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ABSTRACT

Performances of multiresidue analysis of one hundred of pesticides and contaminants, using GC-Q-Orbitrap method in full scan mode were compared to those obtained with GC-triple-quadrupole method in multiple reaction monitoring mode. In terms of sensitivity, 86% of molecules exhibited lower limit of detection values using GC-Q-Orbitrap than using GC-triple-quadrupole. For the GC-Q-Orbitrap method, more than 85% of the pesticides and contaminants showed good recovery [70–120%] in wheat samples, with relative standard deviation values $< 20\%$. GC-Q-Orbitrap method appeared the most sensitive for most pesticides studied in wheat with limit of quantification values ranged between 0.1 μg/kg and 4 μg/kg. Moreover, the matrix effect was acceptable in wheat extracts for 84 molecules but strong suppression of the chromatographic signal was observed for 16 molecules for the GC-Q-Orbitrap method. The injection of unpurified wheat extracts spiked at 10 μg/kg proved the potential of the GC-Q-Orbitrap method for use in performing high-throughput pesticide screening.

1. Introduction

Pesticides, including herbicides, fungicides, and insecticides, are widely used in agriculture to control insect pests, fungi, parasites or weeds (Samsidar et al., 2018). Therefore, pesticide residues are found in food products after harvest (European Union Report on pesticide residues in food, 2014). As some molecules are toxic at very low levels (Maqbool et al., 2016), the European Union has established a maximum residual limit (MRL) (Pico et al., 2006). Triple-quadrupole mass spectrometers coupled with GC or HPLC are usually employed in multiple reaction monitoring (MRM) mode for pesticide residue analyses because of their specificity (Martinez Vidal et al., 2002). However, the number of compounds that can be monitored simultaneously is limited by the dwell time, which limits the peak data number.

Recently, full scan high-resolution mass spectrometry (HRMS) has gained popularity in residue and contaminant analyses for food and environmental samples, especially when high numbers of analytes need to be covered (Kaufmann, 2012, Leendert et al., 2015). Gas chromatography is coupled with different HRMS spectrometers, including time of flight (GC-TOF) and Q-Orbitrap mass spectrometers. The full scan mode enables targeted and nontargeted analyses combined with retrospective analyses in a single workflow. A GC-Q-Orbitrap system provides a high mass resolving power (120,000 full width at half maximum (FWHM) (m/z 200)) combined with a high mass accuracy (<3 ppm), which is needed to avoid isobaric interferences, allowing drastic reduction of the noise and thus decreasing the limit of detection (LOD) (Uclés et al., 2017). GC-Q-Orbitrap spectrometry has been successfully applied for the determination of different complex matrix compositions, such as biofuels and light oils (Kondyli and Schrader, 2019, Hung et al., 2020). In the metabolomic field, human plasma has been studied using both electron ionization and chemical ionization GC-Q-Orbitrap to identify many metabolites (Biswapriya and Olivier, 2020). A high-throughput screening method has also been developed for the toxicological analyses of 288 drugs and poisons in human blood samples for forensic intoxication analysis (Pan et al., 2019). In environmental matrices, various persistent organic pollutants have been identified in fly ash samples using a nontargeted strategy (Yang et al., 2019). Moreover, the performance of GC-Q-Orbitrap has been evaluated for the

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monitoring of organic pollutants in wastewater, demonstrating good linearity, sensitivity and recovery with precise values for 15 targeted polycyclic aromatic hydrocarbons (PAHs) (Dominguez et al., 2020). In food chemistry, several studies have been carried out to quantify pesticide multiresidues and persistent organic pollutants by using GC-Q-Orbitrap in various matrices, such as cereals, fruits and vegetables, as well as in some fishes. A method for the quantification of 8 alkenylbenzenes in different pepper varieties has been successfully validated with limits of quantification (LOQs) close to 0.02 mg/kg (Rivera-Pérez et al., 2020). Chlorinated paraffins and halogenated PAHs have been quantified with low LOQ values in farmed and wild salmons (Kratschmer et al., 2019) and tuna (Wickrama-Arachchige et al., 2020). A method for multiresidue pesticides and polychlorinated biphenyls in cereals and feed ingredients using QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) extraction has been successfully validated with LOQs below 10 μg/kg (Tienstra and Mol, 2018). Moreover, a study focused on GC-Q-Orbitrap performances for pesticide residue analyses in various fruits and vegetables has been carried out (Mol et al., 2016). In full scan mode, optimal acquisition conditions have been obtained at 60,000 FWHM with an automatic-gain-control target at $3E^6$ providing an optimum mass accuracy within 2 ppm, a minimum of 12 scans per peak. GC-Q-Orbitrap in full scan mode has been used to compare QuEChERS purification solid supports on the extract of spices before quantification using the GC-triple-quadrupole method (Hakme et al., 2018). Nontargeted contaminants in the environment have been investigated in honeybees using GC-Q-TOF and GC-Q-Orbitrap, demonstrating that they are useful for detecting a large range of contaminants (Gomez-Ramos et al., 2019).

Some comparisons between the performances of GC-Q-Orbitrap spectrometer and those of low-resolution mass spectrometers (quadrupole and triple-quadrupole analyzers) and with those of high-resolution (TOF analyzer) mass spectrometers have been published. In 2016 (Cortés-Francisco et al., 2016), the sensitivity of a GC-triple-quadrupole method with SIM and the full scan GC-Q-Orbitrap method for 9 PBDE analyses were compared. Both methods gave LOQs below 0.01 μg/kg for the 9 PBDEs in fish and seafood, except for DBE 209, with the GC–MS/MS method.

Currently, multiresidue pesticide quantification in some matrices, such as cereals (He et al., 2015), teas (Ma et al., 2018), spices (Shabeer et al., 2018), and different kinds of fatty matrices (Castillo et al., 2011), remains a challenge due to the presence of large amounts of compounds, such as sterols, pigments, and chlorophyll, which may interfere with the analytes. Cereals have less than 25% moisture and high levels of fatty acid, and fatty matrices contain significant amounts of lipids that may behave the same as some nonpolar pesticides (Lacina et al., 2012). Tea contains antioxidants, aromatic compounds, xanthine and alkaloids. Spices are dry samples and contain flavonoids, terpenes and alkaloids. All these compounds may interfere with targeted analyte detection, which can generate false positives and may interact with the targeted analytes, which decreases the extraction yield. Since early 2000, QuEChERS has been the most widely used extraction-purification method for pesticide analyses of food matrices. Despite the purification step, low-resolution mass spectrometry is not always able to separate matrix interferents from analytes, leading to a loss of sensitivity and false positives.

The main goal of this paper is to evaluate the analytical performances of the GC-Q-Orbitrap method in full scan mode for the determination of 95 pesticide residues and 5 contaminants (PCB congeners) in different complex food matrices, including wheat, rapeseed, cumin and tea. These results will be compared to those obtained with GC-triple-quadrupole method. As previously described, these matrices are challenging in terms of extraction, purification and matrix effects. Therefore, QuEChERS extraction was used to extract 100 molecules from these samples using an adapted purification solid support (dispersive solid phase extraction (d-SPE)) for each matrix.

2. Materials and methods

2.1. Chemicals and reagents

Ultrapure water (18.2 MΩ.cm) was obtained from a Milli-Q water purification system (Millipore Ltd., Bedford, MA, USA). Acetonitrile (MeCN), acetone, and *n*-hexane were purchased from VWR (Fontenay-sous-Bois, France). Formic acid was purchased from Sigma Aldrich (Saint Quentin Fallavier, France). Salt mixtures of 4 g of magnesium sulfate, 1 g of sodium chloride, 0.5 g of sodium citrate dibasic sesquihydrate, and 1 g of sodium citrate tribasic dehydrate were obtained from Agilent (Santa Clara, USA). Preweighted sorbent mixtures from different cleanup methods, PSA/$MgSO_4$, PSA/C18 and Q-Carb®, were purchased from Agilent (Santa Clara, USA). One hundred pesticides and contaminants from a wide variety of chemical families (organochlorines, organophosphorus triazoles, carbamates, pyrethroids, PCBs, etc.), including 91 solid standards (purity > 98%) and 9 standards as single-component solutions (100 mg/L), were purchased from Sigma Aldrich (Steinheim, Germany) and the Dr. Ehrenstorfer Laboratory (Augsburg, Germany). The internal standard (lindane $^{13}C_6$) (purity > 99%) was also obtained from Sigma Aldrich (Saint Quentin Fallavier, France).

2.2. Standard solutions

A mixture containing the 100 pesticides and contaminants was prepared at a concentration of 2000 μg/L in a mixture of hexane/acetone 70/30 (v/v). Standard working solutions from 1 to 200 μg/L were prepared by dilution of the mixture solution at 2000 μg/L in hexane/acetone 70/30 v/v. Lindane $^{13}C_6$ was used as an internal standard (IS) and was prepared at a concentration of 20 μg/L in acetone. Then, 20 μL of IS were added to 180 μL of standard/extract. All stock and working solutions, including IS, were stored in amber vials with Teflon-lined caps at −20 °C.

2.3. Analysis by a GC-triple-quadrupole

An Agilent 7890B gas chromatograph was coupled to a 7000 MS/MS triple-quadrupole system (Agilent Technologies, Santa Clara, USA) equipped with an EI source and two HP-5 MS UI (Agilent Technology, Santa Clara, USA) columns in series (15 m long × 0.25 mm i.d., and 0.25 μm film thickness). The multimode injector was programmed to start at 60 °C for 0.2 min, and then was increased at a rate of 720 °C/min until it reached 310 °C. The carrier gas was helium (high purity, 99.999%) (Air liquid, Bagneux, France) with flow rates of 0.9 and 1.1 mL/min in the first and second columns, respectively. The programmed temperature oven was set as follows: from an initial temperature of 60 °C (1 min) to 170 °C at 35 °C/min and up to 310 °C at a rate of 10 °C/min with a hold time of 2 min at 310 °C. PTV injector was used in splitless mode with an injection volume of 1 μL. The retention time lock setting (RTL) used chlorpyriphos methyl as the locking compound at a retention time of 9.14 min. The ion source and quadrupole analyzer temperatures were fixed at 280 °C. High purity nitrogen (99.999%) (Air liquid, Bagneux, France) was used as the collision gas. The preliminary instrument setup included the optimization of collision energies for each MRM transition in the range of 5–50 eV. Agilent Mass Hunter Quantitative Analysis B07.00 software was used for data acquisition and processing.

2.4. Analysis by GC-Q-Orbitrap

Injections were performed using a GC-Q-Orbitrap system (Q Exactive, Thermo Scientific, Bremen, Germany) consisting of a GERSTEL MPS (Multi-Purpose Sampler) (Mülheim, Germany) autosampler, a trace 1310 GC with PTV injector, an electron ionization (EI) source, and a hybrid Q-Orbitrap mass spectrometer. PTV, Cool Injection System, CIS6 was used with splitless mode injection (1 μL injected) with the following temperature program: t_0: 60 °C, hold time of 0.2 min increased at

720 °C/min until reaching 310 °C with a hold time of 5 min (run time: 20 min). Helium (99.999%, Linde Gas, Schiedam, Netherlands) was used as a carrier gas at a constant flow of 1.0 mL/min. GC separations were performed using an HP-5 MS UI (30 m × 250 μm × 0.25 μm film thickness) (Agilent Technologies, Santa Clara, USA) column using the following temperature program: t_0: 60 °C (1 min), ramp up to 170 °C at 35 °C/min and then increased to 310 °C at a rate of 10 °C/min with a hold time of 2 min at 310 °C. The transfer line was maintained at 280 °C. Electron ionization was performed at 70 eV with the source temperature set at 280 °C. Full scan MS acquisition was performed in profile mode using an *m/z* range of 50–500. Nitrogen gas (Air liquid, Bagneux, France) was used for the C-Trap supply. The mass calibration procedure was performed before each acquisition batch (FC 43, CAS 311–89-7). The internal mass calibration was performed during the measurement of background ions from column bleeding as lock mass ions using (*m/z*) ($C_3H_9Si^+$, 73.04680; $C_3H_9O_2Si_2^+$, 133.01356; $C_5H_{15}O_3Si_3^+$, 207.03235; $C_7H_{21}O_4Si_4^+$, 281.05114; $C_9H_{27}O_5Si^+$, 355.06993). For GC-Q-Orbitrap data processing, X-Calibur 4.0 and Trace Finder 4.1 (Thermo Scientific) were used for peak identification for GC–MS. For evaluation of the comparability of Orbitrap spectra with existing EI-library spectra, NIST 1.4 Mass spectral Library & Search Software (NIST 2014/EPA/NIH) version 2.2 build version June 10, 2014 was used.

2.5. Samples

Samples of wheat, rapeseed, cumin and tea were purchased from a local organic supermarket that had been previously checked to be free of the target pesticides. All samples were mechanically ground to be homogeneous.

2.6. Sample preparation and cleanup

Five grams of homogenized samples (wheat, rapeseed, cumin and tea) were weighed into a 50 mL disposable polypropylene centrifuge tube. For recovery studies, samples were spiked at 10 μg/kg with pesticide and contaminant working solutions at 2000 μg/kg, which corresponds to the MRL for most pesticides. Thereafter, ultrapure water (10 mL) was added, the mixture was stirred vigorously for 1 min, 10 mL of acetonitrile were added, and then, the mixture was immediately shaken for 1 min. Next, a salt mixture containing 4 g of anhydrous magnesium sulfate, 1 g of sodium chloride, 1 g of trisodium citrate dihydrate and 0.5 g of disodium hydrogen citrate sesquihydrate were added for good separation of the water and acetonitrile phases. The tubes were immediately shaken for 1 min and then centrifuged for 5 min at 4,700 rpm at 20 °C. On the one hand, 1 mL of unpurified extract from each matrix was collected; on the other hand, 6 mL of acetonitrile supernatant were transferred into a polypropylene centrifuge tube containing various purification supports (QuEChERS d-SPE cleanup):

(a) d-SPE with PSA (300 mg) and $MgSO_4$ (900 mg) for purification of wheat extracts
(b) d-SPE with PSA (150 mg), C18 (150 mg) and $MgSO_4$ (900 mg) for purification of rapeseed extracts
(c) d-SPE with Q-Carb® containing PSA (150 mg), graphitized carbon black GCB (150 mg) and $MgSO_4$ (855 mg) for purification of tea and cumin extracts

A volume of 4 mL for each extract was collected and acidified with 40 μL of 5% formic acid in acetonitrile. Then, 1 mL of the extract was evaporated to dryness under nitrogen for a solvent change step because of the poor compatibility of acetonitrile with the gas chromatographic method. The evaporated extract was dissolved into a mixture of hexane/acetone 70/30 (v/v). The same solvent change step was applied to the unpurified extract. The same extracts and standard solutions were injected at the same time in both the GC-triple-quadrupole and the GC-Q-Orbitrap systems. Moreover, the purified extracts were also diluted 5-, 10- and 20-fold and injected to evaluate the sensitivity and selectivity of both systems.

3. Results and discussion

The goal of this study was to challenge the sensitivity and selectivity of a well-established targeted GC-triple-quadrupole method with a full scan GC-Q-Orbitrap method for pesticide residue analyses of complex food matrices. The high mass accuracy of the HRMS-Orbitrap provides high selectivity that can avoid matrix interference. The performances in terms of selectivity in full scan mode using this high-resolution mass analyzer were compared to the selectivity of the MRM mode using the triple-quadrupole analyzer.

First, one hundred contaminants (Table S1) of various polarities from a wide variety of chemical families (organochlorines, organophosphorus triazoles, carbamates, pyrethroids, PCBs, etc.) were selected to cover a large panel of analytes. Moreover, almost all pesticides are registered in wheat with MRL values between 10 and 8,000 μg/kg by the European Commission (EU Pesticides Database (v.2.1), 2021). It was most important to use identical chromatographic conditions for both systems to ensure an accurate performance evaluation of both methods. Then, the chromatographic conditions were optimized to elute and separate the 100 targeted analytes for both systems in approximately 20 min. PTV injection was chosen to limit compound degradation, and the same operating conditions were used for both systems. In the same way, identical EI source conditions were set for both systems to limit the influence of the ionization process on the sensitivity even when the ionization source geometries were different.

3.1. GC-triple-quadrupole parameters

For each pesticide and contaminant, two characteristic MRM transitions (quantitative and qualitative) were selected after optimization. Table S1 shows the compound names, retention times, and quantitative and qualitative transitions at the selected collision energy voltages. First, each molecule was analyzed separately in full scan mode to select precursor ions in the first quadrupole, which were submitted to another set of analyses at different collision energy voltages in the second quadrupole to generate the MS/MS product ions. Once all MRM transitions were established for all molecules, the dwell time was optimized to maintain the number of cycles per second at 10 throughout the chromatographic run to obtain well-shaped chromatographic peaks, low detection limits, and sufficient chromatographic data points for all compounds (>10).

3.2. GC-Q-Orbitrap method

A resolving power set at 60,000 FWHM at *m/z* 200 with automatic gain control (AGC) at $1E^6$ was the best compromise between mass accuracy and acquisition rate for this kind of analysis (Hung et al., 2020). Because the injection time (IT) and AGC target regulate the number of ions in the Orbitrap cell, ion injection was stopped when one of the two conditions were met. For the first development, IT was set in automatic mode to maximize the number of ions transferred in the Orbitrap cell.

Starting from the NIST MS Search 2.2 library containing pesticide and contaminant Orbitrap databases, two ions were selected: the most intense for quantification and another intense ion as a qualifier ion for each compound. The qualifier ion should not be a mass isotope of the quantifier ion and should have a $m/z > 100$ if possible. Table S2 summarizes compound names, analyte formulas, quantifier ions, qualifier ions, retention times and mass accuracies.

For GC-Q-Orbitrap spectra, some differences were observed in ion abundance in comparison with those recorded with a quadrupole. As shown in Fig. 1, for triazophos, the ion *m/z* 161 presents the most relative intensity with both analyzers, but the relative intensity of the ion *m/z* 91 was two-fold lower for the Orbitrap analyzer than for the

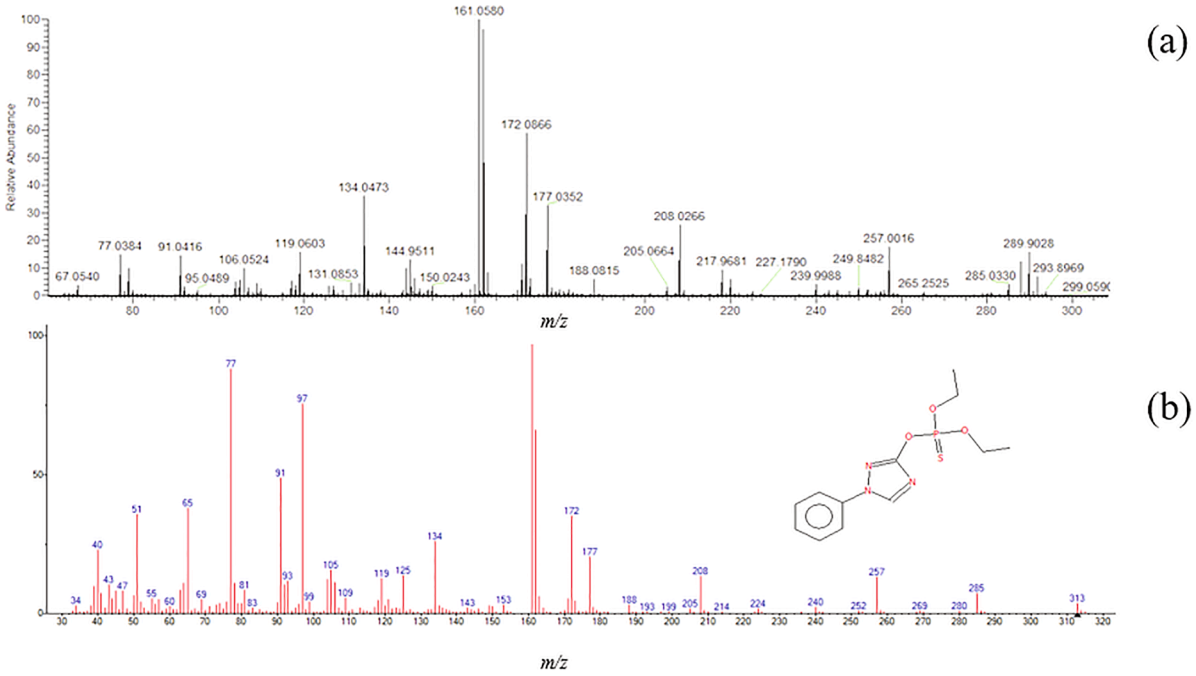

Fig. 1. (a) GC-Q-Orbitrap accurate mass spectrum for triazophos, resolving power of 60,000 FWHM, (b) GC-quadrupole mass spectrum for triazophos from NIST v2.2.

quadrupole analyzer. This phenomenon has already been reported (Mol et al., 2016) and can be attributed to lower trapping efficiency of ions with $m/z < 100$ in the C-trap. Moreover, the development of the method is less time-consuming than for GC-triple-quadrupole, especially when the mass spectra are already available in the database.

3.3. Impact of the resolving power

Depending on the complexity of the studied extracts, chromatographic separation and high resolving power were needed to separate isobaric ions of analytes from the ions of the matrix compounds. If the resolving power is not sufficient, coelution of the isobaric ion signals

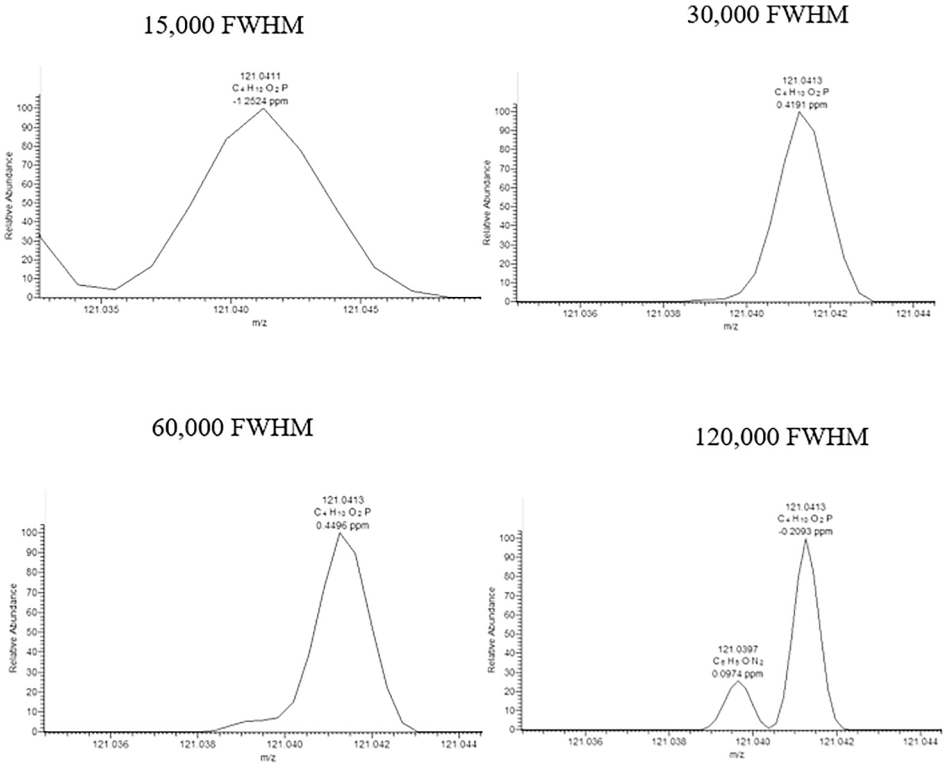

Fig. 2. Mass spectra zoomed in at m/z 121.0418 ± 5 ppm ($C_4H_{10}O_2P^+$) for chlormephos in wheat spiked at 10 μg/kg with a resolving power setting of 15,000 FWHM, 30,000 FWHM, 60,000 FWHM, and 120,000 FWHM at m/z 200.

from analytes and matrix compounds can be observed. However, higher resolving power allows a decrease in scan speed, which, therefore, reduces the number of collected data points per peak. Fig. 2 shows the extracted ion chromatograms for chlormephos ions (*m/z* 121.0418 ± 5 ppm corresponding to the $C_4H_{10}O_2P^+$ fragment) in wheat spiked at 10 µg/kg acquired at 15,000 FWHM, 30,000 FWHM, 60,000 FWHM and 120,000 FWHM. The coelution between the signal of this ion and an interferent isobaric ion peak was observed at 15,000 FWHM and 30,000 FWHM. However, when increasing the resolution at 60,000 FWHM and 120,000 FWHM (at *m/z* 200), both ion signals were partially and totally separated, respectively. As wheat extracts contain many coextractants, a resolving power greater than or equal to 60,000 FWHM was necessary to resolve the coelution signal and avoid overestimation of the targeted compound amount.

3.4. Qualitative results: Comparison of the limits of detection (LOD)

To evaluate the sensitivity of both analyzers, the LOD for the 100 pesticides and contaminants were estimated by injecting different standard calibration levels varying from 0.05 µg/L to 200 µg/L. Histograms for the LOD obtained are presented in Fig. 3. The values for 86 pesticides and contaminants analyzed with GC-Q-Orbitrap are lower than those obtained using the GC-triple-quadrupole. For 9 molecules, the same LODs were determined with both analyzers, and only 5 LOD values were higher for the GC-Q-Orbitrap method than those observed using the GC-triple-quadrupole method. This difference in sensitivity can be attributed to the high-resolution power of the GC-Q-Orbitrap MS analyzer, which drastically decreases the noise level. Because noise remains very low, a very small amount of targeted compound ions can be detected, allowing enhanced sensitivity. For the GC-triple-quadrupole, most molecules with LODs < 0.2 µg/L (aldrin, chinomethionat, chlorothalonil, endrin aldehyde, fenitrothion, haloxyfop-methyl, parathion-ethyl, parathion-methyl, pendimethalin, propham, prothiofos, and quinalphos) yielded signal–noise ratios between 3 and 10. In contrast, all the molecules that had LODs < 0.2 µg/L using the GC-Q-Orbitrap method exhibited S/N ratios >1000 in relation to the very low noise observed with this spectrometer analyzer.

3.5. Quantitative results in wheat

3.5.1. Linearity

At a concentration range of 0.4–40 µg/L, all the molecules analyzed with GC-Q-Orbitrap showed good linearity for the calibration curves (Table 1) with a good correlation coefficient (greater than 0.996). However, at a concentration of 200 µg/L, signal saturation was observed for some molecules. With the GC-triple-quadrupole method, the response for the pesticides and contaminants was quadratic with a weight of 1/x and a wider concentration range (up to 200 µg/L) than that observed in the GC-Q-Orbitrap method. Therefore, the dynamic range of the GC-Q-Orbitrap appeared, in the concentration range studied, less extended due to the saturation of the Orbitrap cell at the highest concentration tested. To achieve comparable results with both methods, calibration curves were established in quadratic mode with a weighting of 1/x.

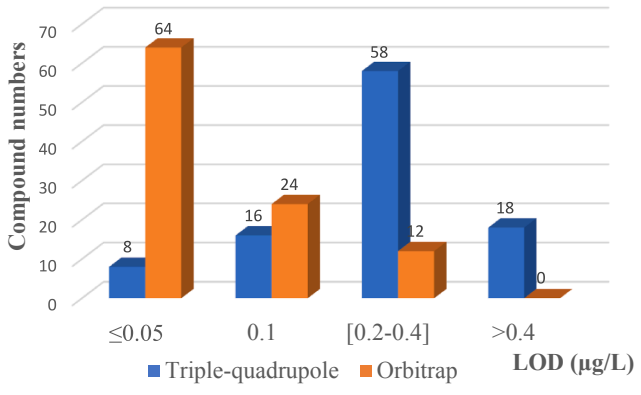

Fig. 3. Evaluation of LOD (µg/L) determined for 100 pesticides and contaminants in a mixture of hexane/acetone using the GC-Q-Orbitrap (orange) and GC-triple-quadrupole (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.5.2. Recovery

Recovery experiments were performed by analyzing wheat samples spiked at a concentration level of 10 µg/kg (n = 5). For the GC-Q-Orbitrap results, more than 85% of the pesticides and contaminants showed good recovery [70–120%], with RSD values < 20% demonstrating good repeatability (European Commission, 2017). Some organochlorine molecules presented intermediate recovery, such as aldrin (62 ± 10%), DDD (2,4′) (61 ± 20%), hexachlorobenzene (61 ± 13%), mirex (64 ± 14%) and procymidone (68 ± 5%). No molecule had a recovery above 120%. The recovery of endrin aldehyde was 0%, and the same recovery was observed with the GC-triple-quadrupole. This result could be attributed to the reaction of the aldehyde function of this molecule with the primary secondary amine used during the purification step (d-SPE, PSA/$MgSO_4$).

For the GC-triple-quadrupole method, the recovery for pesticides and contaminants in wheat spiked at 10 µg/kg, was higher than that obtained with the GC-Q-Orbitrap method for most compounds. Moreover, for 33% of the analytes, the recovery in the wheat matrix was over 120%. This phenomenon can be attributed to the decrease in analyte adsorption in the injection insert due to the coinjection of the wheat matrix compounds (Anastassiades et al., 2003). As described previously (Anastassiades et al., 2003), the addition of protectant analytes can overcome matrix-induced effects during quantitation. Low recoveries (<70%) were observed with both methods (deltamethrin, DDD (2,4′), demeton-S-methyl and tetrachlorvinphos). This outcome is usually due to the interaction of analytes with compounds in the matrix, which reduces the extraction yield. For the GC-Q-Orbitrap method, the recovery was, in most cases, <100%, while for GC-triple-quadrupole method, the recovery was clearly greater than 100%. This phenomenon could be explained by a difference in ionization efficiency (competition between analytes and matrix interferent molecules) due to a difference in ionization source designs. The difference in recovery could be also attributed to a difference in selectivity of GC-triple-quadrupole in mode MRM and GC-Q-Orbitrap in full scan mode. To confirm these opposite trends, the matrix effects will be evaluated.

3.5.3. Limits of quantification

Document (European Commission, 2017) describes the LOQ as the minimum concentration, which means the criteria for a mean recovery within the 70–120% range and an RSD of <20%. Recovery rates outside the range of 70–120% can be accepted if they are consistent (RSD ≤ 20%), but the mean recovery should not be lower than 30% or above 140%. However, if recoveries were between 30% and 70 % or between 120 and 140 % and RSD ≤ 20%, a correction of LOD and LOQ is required even if uncertainty was enlarged. The GC-Q-Orbitrap method cannot be validated for only 4 molecules (chinomethionat, demeton-S-methyl, endrin aldehyde and quinalphos) because the criteria defined above were not met. To include these analytes, spiking at a higher concentration level is required. The LOQ values calculated for the other molecules that complied with the specifications described above ranges between 0.1 µg/kg and 2 µg/kg. These results are very satisfactory because the MRL values for these pesticides and contaminants are ≥ 10 µg/kg. For the GC-triple-quadrupole method, 7 molecules (bifenthrin, carbophenothion, endrin aldehyde, fluorochloridone, haloxyfop-methyl, malathion, mecarbam and phosmet) did not meet the criteria defined above and therefore could not be validated with this method due to the overestimated recovery values. As previously mentioned, the

Table 1
Evaluation of the GC-triple-quadrupole and GC-Q-Orbitrap quantitative results obtained for wheat spiked at 10 μg/kg.

Analyte	Triple Quadrupole					Orbitrap				
	R^2	Recovery (%)	RSD (%)	LOQ (μg/kg)	ME (%)	R^2	Recovery (%)	RSD (%)	LOQ (μg/kg)	ME (%)
2-Phenylphenol	0.9999	120	20	2.0	53	0.9999	101	4	0.1	−45
Alachlor	0.9999	132	14	0.8	62	0.9967	86	5	0.1	−36
Aldrin	0.9999	97	11	2,0	5	1.0000	62	8	0.2	−24
Anthraquinone	1.0000	132	15	0.8	51	1.0000	83	4	0.1	54
Azinphos-ethyl	0.9999	124	8	0.5	70	0.9998	99	6	0.1	−41
Azinphos-methyl	0.9998	90	8	0.4	45	0.9999	117	9	0.2	−43
Bifenthrin	0.9997	143	20	/	84	0.9990	89	4	0.2	−36
Bromophos-ethyl	0.9998	119	20	2.0	69	0.9999	83	9	0.8	−40
Bromophos-methyl	0.9979	128	17	0.2	49	0.9991	85	3	0.2	−40
Butralin	0.9999	96	14	0.8	49	0.9999	115	7	0.4	−60
Carbophenothion	0.9996	147	28	/	75	0.9999	83	6	0.1	3
Chinomethionat	0.9996	61	19	2.0	−7	0.9999	25	20	/	−34
Chlormephos	0.9997	117	20	1.4	−1	0.9997	91	5	0.1	−22
Chlorfenson	0.9991	89	20	0.8	−27	0.9991	40	18	0.5	−47
Chlorobenzilate	0.9994	120	14	0.1	74	0.9997	77	7	0.1	−37
Chlorthal-dimethyl	0.9990	102	9	0.4	11	0.9999	87	8	0.1	−39
Chlorothalonil	0.9998	72	17	2.0	51	0.9989	85	3	0.4	−33
Chlorpropham	0.9998	111	20	0.4	−45	1.0000	94	6	0.1	−74
Chlorpyriphos-ethyl	0.9991	109	19	0.8	28	0.9999	101	6	0.1	−34
Chlorpyriphos-methyl	1.0000	134	10	0.7	39	0.9999	94	5	0.1	−45
Coumaphos	0.9999	80	14	0.8	48	0.9999	91	8	0.1	4
DDD (2,4′)	0.9999	46	14	0.8	−15	0.9999	61	20	0.7	2
DDE (2,4′)	0.9967	68	23	1.2	−27	1.0000	35	10	1.9	−65
DDE (4,4′)	0.9998	60	14	2.0	21	0.9999	44	14	1.2	−35
Deltamethrin	0.9998	59	28	0.6	18	1.0000	48	4	0.4	−11
Demeton-S-methyl	0.9997	40	26	1.7	70	0.9999	19	34	/	−39
Diazinon	0.9997	115	8	0.4	54	0.9998	94	4	0.1	−31
Dichlobenil	0.9993	107	20	0.3	9	0.9997	73	4	0.1	−32
Dichlofenthion	0.9997	108	12	0.1	24	1.0000	90	6	0.1	−16
Dichlorvos	0.9991	74	18	0.4	15	0.9989	71	8	0.1	−28
Dicloran	0.9998	139	14	0.2	29	0.9999	93	8	0.1	−20
Dimethoate	0.9989	140	19	0.2	79	0.9994	113	7	0.1	−34
Diphenylamine	0.9998	93	9	0.2	31	0.9985	70	5	0.2	−32
Disulfoton	0.9967	90	20	1.5	13	1.0000	82	14	0.2	−61
Endosulfan sulfate	0.9998	126	16	0.2	65	0.9993	93	19	0.1	−75
Endrin aldehyde	0.9985	0	57	/	8	0.9995	0	0	/	−64
Ethion	0.9998	125	14	2.5	22	0.9992	73	15	0.1	−26
Ethoprophos	0.9997	126	14	0.2	53	0.9968	91	6	0.1	−28
Etridiazole	0.9997	86	20	0.4	26	1.0000	83	9	0.1	−62
Fenamiphos	1.0000	127	26	0.8	49	0.9999	84	11	0.4	−39
Fenchlorphos	0.9989	118	6	0.8	41	0.9999	83	4	0.1	27
Fenchlorphos-oxon	0.9998	127	7	0.2	68	1.0000	89	6	0.1	−22
Fenitrothion	0.9997	109	17	2.0	−37	0.9997	91	7	0.4	−32
Fenpropathrin	0.9988	136	23	0.4	48	0.9983	96	8	0.1	−57
Fenson	0.9993	135	18	0.4	38	0.9999	111	5	0.1	−61
Fludioxonil	0.9999	88	10	0.2	79	0.9999	77	15	0.2	−11
Fluorochloridone	1.0000	156	23	/	55	0.9999	114	4	0.2	−15
Formothion	1.0000	127	14	2.0	71	1.0000	86	5	0.2	−34
Haloxyfop-methyl	0.9988	156	15	/	64	0.9998	50	23	0.6	−31
HCH (α)	0.9997	120	4	0.4	16	0.9999	91	4	0.1	−29
HCH (β)	0.9997	105	15	0.4	20	0.9999	92	4	0.1	−21
HCH (γ)	0.9989	101	6	0.4	29	0.9997	96	5	0.1	−33
HCH (δ)	1.0000	101	7	0.4	14	0.9997	92	5	0.1	−30
HCH (ε)	0.9997	118	10	0.2	18	0.9999	96	6	0.1	−35
Heptachlor	0.9997	94	16	0.1	8	0.9997	86	11	0.2	−22
Heptenophos	0.9988	135	17	0.2	41	0.9999	96	5	0.1	−38
Hexachlorobenzene	0.9999	76	8	0.4	3	0.9997	61	13	0.4	−29
Isazophos	0.9999	95	20	2.0	27	1.0000	93	6	0.1	−13
Isodrin	0.9997	112	15	0.4	34	0.9988	84	8	0.1	54
Malaoxon	1.0000	136	22	0.4	70	0.9997	72	5	0.1	27
Malathion	0.9983	153	12	/	45	0.9999	101	2	0.2	12
Mecarbam	1.0000	148	22	/	61	0.9999	94	8	0.1	−39
Metalaxyl	0.9999	103	7	0.4	23	0.9995	101	7	0.1	−8
Methacriphos	0.9999	127	18	0.2	25	0.9995	92	4	0.1	11
Methidathion	0.9969	131	20	0.4	44	0.9996	84	9	0.1	−47
Methoxychlor	0.9998	134	17	0.2	33	0.9997	90	5	0.1	30
Mevinphos	0.9983	122	19	0.1	61	0.9999	98	3	0.1	−50
Mirex	0.9999	103	7	0.2	13	0.9991	64	14	0.4	−19
Monochrotophos	0.9990	107	21	0.4	60	0.9993	98	5	0.1	−35
N-Desmethyl-pirimiphos-methyl	0.9999	106	20	2.0	58	0.9990	95	5	0.1	−48
Nitrofen	0.9991	120	11	0.4	86	0.9997	82	10	0.4	−15
Paraoxon-methyl	0.9997	84	17	0.8	63	0.9994	106	12	0.1	−39
Parathion-ethyl	0.9997	106	19	2.0	57	0.9997	100	3	0.1	−34

(*continued on next page*)

Table 1 (*continued*)

Analyte	Triple Quadrupole					Orbitrap				
	R^2	Recovery (%)	RSD (%)	LOQ (µg/kg)	ME (%)	R^2	Recovery (%)	RSD (%)	LOQ (µg/kg)	ME (%)
Parathion-methyl	0.9999	118	16	2.0	52	0.9999	99	7	0.1	−40
PCB 118	0.9992	87	16	0.6	70	0.9990	108	4	0.2	−65
PCB 138	0.9994	71	12	0.4	81	0.9989	91	8	0.2	−65
PCB 153	0.9999	117	25	0.1	52	1.0000	96	9	0.2	−39
PCB 28	0.9990	89	9	0.1	19	1.0000	76	10	0.1	−38
PCB 52	0.9999	101	19	0.1	−25	0.9992	59	10	0.4	−38
Pendimethalin	0.9999	140	23	3.8	65	0.9999	93	15	0.2	−32
Pentachloroanisole	0.9989	106	12	0.4	−10	0.9999	94	4	0.1	−37
Pentachlorobenzene	0.9973	89	7	0.8	8	0.9998	72	3	0.1	−54
Phosalone	0.9999	134	18	0.4	29	0.9997	96	10	0.2	−49
Phosmet	0.9999	155	18	/	57	0.9994	98	5	0.1	−8
Phosphamidon	0.9997	97	15	2.0	−41	0.9990	95	5	0.1	−31
Pirimiphos-ethyl	0.9997	107	11	0.8	51	0.9998	87	8	0.1	−23
Procymidone	0.9973	135	13	1.2	6	1.0000	68	5	0.6	−41
Profluralin	0.9989	92	17	0.8	40	0.9999	101	11	0.4	−33
Propham	0.9973	113	20	2.0	30	0.9992	98	2	0.1	−33
Prothiofos	0.9995	94	13	2.0	3	0.9973	36	14	0.6	−29
Quinalphos	0.9981	64	27	2.0	52	0.9984	23	13	/	−25
Quintozene	0.9997	99	12	0.4	7	0.9988	87	12	0.2	−27
Sulfotep	0.9984	118	15	0.6	12	0.9999	94	6	0.2	−25
Tecnazene	0.9983	103	9	0.4	17	1.0000	87	3	0.2	−38
Tetrachlorvinphos	0.9998	45	16	0.7	−40	0.9997	34	15	1.2	−50
Tetradifon	0.9999	139	19	0.4	69	0.9998	70	17	0.1	−37
Tolclofos-methyl	0.9999	105	12	0.5	34	0.9999	87	5	0.1	−46
Triazophos	0.9998	140	20	1.2	65	0.9999	88	3	0.1	−40
Trifluralin	0.9973	140	17	0.7	27	0.9999	101	4	0.1	−24
Vinclozolin	0.9999	129	8	0.6	32	1.0000	89	8	0.2	−29

*/: not quantified

recovery value for endrin aldehyde was 0%, which meant it could not be quantified using this sample preparation. The LOQ values calculated for the other molecules that met the conditions described above ranged between 0.1 µg/kg and 4 µg/kg.

The LOQ values for both methods are presented in Fig. 4. This figure demonstrates that the LOQ values obtained with the GC-triple-quadrupole are slightly higher than those obtained with the GC-Q-Orbitrap method. These results demonstrate that the GC-Q-Orbitrap method is more sensitive than the GC-triple-quadrupole method for most pesticides and contaminants studied in wheat.

3.5.4. *Matrix effects*

As a consequence of coeluting sample components, the targeted analyte signal may be enhanced or suppressed compared to the signal from the same targeted analyte when injected in pure solvent. The matrix effect is evaluated by comparing the slope of the calibration curves for the standards in solvent against standards prepared in matrix extracts. The matrix effect (ME) is calculated using Eq. (1):

$$\text{Matrix effect(ME)} = ((\text{slope matrix}/\text{slope solvent}) - 1) \times 100 \quad (1)$$

The soft matrix effect (suppression or enhancement of 0–20%) is negligible. However, if some of the analytes had a suppression or enhancement of 20–50%, the matrix effect appeared as medium. When the matrix effect (suppression or enhancement > 50%) is strong, it is necessary to use some methods to overcome the ME, such as employing a matrix-matched calibration or sample dilution. ME % values are presented in Table 1.

For GC-triple-quadrupole analyses, 64 molecules had a medium matrix effect, and 36 molecules had a strong matrix effect; in most cases, they were positive. The enhancement of a signal is generally attributed to a decrease in analyte adsorption in the injector in the presence of matrix compounds, such as the addition of protectants in the sample vial before injection (Anastassiades et al., 2003). Suppression of the signal is often due to analyte degradation that can occur during extraction steps or in the EI source. When an enhanced signal was observed, in most cases with the GC-triple-quadrupole method, the opposite phenomenon was observed for the GC-Q-Orbitrap where the signal was suppressed. For the GC-Q-Orbitrap methods, the matrix effect for 84 molecules was acceptable, with values ranging between -50% and 50%. Strong suppression of the chromatographic signal was observed for 16 molecules. This phenomenon could be attributed to competition between targeted analyte ions and matrix compound ions during their transfer in the C-trap. A possibility to prevent this phenomenon would be a SIM approach (selected ion monitoring) mode to overcome the signal suppression by selecting the ions transferred in the C-trap using the quadrupole implemented beforehand. In contrast to the full scan mode, this targeted approach limits the number of compounds that can be analyzed and the possibility of reprocessing the analysis data to detect the presence of other pesticides and contaminants in the injected extracts after acquisition.

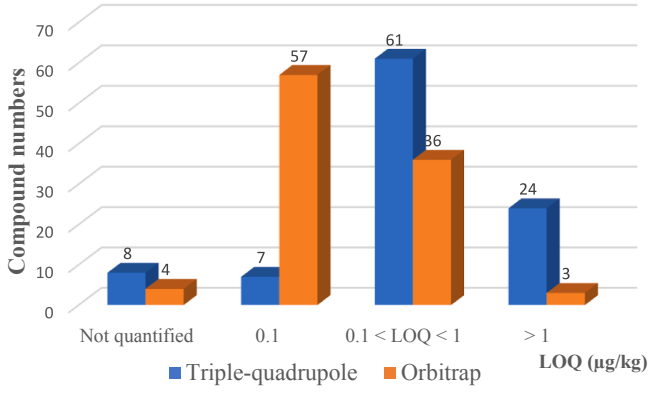

Fig. 4. Evaluation of LOQ (µg/kg) determined for 100 pesticides and contaminants in wheat spiked at 10 µg/kg using the GC-Q-Orbitrap (orange) and GC-triple-quadrupole (blue). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

3.5.5. *Injection of unpurified wheat extract*

Wheat extract spiked at 10 µg/kg without a purification step was injected using the GC-Q-Orbitrap method. Most of the pesticides and

contaminants (97%) were detected. Ten replicates of injection were performed without loss of sensitivity. According to the MRL, GC-Q-Orbitrap has been demonstrated to be a powerful method for the rapid screening of pesticides and contaminants in wheat without a purification step. Nevertheless, contamination of the inlet can occur with unpurified samples, and diluting can minimize this phenomenon. Then, the unpurified extracts spiked at 10 μg/kg were injected after different dilutions (5, 10 and 20 times). More than 70% of the pesticides and the contaminants were quantified in solution diluted 10-fold. The injection of QC standards after 10 unpurified extract injections has shown that the QC values were between 70 and 130 %. Nevertheless, after 30 unpurified extract injections a change of inlet and a cleaning of the ionization source appeared necessary.

3.5.6. Injection of wheat extracts of real sample

To prove the effectiveness of the two methods (GC-Q-Orbitrap and GC-triple quadrupole), they were applied to ten different real wheat samples. Results obtained with GC-Q-Orbitrap and those obtained with GC-triple quadrupole showed that only five pesticide residues were detected (chlorpyrifos ethyl, chlorpyrifos methyl, phosmet, chlorpropham and deltamethrin). The amount of detected pesticides in wheat extracts did not exceeded the MRL values of these pesticides in wheat samples which were 10, 10, 50, 10 and 1,000 μg/kg respectively.

Using GC-Q-Orbitrap, chlorpyrifos ethyl and chlorpyrifos methyl were detected in all the wheat samples, with concentration ranging from 2.6 to 6.3 μg/kg. Phosmet was detected at a concentration range from 18.9 to 21.5 μg/kg, chlorpropham was detected in three sample at a concentration range from 2.3 to 6.9 μg/kg and deltamethrin was detected in one sample at a concentration of 33.5 μg/kg. Almost similar values were obtained using the GC-triple quadripole: chlorpyrifos ethyl and chlorpyrifos methyl were detected in all the wheat samples, with concentration ranging from 3.1 to 7.7 μg/kg. Chlorpropham was detected in three sample at a concentration range from 3.0 to 8.6 μg/kg and deltamethrin was detected in one sample at a concentration of 36.6 μg/kg. Phosmet is detected using GC-triple quadripole method but could not be quantified due to the too high recovery value up to 140% obtained for pesticide. So, the results obtained with both approaches (MRM mode using GC-triple quadripole and full scan mode using GC-Q-Orbitrap) were consistent.

3.6. Injection of other complex matrix extracts

The final part of our study was dedicated to the influence of various matrices on the detection of both methods. The same extracts of

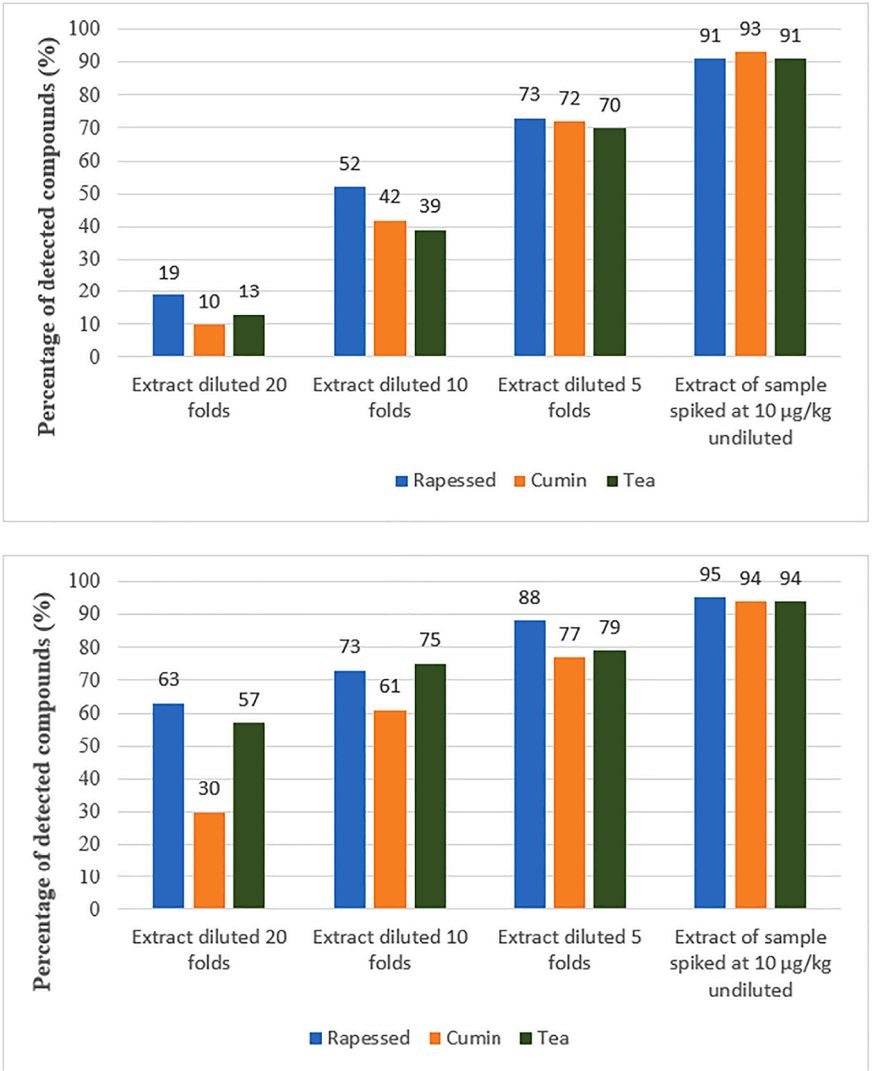

Fig. 5. Comparison of the percentage of detected compounds with different dilutions (5-, 10- and 20-fold) using the GC-triple-quadrupole (a) and GC-Q-Orbitrap (b) in the complex matrices spiked at 10 μg/kg: rapeseed (blue), cumin (orange) and black tea (green). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

rapeseed, cumin or tea samples spiked at 10 μg/kg were analyzed using the GC-triple-quadrupole and GC-Q-Orbitrap methods. For the latter method, optimized parameters, determined in this study, were selected: 60,000 FWHM and $1E^6$ for the AGC target value. For data treatment, tolerance for the mass (±5 ppm) and retention time (±0.1 min) was used. The extracts from these different matrices underwent different dilutions, 5-, 10- and 20-fold, to assess the sensitivity and selectivity of both methods. The histograms presented in Fig. 5 summarize the results obtained for the three matrices.

The results showed that for undiluted extracts for the three matrices, similar percentages of detected compounds were obtained regardless of the method used. The endrin aldehyde was recovered in rapeseed extracts. This result can be explained by the nature of the d-SPE material used for rapeseed purification that contains less amount of PSA. Concerning diluted extract analyses, the GC-Q-Orbitrap sensitivity appeared to be clearly higher than the GC-triple-quadrupole sensitivity due to the very low noise observed with the GC-Q-Orbitrap method. For the extract diluted 20-fold, the number of pesticides and contaminants still detected ranged from 30 to 63% (Fig. 5). Moreover, when injecting extracts diluted 20-fold into the GC-Q-Orbitrap system, some ions provided in matrices were clearly separated from the analyte ions.

4. Conclusion

In this study, the GC-Q-Orbitrap (60,000 FWHM at *m/z* 200) method and GC-triple-quadrupole method were evaluated and compared for the screening and quantification of 100 pesticides and contaminants in different complex food matrices, such as wheat, rapeseed, cumin and black tea. The GC-Q-Orbitrap method development in full scan mode was found to be less time-consuming than the GC-triple-quadrupole method. The GC-Q-Orbitrap and GC-triple-quadrupole methods were able to detect 100% of the pesticides and contaminants with an LOD of < 0.4 μg/L and < 2 μg/L, respectively. In terms of sensitivity, the LOD values were lower for 86 pesticides and contaminants analyzed with the GC-Q-Orbitrap method than those obtained using the GC-triple-quadrupole method. Good linearity for the calibration curves at a concentration range of 0.4–40 μg/L with a good coefficient and correlation (greater than 0.996) was obtained for almost all the molecules studied. However, the GC-Q-Orbitrap method exhibited a smaller dynamic range than the GC-triple-quadrupole method. More than 85% of the pesticides and contaminants showed good recovery [70–120%] with the GC-Q-Orbitrap method, which can be attributed to better selectivity. Moreover, a negative matrix effect was observed with the GC-Q-Orbitrap method. This phenomenon may be due to competition between targeted analyte ions and matrix compound ions during their transfer in the C-trap, which that can be overcome using a SIM approach. In contrast to the full scan mode, this targeted approach limits the number of compounds that can be analyzed and the possibility of reprocessing the analysis data to detect the presence of other pesticides and contaminants in the injected extracts after acquisition. The injection of unpurified wheat extracts spiked at 10 μg/kg proved the potential of the GC-Q-Orbitrap method for use in performing high-throughput screening for pesticides and contaminants in food matrices.

CRediT authorship contribution statement

Saida Belarbi: Investigation, Validation, Writing - original draft, Visualization. **Martin Vivier:** Conceptualization, Writing - review & editing. **Wafa Zaghouani:** Writing - review & editing. **Aude De Sloovere:** Project administration, Funding acquisition. **Valérie Agasse-Peulon:** Writing - review & editing, Supervision. **Pascal Cardinael:** Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodchem.2021.129932.

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