ethion	Organophosphorus	384.48	27.55 ± 0.15	231	97, 153, 125
Triazofos	Organophosphate	313.31	27.93 ± 0.09	161	77, 97, 162
Tebuconazole	Triazole	307.82	28.90 ± 0.08	125	70, 250, 83
Fenpropathrin	Pyrethroid	349.42	29.95 ± 0.07	97	55, 181, 43
Lambda-cyhalothrin	Pyrethroid	449.85	30.98 ± 0.43	181	197, 208, 141
Cypermethrin	Pyrethroid	416.30	33.76 ± 0.16	163	181, 165, 91

3.4. Correlation between MS techniques

For a comprehensive qualitative analysis, the pesticide cereals contents were subjected to two different MS techniques; DART-ToF-MS and GC-MS. As “soft” and “hard” MS ionization methods, DART-ToF-MS and

GC-MS are strong nominated for comprehensive studies of the unknown molecules. As shown in Tables 2 and 3, the results revealed that 19 pesticides were successfully identified by both techniques in all samples; 16 by DART-ToF-MS and 13 using GC-MS, while ten pesticides, pirimicarb, diazinon, dichlorvos, chlorpyrifos-methyl, pirimiphos-methyl,

malathion, ethion, triazofos, tebuconazole and fenprothrin were characterized by both techniques. This indicates that 16–32 % of the pesticides presented in cereals cannot be identified by a single MS technique. Through this result, we conclude that the two MS methods are complementary to each other and both can be used for comprehensive identification of the presence of pesticides in cereals.

3.5. Method validation

System suitability parameters such as linearity, precision, LOD, LOQ and recovery were tested according to the criteria as per ICH guidelines (International Conference on Harmonization (ICH, 2005)). Calibration curves of all pesticides were obtained by both external and internal standard methods. Tributyl phosphate has been added for all of the standards and real samples as an internal standard compound. Although the external standard method showed reasonable suitability for almost all analytes, the determination of the pesticides using the internal standard addition method exhibited better sensitivity measured by lower detection values and wider linear ranges.

The calibration graphs of each pesticide at five concentration levels were established using the two methods at optimum conditions. The external calibration curves were proposed over the linear concentration range when peak areas were used for signal evaluation, while the internal calibration graphs were established based on the ratio of the pesticide to the tributyl phosphate peak areas. All of the standard solutions in each linearity level were injected in triplicate. The regression coefficient factors were found to be higher than 0.9980 in all cases, indicating good values of method linearity. Consecutive dilutions for the standard mixtures were made to determine the LOD and LOQ based on the ICH guidelines. LOD and LOQ represent the concentrations of the analytes that would yield signal-to-noise ratios of 3/1 and 10/1 for LOD and LOQ, respectively. The estimated values of LOD for the pesticides ranged from 4 $\mu\text{g kg}^{-1}$ for ethion to 9 $\mu\text{g kg}^{-1}$ for malathion using the internal standard addition method. On the other hand, the measured values of LOQ ranged from 15 to 34.8 $\mu\text{g kg}^{-1}$, which are represented as the lowest concentrations in the linear range of each pesticide. The results of quality parameters for the thirteen-pesticide including linear equations, regression factors, LOD values, and linear ranges are summarized in Table 4.

3.6. Cereals samples analysis

To determine the applicability of the proposed extraction and GC-MS methods, a total of 30 different types and countries of origin cereals were analyzed. The real samples which are commonly consumed in Saudi Arabia were collected from the local markets in 2019. The most abundant ions (base peaks presented in Table 3) that showed no chromatographic interference and had the highest signal-to-noise ratio were selected for quantification purposes. Among the studied cereals, only four samples were free from any pesticide (samples no. 1, 2, 7 and 14),

otherwise, at least one pesticide was identified in the rest of the studied cereals. The amounts of the detected pesticides (above LOQ values) in all cereals were obtained between 10 and 2409 $\mu\text{g kg}^{-1}$. Of the 13 identified pesticides, only aldrin and particularly dichlorvos were detected in most samples. In some cases, more than 5 pesticides (up to 8) were detected in a number of cereal samples, which means a mixture of pesticides is commonly used to treat a wide range of pests. Representative GC-MS chromatograms for some real samples are displayed in Fig. 4.

Of the two most consumable kinds of cereal; rice and wheat, three pesticides were detected in almost all rice samples; dichlorvos, aldrin and cypermethrin. On the other side, with the exception of sample no. 8, the results showed that the wheat samples were contaminated with the lowest amounts of pesticides among all studied cereals. Regarding the cereal's sources, as unexpected, the local cereals did not exhibit higher contents of pesticides than imported ones due to transportation and storage conditions. The complete results have been illustrated in Table 5. In conclusion, we did not note any strong relationship between the type or the source of the cereals and the detected pesticides.

The measured LOQ values of all studied pesticides are lower than the maximum residue limits established by the Codex Alimentarius Commission, International Food Standards (FAO/WHO) for most cereal grains (Codex, 2020). According to these international standards, the contents of pesticides in certain samples were higher than the maximum residue level. The pesticides that exceeded the maximum residue limits are dichlorvos in sample 17, diazinon in sample 16, chlorpyrifos-methyl in samples 3 and 20, pirimiphos-methyl in sample 20, aldrin in samples 20 and 26, and cypermethrin in samples 8, 11, 16, 17, 18, 20, 21 and 28. The recovery values presented in Table 4 were evaluated in order to validate the found contents of the pesticides in the cereals extracts. The recovery levels of pesticides were located between 75.28 and 122.02 % with good repeatability verified by %RSD < 14 % (n = 3) in all cases. These values demonstrate good extraction efficiency.

3.7. Comparison with other works

The efficiency of the proposed methods has been compared with other techniques recently reported utilizing QuEChERS in terms of several parameters such as the *d*-SPE cleanup QuEChERS sorbents, linearity ranges, LOQ and recovery percentage (He et al., 2015; Han et al., 2017; Melo et al., 2020; Cabrera et al., 2016; Guo et al., 2019; Hou et al., 2013). Details of the comparison are shown in Table 6. As extraction sorbents, all of the reported works used either PSA or C18 or a mixture of both sorbents and sometimes in addition to other sorbents i.e. MWCNTs. In this work, a mixture of PSA and C18 has been compared with MWCNT in the *d*-SPE cleanup of QuEChERS. The proposed QuEChERS followed by the GC-MS method exhibited wider linearity ranges and comparable LOQ and recovery values compared to the other reported works.

To our information, the DART-ToF-MS technique has not used for the

Table 4

Calibration data, the values of LOD, the linear ranges for the studied pesticides, and the recovery values of the proposed analytical method.

Pesticide	Equation (external standard)	R ²	Equation (internal standard)	R ²	LOD ($\mu\text{g kg}^{-1}$)	Linear range($\mu\text{g kg}^{-1}$)	Recovery (%)
Dichlorvos	y = 156095x - 215914	0.9995	y = 0.0211x - 0.011	0.9991	7	24–6250	102.98
Diazinon	y = 91928x - 103768	0.9996	y = 0.0126x - 0.0109	0.9992	5.5	21–5680	76.41
Pirimicarb	y = 182205x - 175519	0.9996	y = 0.0235x - 0.0187	0.9991	5	20.7–5000	87.98
Chlorpyrifos-methyl	y = 110667x - 135272	0.9996	y = 0.0153x - 0.0137	0.9990	5.8	22.5–6250	75.28
Pirimiphos-methyl	y = 163873x - 218316	0.9996	y = 0.0214x - 0.0192	0.9990	6	22–5200	79.17
Malathion	y = 286572x - 542056	0.9990	y = 0.0372x - 0.0641	0.9992	9	34.8–6250	122.02
Aldrin	y = 68860x - 61166	0.9993	y = 0.0089x - 0.0046	0.9991	6.2	23.7–5680	86.88
Ethion	y = 260067x - 506102	0.9989	y = 0.0337x - 0.0622	0.9991	4	15–5200	96.10
Triazofos	y = 75494x - 231032	0.9999	y = 0.0096x - 0.0196	0.9988	5.3	18.2–5650	107.44
Tebuconazole	y = 160454x - 332236	0.9987	y = 0.0207x - 0.0426	0.9987	5	17.7–5680	119.66
Fenprothrin	y = 232365x - 405398	0.9992	y = 0.03x - 0.0505	0.9991	4.5	17.3–5200	121.79
Lambda-cyhalothrin	y = 135108x - 466352	0.9996	y = 0.0172x - 0.0415	0.9980	6.5	26–5000	83.55
Cypermethrin	y = 20761x - 78747	0.9992	y = 0.0025x + 0.0005	0.9994	8	32–6250	104.71

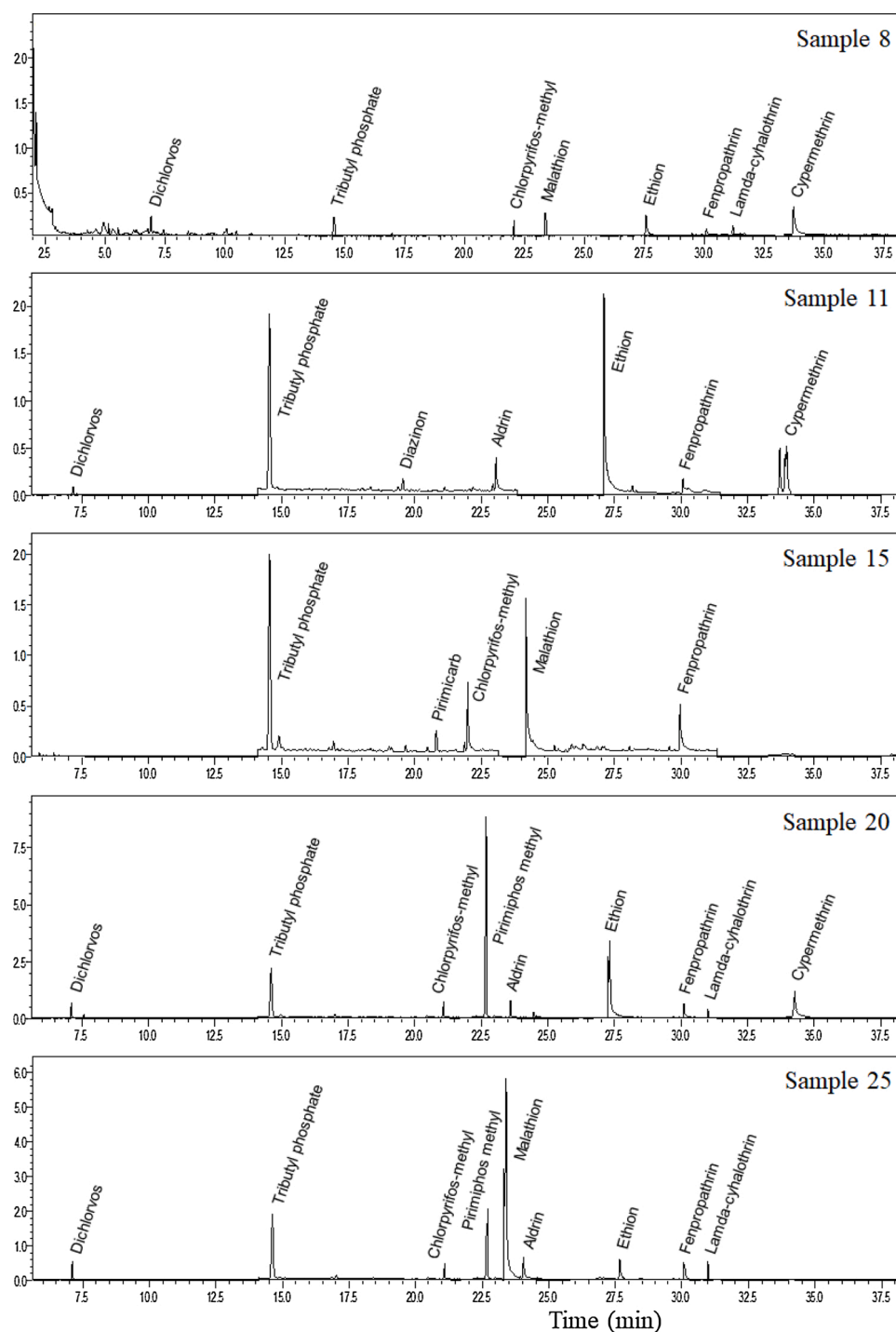


Fig. 4. Representative GC-MS chromatograms for some of the studied samples.

screening of pesticides in cereals. Based on the experimental findings and the deduction from the comparison, the DART-ToF-MS method utilizes simpler, cheaper, more rapid and environmentally benign alternatives for the identification of multiclass pesticide residue levels in cereals and other related matrices. However, direct analysis of cereals without prior-extraction steps and the possibility for quantification of the residual pesticides using DART-ToF-MS need for more examinations and still under investigation.

4. Conclusions

Due to the complexity of the matrix, the pretreatment step is

necessary for the determination of the residual pesticides in cereals. In this work, QuEChERS has been developed as a quick, cheap, simple and efficient procedure for the reduction of the interfering compounds from the cereal grains. For a comprehensive analysis of multi-residue pesticide in 30 different types of cereals, the purified samples were subjected for two different MS techniques; DART-ToF-MS and GC-MS. To our information, these outcomes establish the first data on the presence of pesticides in cereal samples using the DART-ToF-MS technique. However, direct analysis of cereals without prior-extraction steps and the possibility for quantification of the residual pesticides using DART-ToF-MS need for more investigation.

Table 5

The average content of the detected pesticides in cereal samples.

	Pesticides concentration ($\mu\text{g kg}^{-1}$) \pm %RSD														
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15
Dichlorvos	ND	ND	ND	Trace	ND	ND	ND	33	ND	79	14	Trace	ND	ND	ND
Diazinon	Trace	ND	ND	ND	ND	ND	ND	ND	ND	ND	22	ND	ND	ND	ND
Pirimicarb	Trace	ND	ND	ND	Trace	Trace	ND	Trace	Trace	Trace	ND	ND	Trace	ND	99
Chlorpyrifos-methyl	ND	ND	245	ND	ND	ND	ND	37	ND	ND	ND	ND	ND	ND	50
Pirimiphos-methyl	ND	ND	ND	ND	Trace	ND	ND	Trace	Trace	ND	Trace	Trace	ND	ND	Trace
Malathion	ND	ND	ND	ND	ND	ND	ND	678	ND	ND	ND	ND	ND	ND	278
Aldrin	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	52	ND	ND	ND	ND
Ethion	ND	ND	ND	ND	ND	ND	ND	54	ND	ND	13	ND	Trace	ND	ND
Triazofos	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Tebuconazole	ND	ND	11	ND	ND	15	ND	ND	ND	ND	Trace	69	ND	ND	ND
Fenpropathrin	ND	ND	ND	ND	ND	ND	ND	99	ND	ND	10	ND	11	ND	15
Lambda-cyhalothrin	ND	ND	ND	ND	ND	ND	ND	83	ND	ND	ND	ND	ND	ND	ND
Cypermethrin	ND	ND	ND	ND	ND	ND	ND	169	ND	ND	2409	ND	ND	ND	ND
	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Dichlorvos	63	712	61	60	71	49	45	56	49	70	102	46	41	41	43
Diazinon	434	ND	ND	ND	ND	ND	ND	ND	ND	Trace	ND	ND	ND	ND	ND
Pirimicarb	ND	ND	ND	Trace	Trace	ND	ND	ND	Trace	Trace	ND	ND	ND	Trace	ND
Chlorpyrifos-methyl	ND	ND	ND	ND	69	ND	ND	ND	ND	27	ND	ND	ND	ND	ND
Pirimiphos-methyl	Trace	Trace	Trace	Trace	306	ND	ND	ND	ND	14	ND	ND	Trace	ND	ND
Malathion	ND	ND	ND	ND	ND	ND	ND	ND	ND	81	ND	Trace	ND	ND	ND
Aldrin	Trace	39	17	Trace	59	13	Trace	ND	Trace	30	190	Trace	Trace	Trace	10
Ethion	ND	Trace	ND	ND	43	ND	ND	ND	ND	29	Trace	ND	ND	ND	ND
Triazofos	ND	ND	ND	ND	ND	ND	ND	ND	17	ND	ND	ND	ND	ND	ND
Tebuconazole	32	24	ND	ND	ND	ND	46	ND	ND	ND	ND	ND	ND	ND	ND
Fenpropathrin	1182	ND	ND	71	69	ND	Trace	ND	ND	47	ND	ND	Trace	ND	ND
Lambda-cyhalothrin	ND	ND	ND	ND	12	ND	ND	ND	ND	22	ND	ND	ND	ND	ND
Cypermethrin	71	116	49	ND	170	74	ND	ND	29	ND	ND	ND	38	ND	ND

Trace: the concentration is located between the LOD and LOQ.

ND: not detected.

Table 6

Comparison of the proposed QuEChERS method with other reported works based on QuEChERS for the extraction and determination of multiclass pesticides in cereal samples.

Type of samples	Sorbent	Analytical method	Linear range $\mu\text{g kg}^{-1}$	LOQ $\mu\text{g kg}^{-1}$	Recovery (%)	Ref.
Corn, wheat flour and rice	Mixture of C18 and PSA	GC-MS/MS	2–200	5–50	70–120	(He et al., 2015)
Rice, wheat and corn	Mixture of MWCNTs, PSA and C18	GC-MS/MS	10–1000	0.2–4.3	70–120	(Han et al., 2017)
Rice	PSA	HPLC-MS/MS	5–60	5	77.1–111.5	(Melo et al., 2020)
Rice	C18 compared with different sorbents such as chitosan, florisol, alumina and PSA	LC-MS/MS	5–20	1–10	70–120	(Cabrera et al., 2016)
Rice, corn and wheat	C18	HPLC-MS/MS	0.20–40	–	73.8–115	(Guo et al., 2019)
Rice	Mixture of PSA and C18	GC-MS/MS	10–200	–	70–122.7	(Hou et al., 2013)
Wheat, corn, rice, millet, barley, fenugreek, oat, lentils and chickpeas	Mixture of PSA and C18 compared with MWCNTs	DART-ToF-MS and GC/MS	15–6250	15–34.8	75.3–122	This work

Authorship statement

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing, or revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the Journal of Food Composition and Analysis.

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Declaration of Competing Interest

The authors have declared no conflict of interest.

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Appendix A. Supplementary data

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