separations

MDPI

Article

Simultaneous Determination of Multiresidues of Pesticides and Veterinary Drugs in Agricultural Soil Using QuEChERS and UHPLC–MS/MS

Michele C. Vicari [1], Janice F. Facco [1], Sandra C. Peixoto [1,2], Gabriel S. de Carvalho [1], Luana Floriano [1], Osmar D. Prestes [1], Martha B. Adaime [1] and Renato Zanella [1,*]

[1] Laboratory of Pesticide Residues Analysis (LARP), Chemistry Department, Federal University of Santa Maria (UFSM), Santa Maria 97105-900, RS, Brazil
[2] Universidade Franciscana (UFN), Santa Maria 97010-032, RS, Brazil
* Correspondence: renato.zanella@ufsm.br; Tel.: +55-5532208011

Abstract: Soil is one of the main destinations for pesticides and veterinary drugs used in agriculture and animal production. The negative consequences of the accumulation of these compounds in the environment make it important to monitor these compounds in the soil. In this study, we compared different extraction procedures using solvent shaking, ultrasound, or QuEChERS, and their combinations, for the simultaneous determination of 75 pesticide and seven veterinary drug residues in agricultural soil by ultra-high performance liquid chromatography coupled to serial mass spectrometry (UHPLC–MS/MS). The method using QuEChERS combined with shaking showed the best results for soil using the addition of water, followed by extraction with acetonitrile acidified with acetic acid and shaking in a shaker. For partitioning, anhydrous magnesium sulfate and anhydrous sodium acetate were used. The extract was centrifuged, filtered, and diluted (1:4, v/v) in water for determination by UHPLC–MS/MS. Method validation showed adequate accuracy and precision results, with recoveries between 70 and 120% and RSD $\leq$ 20% for the vast majority of the compounds evaluated at the spike levels of 10, 25, 50, and 100 μg kg^{-1}. The method limits of detection (LOD) and quantification (LOQ) ranged from 3.0 to 7.5 μg kg^{-1} and from 10 to 25 μg kg^{-1}, respectively. The method was applied to different agricultural soil samples and proved to be efficient for routine analysis.

Keywords: soil; pesticides; veterinary drugs; sample preparation; LC–MS/MS

Citation: Vicari, M.C.; Facco, J.F.; Peixoto, S.C.; de Carvalho, G.S.; Floriano, L.; Prestes, O.D.; Adaime, M.B.; Zanella, R. Simultaneous Determination of Multiresidues of Pesticides and Veterinary Drugs in Agricultural Soil Using QuEChERS and UHPLC–MS/MS. *Separations* **2024**, *11*, 188. https://doi.org/10.3390/separations11060188

Academic Editor: Maria Elizabeth Tiritan

Received: 7 May 2024
Revised: 31 May 2024
Accepted: 6 June 2024
Published: 14 June 2024

1. Introduction

In recent decades, the increase in agricultural activity has led to a growing demand for pesticides. However, many pesticides have been classified as persistent and highly toxic, and can cause numerous damages to the environment and to non-target species. Soil contamination by pesticides is a growing concern due to the damage caused, which can compromise essential soil functions, biodiversity, and food safety [1]. Animal production is one of the most significant activities in Brazilian agribusiness, and to ensure the productivity and competitiveness of the sector, veterinary drugs have been widely used to ensure animal health, as well as allowing an increase in production [2]. Although the excretion rates of veterinary antimicrobials depend on the substance administered, the mode of application, the animal species, and the treatment time, it is estimated that up to 90% of the administered dose is eliminated in its unmetabolized form or as active metabolites, since the absorption of these substances generally occurs incompletely in the body [3,4].

Agricultural soils adjacent to concentrated animal feeding operations and animal husbandry are often fertilized with animal manure. The prevalence of veterinary antibiotics in agricultural soil can, in the long term, affect the effectiveness of these antibiotics in the human health sector [5]. Veterinary antibiotics have often been detected in livestock

manure and composted soil and have reached concentrations in soil well above 100 μg kg^{-1}. There are also occurrences in surface and groundwater that can be clearly attributed to veterinary uses, but the concentrations are generally in the ng L^{-1} range and are therefore considerably lower than those found in soils [6].

Deficiencies in good practice in the use of pesticides and veterinary drugs result in the occurrence of residues which, at levels above the maximum residue limits (MRLs), can pose a risk to human health. These risks are closely related to non-compliance with the manufacturer's instructions for use contained in the product's package leaflet, such as indication of use for the target species, dosage, route of administration, and grace period [7]. There is a great lack of legislation establishing maximum limits for veterinary drugs in soil. In 2001, the European Agency for the Evaluation of Medical Products (EMEA) set a general limit of 100 μg kg^{-1} for veterinary drugs in soil. This value was established on the basis of toxicological studies carried out on drugs authorized in the United States and is below the harmful levels observed in earthworms, microbes, and plants [8]. With regard to pesticides, soil monitoring is not required by the European Union (EU) and there is little information on the maximum limits allowed in soil. The Vietnamese government [9] set the maximum permissible limits for pesticide residues in soil ranging from 10 to 100 μg kg^{-1}. In view of the above, it can be seen that there is a knowledge gap regarding environmental risk indicators for pesticides and veterinary drugs in soil. Due to the large number of active ingredients in use, there is a need to establish maximum permitted values for these compounds in soil.

Pesticide soil quality standards should be defined situationally, considering that pesticide fate in the soil and human exposure to soil pesticides vary greatly with specific patterns [10], the process of setting pesticide standards in soil lacks the integration of the effectiveness of plant protection, and the prevention of human health risks [11]. Pesticides reach the soil not only through direct incorporation, but also through seed treatment, the control of pathogenic fungi and pests, and the elimination of invasive plants, among other routes. Contamination can also occur indirectly, through the spraying of plants and the falling of fruit and leaves that have received pesticide application. Due to the high complexity of environmental processes, the study of the environmental effect of pesticides is also extremely complex. Generally, the sorption of pesticides in soil is stronger compared to other matrices, such as fruits and vegetables. The environmental fate of pesticides is determined by their chemical and physical properties, as well as environmental characteristics [12]. Soil stands out as an important matrix for environmental monitoring, since pesticides are often applied directly or found in the soil after being applied to plants. Many of the veterinary drugs administered are not completely metabolized in the animal body, being excreted partly in the form of the original compound and partly metabolized. In addition to the excretions of grazing animals, manure is often dumped directly onto pastures or used as fertilizer in agriculture. Environmental contamination can also occur due to poor storage conditions or irregular disposal. The behavior and fate of veterinary drugs in the environment are regulated, just like pesticides, by chemical, physical, and biological processes [13]. The behavior of drugs and veterinary drugs in the environment has not yet been widely studied and there is a lack of quantitative data to estimate the extent of this contamination, the mobility of these compounds, and their environmental impacts on the environment and animals [14].

Selective extraction of pesticides from soil is based on physicochemical properties such as solubility, polarity, molecular mass, Kow, Koc, and volatility [15]. More selective extraction techniques can eliminate or reduce the need to clean the extract. The extraction of analytes from solid samples remains a critical step in the analysis of contaminants and aspects such as selectivity, recovery of the analyte, volume of organic solvent required, toxicity of the solvent, extraction time, and number of extraction cleaning steps, as well as the associated costs and simplicity of execution, must be considered. Table 1 presents examples of different sample preparation techniques applied for the determination of pesticide and veterinary drug residues in soil samples. Among these techniques, the

solid–liquid extraction stands out, which includes shaker and ultrasonic-assisted extraction (UAE) techniques [16], as well techniques developed more recently in order to reduce solvent consumption and increase extraction efficiency, including microwave-assisted extraction (MAE), pressurized-liquid extraction (PLE), supercritical fluid extraction (SFE), solid phase microextraction (SPME), and the QuEChERS method [17–19].

Table 1. Different sample preparation procedures for determining pesticide and veterinary drug residues in soil samples.

Extraction (Time)	Analyte (no.)	Extraction Solvent (mL)	Ref.
Soxhlet (24 h)	Organochlorines (13)	DCM (100)	[20]
Soxhlet (16 h)	Organochlorines (20)	Acetone:hexane (1:1, *v*/*v*) (250)	[21]
Shaker (1 h)	Pesticides multiclass (6)	MeCN (50)	[22]
Shaker (30 min)	Pesticides multiclass (37)	Acetone with 1% HAc (30)	[23]
Shaker (4 h)	Pesticides multiclass (9)	MeOH or MeOH/EtAc (70:30, *v*/*v*) (20)	[24]
Shaker (16 h)	Pesticides multiclass (30)	MeCN (50) + H_2O (200)	[25]
Shaker (6 min)	Veterinary antibiotics (58)	$Na_2EDTA{\cdot}2H_2O$ (0.4 g)/MeCN:phosphate buffer (1:1, *v*/*v*) (40)	[26]
Shaker (10 min)	Veterinary antibiotics (34)	MeCN:MeOH (1:1, *v*/*v*) with 0.2% formic acid + Na_2EDTA–McIlvaine buffer (20)	[27]
UAE	Organochlorines (17)	MeOH (15)	[28]
	Pesticides multiclass (51)	EtAc (10)	[29]
	Pesticides multiclass (54)	MeCN:H_2O (1:1, *v*/*v*) (20)	[30]
	Veterinary antibiotics (9)	MeOH:MeCN:EDTA:McIlvaine buffer (30:20:25:25) (5)	[31]
	Sulfonamides (4)	MeOH (18) + HCl 0.1 mol L^{-1} (2)	[32]
	Organochlorines (12)	Petroleum ether:acetone (1:1, *v*/*v*) (50)	[33]
	Veterinary antibiotics (24)	ACN:McIlvaine buffer (pH 4.0)(1:1, *v*/*v*) (15)	[34]
MAE	Herbicides (9)	H_2O:MeOH (10)	[35]
	Organochlorines (10)	Acetone:hexane (1:1, *v*/*v*) (25)	[36]
	Organophosphates (6)	H_2O:MeOH (1:1) (1–2 mL) and 0.02 M KH_2PO_4; hexane (5)	[37]
	Tetracyclines (3)	ACN:McIlvaine buffer:0.1 M EDTA (2:1:1, *v*/*v*/*v*)	[38]
PLE	Pesticides multiclass (30)	Acetone:DCM (1:1, *v*/*v*)	[39]
	Pesticides multiclass (122)	EtAc:MeOH (3:1, *v*/*v*)	[40]
	Pesticides multiclass (24)	H_2O:MeCN (1:2, *v*/*v*)	[41]
	Antibiotics (23)	Citrate–phosphate buffer pH 7.0 and MeOH (1:1, *v*/*v*)	[42]
SPME	Organochlorines (8)	H_2O (5)	[43]
	Pesticides multiclass (20)	MeOH, evaporation, dissolution in acetone, and dilution 1:50 in H_2O	[44]
SFE	Pesticides multiclass (36)	H_2O	[45]
	Pesticides multiclass (31)	CO_2 added with MeOH	[46]
	Pesticides multiclass (107)	CO_2 added with MeOH	[47]
QuEChERS original	Carbamates	H_2O (3) + MeCN (5)	[48]
	Metaflumizone	H_2O (5) + MeCN (10)	[49]
	Procymidone	H_2O (3) + MeCN (10)	[50]
	Oxadiargil	MeCN (15)	[51]
	Imidacloprid and thiamethoxam	MeCN (20)	[52]
	Pesticides (36)	H_2O (5) + MeCN (10)	[53]
QuEChERS acetate	Organochlorines (19)	H_2O (10) + MeCN with 1% HAc (10)	[54]
	Pesticides (12)	H_2O (10) + MeCN with 1% HAc (10)	[55]
QuEChERS citrate	Pesticides multiclass (38)	H_2O (4) + MeCN (20)	[56]
	Pesticides multiclass (24)	MeCN (20)	[41]
	Organophosphates (10)	MeCN (20)	[57]
	Organochlorines (14)	H_2O (3) + MeCN (7)	[58]
	Insecticides (3)	H_2O (5) + MeCN with 1% HAc (5)	[59]
	Pesticides multiclass (216)	MeCN with 1% formic acid (*v*/*v*) (10)	[60]

Table 1. *Cont.*

Extraction (Time)	Analyte (no.)	Extraction Solvent (mL)	Ref.
QuEChERS modified	Herbicides, insecticides, and fungicides (7)	Aqueous saturated calcium hydroxide (20) + MeCN (10)	[61]

DCM: dichloromethane; EDTA: ethylenediaminetetraacetic acid; EtAc: ethyl acetate; H_2O: water; HAc: acetic acid; MAE: microwave-assisted extraction; MeCN: acetonitrile; MeOH: methanol; McIlvaine buffer: a sodium phosphate dibasic dihydrate–citric acid solution; PLE: pressurized-liquid extraction; SFE: supercritical fluid extraction; SPME: solid phase microextraction; UAE: ultrasonic-assisted extraction.

The QuEChERS method has been used successfully in soil samples, as it has advantages such as simplicity, speed, low cost, and the ability to provide high-quality analytical results [62–64]. In addition to using the original QuEChERS method, modifications using extractions with acidic buffers, such as acetate and citrate, have been used to obtain adequate recoveries for compounds sensitive to pH variation [65–67]. In addition, the addition of water to obtain adequate humidity and the use of different adsorbents in the extract cleaning stage have been described for the extraction of pesticides from soils with adequate results.

The ultra-high performance liquid chromatography coupled to serial mass spectrometry (UHPLC–MS/MS) technique has been widely used for the determination of pesticides and veterinary drugs in various matrices, as it has high selectivity and sensibility. The acquisition of results using the selected reaction monitoring (SRM) mode adds selectivity for analysis at low concentrations, since two transitions per analyte are monitored [68]. Thus, considering the importance of using soil for food production, the intensive use of pesticides for pest control, and the use of animal waste containing veterinary drugs and the consequent possibility of these compounds contaminating humans and the environment, this work compared different extraction procedures in order to establish and validate a suitable sample preparation method for the multiresidue determination of 75 pesticides and seven veterinary drugs in agricultural soil samples by UHPLC–MS/MS, demonstrating the applicability of the proposed method in routine analysis.

2. Materials and Methods

2.1. Reagents and Materials

The solid standards of the pesticides and veterinary drugs selected for this study were purchased from LGC Standards (Augsburg, Germany) with a purity of between 91.5 and 99.9%. The analytical stock solutions of each compound, at a concentration of 1000 mg L^{-1}, were prepared in acetonitrile, taking into account the purity of the solid standards. The working solution at a concentration of 5.0 mg L^{-1} containing all the compounds studied, including the surrogate standard (SS), deuterated linuron (linuron d6), was prepared in acetonitrile. Triphenylphosphate, used as the internal standard (IS), was acquired from Sigma-Aldrich (St. Louis, MO, USA).

LC–MS-grade methanol and acetonitrile, anhydrous sodium acetate p.a., and anhydrous magnesium sulfate ($MgSO_4$) p.a. were purchased from J.T. Baker (Phillipsburg, NJ, USA). Glacial acetic acid 99.9% and sodium chloride were purchased from Merck (Rio de Janeiro, Brazil). Formic acid 98%, sodium citrate dihydrate ($C_6H_5Na_3O_7{\cdot}2H_2O$), and sodium hydrogen citrate sesquihydrate ($C_6H_6Na_2O_7{\cdot}1.5H_2O$), all p.a., were purchased from Sigma-Aldrich (St. Louis, MO, USA). Bondesil C18 and Bondesil PSA sorbents, both with a particle size of 40 µm, were purchased from Agilent Technologies (Santa Clara, CA, USA). Argon, 99.9992% pure, used as the collision gas in the UHPLC–MS/MS system, was purchased from Air Products (Guaiba, Brazil). Ultrapure water (resistivity of 18.2 MΩ cm) was obtained with the Milli-Q Direct UV3® system from Millipore (Molshein, France). Other materials included nylon filters of 13 mm i.d. and porosity of 0.2 µm, used for extract filtration before analysis, and glass vials with a capacity of 2 mL, both purchased from Agilent Technologies (Santa Clara, CA, USA), polypropylene tubes (15 and 50 mL) with screw caps (Sarstedt, Nümbrecht, Germany), and common laboratory glassware.

2.2. Soil Samples

The agricultural soil sample used as a blank sample to develop the method was collected from a site with no agropastoral activity and had the following characteristics: pHwater (1:1) = 4.9; Ca = 5.9 centimoles of charge (cmolc)/dm^3; Mg = 1.4 cmolc/dm^3; Al = 0.8 cmolc/dm^3; H + Al = 9.7 cmolc/dm^3; cation exchange capacity (CTC) = 8.1 cmolc/dm^3; Al saturation = 9.9%; Shoemaker–McLean–Pratt (SMP) buffer, a solution of p-nitrophenol, potassium chromate, calcium chloride, calcium acetate, and triethanolamine, pH = 5.3; organic matter (% MO) = 2.2 (m/v); % clay = 20 (m/v); and texture = 3.0. Before use, soil samples were homogenized, air-dried at room temperature, grinded, and sieved (2 mm mesh). The sample showed no residues of the pesticides and veterinary drugs under study and was used as a blank sample.

2.3. Instrumentation

This work was carried out using a UHPLC–MS/MS system from Waters Technologies (Milford, USA) equipped with a binary pump, sample manager Acquity, triple quadrupole mass spectrometer model Xevo TQ, electrospray ionization (ESI) source, and data acquisition using MassLynx software (version 4.1).

Precision analytical balances were used, models AUW-220D and UX-420H (Shimadzu, Kyoto, Japan), as well as the following instruments: centrifuges 80-2B (Centribio Co., Ltd., Shanghai, China) and NT 825 (Nova Técnica, Piracicaba, Brazil); Biomixer QL-901 vortex mixer (Microtécnica, Curitiba, Brazil); TE-394/1 air circulation oven (Tecnal, Piracicaba, Brazil); TE-240/1 pendulum shaker table (Tecnal, Piracicaba, Brazil); and Sonorex RK 510 ultrasound, 40 kHz frequency, and 135 W power (Bandelin, Berlin, Germany).

2.4. UHPLC–MS/MS Analysis

The analytes were determined using UHPLC–MS/MS under the following conditions: Acquity UPLC® BEH C18 column (50 mm × 2.1 mm i.d.; 1.7 µm), maintained at 40 °C; mobile phase (A) water:methanol (98:2, v/v) and (B) methanol, both containing 0.1% (v/v) formic acid to improve the ionization of the analytes; elution gradient: 5% B from 0 to 0.25 min; changing until reaching 100% B at 7.75 min and remaining until 8.50 min; returning to 5% B at 8.51 min and remaining until 10 min; mobile phase flow rate: 0.25 mL min^{-1}; injection volume: 10 µL; ionization source: electrospray (ESI); and triple quadrupole mass spectrometric detector, operating in selected reaction monitoring (SRM) mode. Other selected parameters were as follows: capillary voltage: 2.0 kV; desolvation temperature: 500 °C; desolvation gas flow rate (N_2): 600 L h^{-1}; spray flow rate (N_2): 80 L h^{-1}; collision gas flow rate (argon): 0.15 mL min^{-1}; and source temperature: 150 °C. Most of the compounds were analyzed in ESI+ mode, with the exception of 2,4-dichlorophenoxyacetic acid (2,4-D), chloramphenicol, and fipronil, which were analyzed by ESI–. Table S1 shows the compounds studied and the respective retention time (t_R), precursor and product ions, and collision energy of the transitions monitored by UHPLC–MS/MS. Two characteristic transitions were selected for each compound, with the most intense transition being used for quantification and the second most intense transition for confirmation of identity.

2.5. Sample Preparation Evaluation

The evaluation of the extraction tests carried out in this study used 10 g of blank soil samples weighed into 50 mL conical-bottom Falcon-type polypropylene (PP) tubes, spiked at a concentration of 100 µg kg^{-1}, and each test was carried out in triplicate. After spike, the samples were left to stand for 1 h before the extraction procedure was carried out. Acetonitrile was selected as the extraction solvent in all the tests evaluated (ultrasound, shaker, QuEChERS method, and their combinations), as it allows the extraction of compounds with different polarities and, when acidified, allows satisfactory recoveries of pesticides that generally present stability problems. In this study, different sample preparation approaches (Table 2) were investigated in order to obtain the most efficient extraction method for the analytes in the soil matrix. The recovery of the analytes at a

concentration level of 100 μg kg^{-1} was evaluated in triplicate using ultrasound (tests 1A and 1B), shaker (tests 2A and 2B), the QuEChERS method, and combinations of these tests (tests 3–6). After the partitioning step, the tube was centrifuged at 2140× *g* and 20 °C for 8.0 min, and the extracts were diluted 1:4 (*v*/*v*) with water and filtered for analysis.

Table 2. Tests carried out to select the extraction procedure based on different procedures with and without the addition of water before extraction.

Test	Extraction Using Ultrasound (10 g Sample)				
1A	10 mL MeCN	Ultrasound 5, 10, 15, 20, and 30 min	4.0 g $MgSO_4$	Vortex 1 min	Extract diluted in water (1:4, *v*/*v*) without clean-up
1B	10 mL water [41] 10 mL MeCN				
Test	Extraction Using Shaker (10 g sample)				
2A	10 mL MeCN	Shaker 5, 10, 15, 20, and 30 min	4.0 g $MgSO_4$	Vortex 1 min	Extract diluted in water (1:4, *v*/*v*) without clean-up
2B	10 mL water [41] 10 mL MeCN				
Test	Original QuEChERS Method (10 g sample)				
3A	10 mL MeCN	Vortex 1 min	4.0 g $MgSO_4$ + 1.0 g NaCl	Vortex 1 min	1 mL extract + 150 mg $MgSO_4$ + 25 mg PSA
3B					Without clean-up
3C	10 mL H_2O → rest for 10 min → 10 mL MeCN	Vortex 1 min	4.0 g $MgSO_4$ + 1.0 g NaCl	Vortex 1 min	Without clean-up
3D				Ultrasound 15 min	
3E		Shaker 15 min		Vortex 1 min	
Test	Citrate QuEChERS Method (10 g sample)				
4A	10 mL MeCN	Vortex 1 min	4.0 g $MgSO_4$ + 1.0 g NaCl + 1.0 g $C_6H_5Na_3O_7{\cdot}2H_2O$ + 0.5 g $C_6H_6Na_2O_7{\cdot}1.5H_2O$	Vortex 1 min	1 mL extract + 150 mg $MgSO_4$ + 25 mg PSA
4B					Without clean-up
4C	10 mL H_2O → rest for 10 min → 10 mL MeCN	Vortex 1 min	4.0 g $MgSO_4$ + 1.0 g NaCl + 1.0 g $C_6H_5Na_3O_7{\cdot}2H_2O$ + 0.5 g $C_6H_6Na_2O_7{\cdot}1.5H_2O$	Vortex 1 min	Without clean-up
4D				Ultrasound 15 min	
4E		Shaker 15 min		Vortex 1 min	
Test	Acetate QuEChERS Method (15 g sample)				
5A	15 mL MeCN with 1% HAc	Vortex 1 min	6.0 g $MgSO_4$ + 1.5 g CH_3COONa	Vortex 1 min	1 mL extract + 150 mg $MgSO_4$ + 50 mg PSA
5B					Without clean-up
5C	15 mL H_2O → rest for 10 min → 15 mL MeCN with 1% HAc	Vortex 1 min	6.0 g $MgSO_4$ + 1.5 g CH_3COONa	Vortex 1 min	Without clean-up
5D				Ultrasound 15 min	
5E		Shaker 15 min		Vortex 1 min	
Test	Proposed QuEChERS Method (10 g sample)				
6A	10 mL MeCN with 1% HAc	Vortex 1 min	4.0 g $MgSO_4$ + 1.7 g CH_3COONa	Vortex 1 min	1 mL extract + 600 mg $MgSO_4$ + 500 mg C18
6B					Without clean-up
6C	10 mL H_2O → rest for 10 min → 10 mL MeCN with 1% HAc	Vortex 1 min	4.0 g $MgSO_4$ + 1.7 g CH_3COONa	Vortex 1 min	Without clean-up
6D				Ultrasound 15 min	
6E		Shaker 15 min		Vortex 1 min	

The QuEChERS tests described in Table 2 were carried out using the original QuEChERS method [69], the acetate QuEChERS method [70], the citrate QuEChERS method [71], and the modified QuEChERS method proposed in this study. In order to verify the efficiency of the extract cleaning step, the tests were evaluated with and without clean-up. The effect of adding ultrapure water before extraction with MeCN [49,60] and using a shaker and ultrasound instead of vortex stirring in the first stage of the QuEChERS method were also evaluated.

2.6. Established Sample Preparation Procedure

The selected sample preparation procedure (Figure 1) was based on the modified QuEChERS method proposed in this study. An aliquot of 10 g of soil sample was weighed directly into 50 mL PP tubes followed by the addition of 50 µL of surrogate standard and 10 mL of water. The tube was vortexed for 1 min and left to stand for 10 min before the extraction step using 10 mL of acetonitrile containing 1% (*v*/*v*) acetic acid followed by agitation on a pendulum shaker for 15 min. For the partitioning step, 4 g of anhydrous magnesium sulphate and 1.7 g of sodium acetate were added to the extract and the tube was vortexed for 1 min. After centrifugation at 2140× *g* and 20 °C for 8 min and filtration (0.2 µm), the extract was diluted with water in a ratio of 1:4 (*v*/*v*) and 20 µL of the 1 mg L^{-1} solution of the internal standard was added for analysis by UHPLC–MS/MS. No cleaning of the extract was necessary, even though it was a complex matrix.

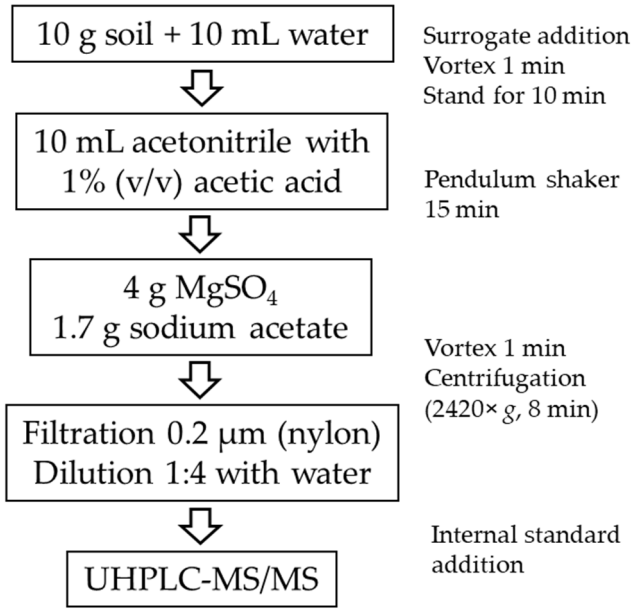

Figure 1. Flowchart of the proposed QuEChERS method.

2.7. Method Validation

Validation was carried out in accordance with the SANTE [72] guidelines considering the parameters of selectivity, linearity, analytical curve, matrix effect, detection and quantification limits, accuracy, and precision, evaluated in the repeatability and intermediate precision assay. The method selectivity was assessed by comparing the chromatograms obtained by UHPLC–MS/MS for the blank sample extracts and the spiked sample extracts at a concentration of 10 µg L^{-1}, with the aim of verifying the presence of interfering compounds at the retention time of selected pesticides. The linearity was evaluated considering the coefficient of determination (r^2) results using the analytical curves prepared in solvent and in the blank extract of the matrix at 0.5, 1, 2, 5, 10, 20, and 30 µg L^{-1}, in triplicate. Linearity was considered satisfactory for compounds that presented $r^2 \geq 0.990$. To evaluate the accuracy, through recovery, and precision, in terms of relative standard deviation (RSD), in the assay of repeatability carried out on the same day, recovery tests were performed

at the spike levels of 10, 25, 50, and 100 μg kg^{-1}, with 7 replicates. For the intermediate precision assay, recovery and RSD were evaluated by carrying out the analytical procedure on 3 different days, with 7 repetitions for each day, at the 50 μg kg^{-1} level. Accuracy and precision were considered satisfactory if recovery results were from 70 to 120%, with RSD $\leq$ 20%. The practical limit of quantification (LOQ) was determined from the spike tests, considering the LOQ the lowest spike level with acceptable accuracy and precision. The limit of detection (LOD) was obtained by dividing the LOQ value by 3.33. The matrix effect was estimated by comparing the slopes of the analytical curves obtained from the matrix-matched extract with those obtained from the solvent (acetonitrile) [73]. Validation results are presented in Table 3.

Table 3. Method validation data of selected pesticides and veterinary drugs in soil.

Compounds		Method LOD (μg kg^{-1})	Method LOQ (μg kg^{-1})	Repeatability: Recovery (RSD), %				Interm. Prec.: R (RSD), %	Matrix Effect (%)
				Spike Levels (μg kg^{-1}), n = 7				(μg kg^{-1}), n = 7	
				10	25	50	100	50	
1	2,4-D	7.5	25		92 (11)	71 (15)	79 (12)	77 (11)	86
2	Atrazine	3.0	10	91 (7)		88 (10)	90 (8)	85 (9)	2
3	Azoxystrobin	3.0	10	83 (14)		90 (15)	99 (15)	84 (14)	−4
4	Bentazone	3.0	10	101 (13)		96 (13)	104 (9)	78 (13)	−11
5	Bispyribac sodium	3.0	10	84 (11)		83 (14)	101 (14)	79 (12)	−19
6	Bitertanol	7.5	25		96 (13)	15 (14)	104 (14)	93 (14)	28
7	Boscalid	7.5	25		101 (15)	106 (15)	77 (13)	75 (12)	−45
8	Bromuconazole	7.5	25		74 (14)	77 (13)	83 (12)	79 (10)	4
9	Buprofezin	3.0	10	90 (13)		83 (9)	85 (9)	81 (11)	60
10	Carbaryl	3.0	10	82 (12)		100 (8)	88 (15)	87 (11)	21
11	Carbendazim	7.5	25		71 (12)	85 (14)	79 (12)	77 (9)	−17
12	Carbofuran	7.5	25		79 (12)	112 (12)	75 (12)	78 (13)	−40
13	Carbofuran-3OH	7.5	25		79 (13)	123 (5)	89 (13)	80 (13)	19
14	Chloramphenicol	3.0	10	116 (12)		90 (14)	104 (14)	83 (11)	8
15	Chlorpropham	7.5	25		93 (12)	82 (14)	83 (13)	95 (11)	21
16	Chlorpyrifos-ethyl	7.5	25		95 (11)	113 (15)	95 (12)	82 (13)	−19
17	Chlorpyrifos-methyl	3.0	10	77 (12)		117 (14)	111 (11)	79 (12)	267
18	Clomazone	3.0	10	83 (11)		88 (9)	85 (9)	85 (12)	−17
19	Clorimuron-ethyl	7.5	25		75 (14)	101 (9)	71 (9)	92 (9)	12
20	Cyanazine	3.0	10	88 (14)		87 (7)	88 (5)	101 (13)	0.3
21	Diazinon	3.0	10	90 (14)		90 (5)	91 (6)	91 (11)	4
22	Difenoconazole	7.5	25		101 (10)	97 (12)	97 (12)	87 (14)	1
23	Dimethoate	7.5	25		74 (15)	116 (13)	118 (11)	105 (13)	132
24	Epoxiconazole	3.0	10	91 (14)		73 (10)	95 (9)	89 (12)	−8
25	Fenarimol	7.5	25		87 (12)	77 (12)	98 (14)	79 (11)	−16
26	Fenpropathrin	3.0	10	103 (9)		108 (12)	105 (13)	92 (4)	287
27	Fenpropimorph	3.0	10	79 (10)		85 (9)	86 (10)	84 (13)	88
28	Fenthion	7.5	25		103 (13)	73 (14)	95 (13)	87 (12)	14
29	Fipronil	3.0	10	90 (15)		87 (9)	83 (14)	89 (11)	−18
30	Fluquiconazol	3.0	10	81 (12)		106 (12)	93 (11)	82 (13)	−14
31	Fluroxypyr	7.5	25		75 (13)	76 (14)	72 (8)	85 (12)	1
32	Flutolanil	7.5	25		71 (12)	71 (4)	85 (13)	88 (13)	21
33	Imazalil	3.0	10	94 (14)		76 (14)	84 (13)	71 (11)	−14
34	Imidacloprid	7.5	25		75 (14)	77 (14)	89 (14)	79 (12)	16
35	Iprovalicarb	3.0	10	107 (13)		101 (15)	112 (13)	105 (10)	−11
36	Linuron	7.5	25		89 (11)	110 (14)	83 (12)	83 (9)	10
37	Linuron d6 (SS)	7.5	25		90 (13)	101 (13)	92 (13)	78 (13)	−12
38	Malathion	7.5	25		89 (7)	95 (13)	77 (13)	79 (10)	−42

Table 3. *Cont.*

Compounds		Method LOD (μg kg^{-1})	Method LOQ (μg kg^{-1})	Repeatability: Recovery (RSD), %				Interm. Prec.: R (RSD), %	Matrix Effect (%)
				Spike Levels (μg kg^{-1}), n = 7				(μg kg^{-1}), n = 7	
				10	25	50	100	50	
39	Mecarbam	7.5	25		71 (8)	91 (14)	83 (18)	89 (13)	87
40	Mepronil	3.0	10	85 (12)		102 (8)	90 (11)	83 (11)	4
41	Metalaxyl	3.0	10	84 (10)		98 (13)	91 (7)	86 (14)	−3
42	Metconazole	3.0	10	76 (13)		71 (12)	89 (11)	84 (10)	−14
43	Methiocarb sulfone	3.0	10	96 (14)		94 (9)	92 (6)	90 (10)	48
44	Methiocarb sulfoxid	7.5	25		70 (7)	114 (11)	82 (8)	79 (11)	−13
45	Metsulfuron-methyl	3.0	10	100 (14)		71 (4)	93 (12)	77 (12)	16
46	Mevinphos	7.5	25		73 (10)	110 (12)	78 (13)	79 (9)	101
47	Miclobutanil	3.0	10	83 (13)		84 (12)	84 (12)	84 (8)	−7
48	Monensin	3.0	10	88 (11)		120 (8)	90 (4)	91 (11)	−22
49	Monocrotophos	3.0	10	72 (9)		102 (8)	101 (13)	94 (13)	−17
50	Monolinuron	7.5	25		77 (7)	90 (13)	99 (10)	89 (15)	−25
51	Paraoxon-ethyl	3.0	10	89 (12)		88 (15)	77 (12)	86 (14)	39
52	Pirimicarb	7.5	25		111 (10)	107 (9)	79 (10)	78 (5)	18
53	Pirimiphos-methyl	3.0	10	85 (13)		86 (11)	85 (7)	98 (14)	−10
54	Profenofos	7.5	25		78 (11)	103 (13)	105 (13)	83 (14)	−13
55	Propargito	3.0	10	84 (13)		117 (8)	117 (6)	73 (8)	32
56	Propiconazole	3.0	10	77 (12)		86 (10)	91 (11)	85 (11)	−6
57	Propoxur	3.0	10	78 (13)		111 (12)	79 (13)	78 (7)	10
58	Propyzamide	3.0	10	91 (14)		96 (13)	95 (14)	87 (9)	15
59	Pyraclostrobin	7.5	25		83 (14)	105 (14)	117 (13)	85 (11)	−2
60	Pyrazophos	3.0	10	106 (10)		90 (14)	90 (11)	81 (13)	2
61	Pyridaben	7.5	25		79 (13)	101 (15)	89 (15)	94 (12)	12
62	Pyridaphenthion	7.5	25		87 (12)	102 (13)	101 (13)	108 (9)	−3
63	Pyridate	7.5	25		92 (11)	114 (11)	72 (14)	86 (8)	88
64	Pyrimethanil	3.0	10	84 (12)		82 (4)	79 (7)	91 (9)	0.4
65	Quinoxyfen	7.5	25		109 (5)	117 (10)	72 (9)	77 (8)	−13
66	Robenidin	7.5	25		82 (14)	107 (13)	90 (6)	85 (7)	6
67	Salinomycin	3.0	10	88 (13)		116 (5)	75 (9)	75 (4)	−62
68	Simazine	3.0	10	92 (15)		107 (12)	85 (11)	87 (9)	−7
69	Sulfadimethoxin	3.0	10	96 (7)		88 (7)	79 (6)	84 (12)	3
70	Sulfamethazin	7.5	25		89 (13)	97 (14)	78 (14)	76 (13)	16
71	Sulfathiazol	7.5	25		71 (14)	71 (8)	77 (12)	77 (11)	−7
72	Tebuconazole	3.0	10	83 (13)		84 (11)	88 (11)	83 (7)	22
73	Terbuthylazine	3.0	10	94 (10)		112 (14)	79 (10)	87 (14)	−16
74	Tetraconazole	3.0	10	89 (14)		89 (9)	93 (13)	89 (9)	−17
75	Thiacloprid	3.0	10	94 (13)		110 (9)	97 (4)	95 (10)	−12
76	Thiamethoxam	7.5	25		99 (11)	101 (14)	105 (8)	86 (8)	−18
77	Tolcofos-methyl	3.0	10	76 (15)		103 (13)	91 (14)	93 (12)	7
78	Triadimefon	3.0	10	95 (13)		78 (6)	96 (14)	79 (11)	−35
79	Triazophos	3.0	10	81 (12)		83 (12)	93 (8)	89 (10)	−4
80	Trichlorfon	7.5	25		74 (7)	103 (7)	93 (12)	90 (13)	10
81	Trifloxystrobin	3.0	10	80 (14)		104 (14)	104 (14)	95 (11)	−3
82	Triflumizole	7.5	25		75 (14)	86 (10)	86 (8)	79 (9)	−20
83	Vamidothion	7.5	25		87 (9)	99 (11)	87 (11)	78 (13)	12

Interm. Prec. = intermediate precision; R = recovery; RSD = relative standard deviation; LOD = limit of detection; LOQ = limit of quantification; SS = surrogate standard.

2.8. Application of the Proposed Method to Agricultural Soil Samples

The method developed was applied to determine pesticide and veterinary drug residues in 60 soil samples collected around the coordinates 29°41′0″ S 53°48′0″ W in the central region of the Rio Grande do Sul State, Brazil. All the samples were collected from

recently cultivated areas where there were reports of organic fertilizer being used. In each sampling unit, after removing the surface litter at the sampling spot, 10 soil sub-samples were collected with an auger to a depth of 15 cm and placed in the same clean bucket. Each sample was homogenized and reduced to approximately half a kilogram by quartering, air-dried at room temperature, grinded, and sieved (2 mm mesh) before analysis.

3. Results and Discussion

3.1. Sample Preparation Method

The extraction tests were carried out using blank soil samples, spiked at a concentration of 100 μg kg^{-1}, and each test was carried out in triplicate. After spiking in a 50 mL Falcon tube, the samples were homogenized and kept for 1 h before the extraction procedure was carried out. ACN was used as the extraction solvent for all the tests (ultrasound, shaker, and QuEChERS method), as it allows the extraction of a wide range of compounds with different polarities and, when acidified, allows satisfactory recoveries of pesticides that generally have stability problems, as well as being suitable for analysis by UHPLC–MS/MS.

The results obtained by ultrasound extraction (Test 1A) were unsatisfactory, as less than 60% of the compounds showed recoveries of 70 to 120%, with RSD $\leq$ 20%. The tests that used hydration of the sample before extraction (Test 1B) showed an increase in the number of compounds recovered in the appropriate range, and the test with the highest percentage (60%) of compounds recovered was the one that used 15 min of ultrasound. The tests carried out with a shaker (Test 2A) only showed adequate results for around 40% of the compounds. The inclusion of a hydration step before extraction (Test 2B) increased this percentage to around 65%.

The initial tests using the QuEChERS method were based on the original procedures, citrate, acetate, and the proposed method, as described in Table 2, identified as tests 3A, 4A, 5A, and 6A, respectively. Next, in order to assess the need for the extract cleaning step, the same tests were repeated excluding the cleaning step (tests 3B–6B).

Looking at Figure 2, it can be seen that for all the pairs of tests carried out, there were no significant differences in the percentage of compounds recovered and that tests 3B, 5B, and 6B, which did not use the extract cleaning step, showed the best results. Therefore, it can be said that the extract cleaning step with dispersive sorbents did not improve the recovery of the analytes evaluated. The primary secondary amine (PSA) sorbent has a bidentate structure with a high chelating effect due to the presence of primary and secondary amino groups, removing part of the coextractives. As a result, the retention of free fatty acids, sugars, and pigments present in the matrix is very strong [74]. On the other hand, C18 is a sorbent that is effective in removing starch and sugar from some samples [75]. These coextractives are generally not present in soil and so the cleaning process did not improve the recovery values. Based on these results, it can be concluded that the extract cleaning step is not necessary, making the procedure quicker and reducing the cost of analysis.

Based on these initial results, new tests were carried out without using the extract cleaning step, and the influence of adding water to the soil before extraction with acetonitrile was evaluated according to tests 3C to 6C, described in Table 2. The addition of water to the samples before the extraction stage is used to weaken the interactions of the analytes with the matrix and ensure adequate partitioning in samples with low amounts of water [76]. Based on the results shown in Figure 2, it can be seen that in the tests where the sample was hydrated, the number of compounds that showed satisfactory recovery values was higher than in the tests where no water was added, reaching 77% of the compounds recovered in the range between 70 and 120% using the QuEChERS acetate method.

The different QuEChERS methods were tested including 15 min of ultrasound in the extraction stage (tests 3D–6D) and using a shaker for 15 min (tests 3E to 6E), as described in Table 2, with the 15 min time chosen because it showed the best recovery results in tests 1 and 2.

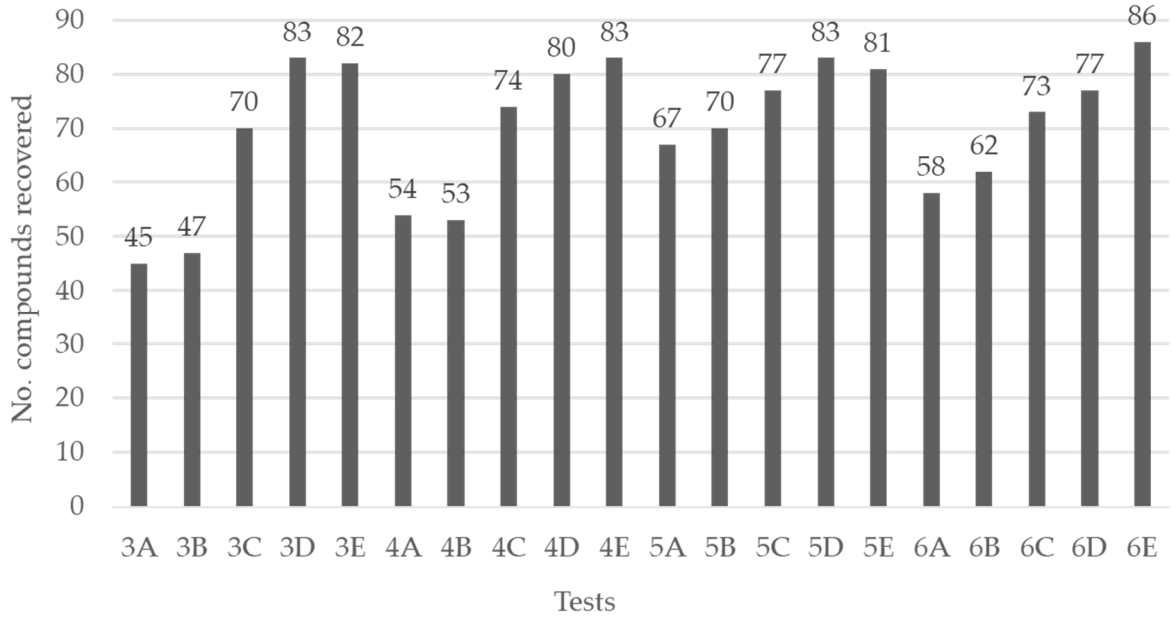

Figure 2. Summary of the results obtained in the tests with original (Test 3), citrate (Test 4), and acetate QuEChERS methods (Test 5), and the proposed QuEChERS method (Test 6), as described in Table 2.

The results shown in Figure 2 demonstrate an increase in the number of compounds recovered in the range of 70 to 120% with the use of shaker or ultrasound for 15 min in all the different QuEChERS methods used. In addition, it is worth noting that test 6E, based on the proposed QuEChERS method and 15 min of shaking, showed the highest percentage (86%) of compounds with satisfactory recovery, and was chosen for validation.

According to the results obtained, the best conditions used were as follows: a procedure based on the proposed QuEChERS method, with ultrapure water added to the sample, followed by extraction with acetonitrile acidified with acetic acid, shaking for 15 min, using magnesium sulphate and sodium acetate in the partitioning stage, and without cleaning the extracts.

3.2. Validation of the Method

The proposed method was evaluated for the determination of 75 pesticides and seven veterinary drugs in agricultural soil. The validation parameters were obtained according to SANTE [72]. Recovery tests were carried out at the spike levels of 10 or 25, 50, and 100 μg kg^{-1}. For compounds that did not show a reasonable signal at a concentration of 10 μg kg^{-1}, it was decided to use the spike level of 25 μg kg^{-1}. The recovery and RSD values obtained are shown in Table 3. From the results obtained, it can be observed that all pesticides and veterinary drugs evaluated showed recovery between 70 and 120%, with RSD $\leq$ 20%, in all spike levels, as recommended by SANTE guidelines [72].

The matrix effect in UHPLC–MS/MS systems stems from the suppression or enhancement of the analytical response caused by the co-elution and consequent simultaneous ionization of matrix constituents. Depending on the composition of the sample and the properties of the analytes, the matrix extract (ME) can be observed to a lesser or greater degree, directly affecting the accuracy of the method. Mild ionization or suppression effects (0 to 20%) are considered negligible. When the ME is moderate (20–50%) or strong (>50%), some approaches based on matrix effect compensation can be used, such as the diluted calibration curve with blank extract [73]. The ME was calculated using the following equation:

$$\mathrm{ME}(\%) = \left(\frac{\mathrm{Smatrix}}{\mathrm{Ssolvent}} - 1\right)$$

where S_{matrix} and $S_{solvent}$ are the slopes of the calibration curves prepared in the matrix and solvent, respectively. Table 3 shows the matrix effect values obtained for the soil sample. It can be seen that for most of the analytes the ME was not significant; however, certain analytes showed moderate suppression (boscalid, carbofuran, malathion, monesin, and monolinuron) or signal increase (bitertanol, carbaryl, chlorpropham and flutolanil, methiocarb sulfone, paraoxon-ethyl, propargite, and tebuconazole) of the analytical signal. In addition, a significant suppression effect was observed for salinomycin, and significant signal increases for 2,4-D, buprofezin, chlorpyrifos methyl, dimethoate, fenpropathrin, fenpropimorph, and mecarbam. It is known that the ME observed for the QuEChERS method is commonly pronounced, since ionization suppression is greater, especially for complex matrices [77]. Therefore, curves in the blank matrix extract were used to compensate for the ME.

LOQ values were determined using the lowest point on the analytical curve for each analyte, which, when spiked in the matrix, shows recovery results of between 70 and 120% with RSD $\leq$ 20% [72]. The method LOQ value for most of the compounds was 10 μg kg^{-1}. To date, there is no specific legislation with maximum permitted limits (MRLs) for these compounds in soil.

3.3. Application of the Validated Method

The developed method was applied to 60 soil samples collected in the central region of the Rio Grande do Sul State, Brazil. Among the samples analyzed, 24 contained pesticide residues in concentrations from 8 to 36 μg kg^{-1}. Chloramphenicol was the only veterinary drug found in four samples in concentrations of 12 to 25 μg kg^{-1}. The fungicide carbendazim was found in four samples at concentrations above 20 μg kg^{-1}. Two samples contained the fungicide tebuconazole above 25 μg kg^{-1}, two contained the insecticide and nematicide carbofuran from 8 to 12 μg kg^{-1}, seven had the fungicide epoxiconazole from 8 to 16 μg kg^{-1}, and seven had the insecticide imidacloprid from 15 to 36 μg kg^{-1}. The fungicides azoxystrobin and pyraclostrobin, and the insecticide profenofos, were found at concentrations < LOQ in one, three, and one samples, respectively.

4. Conclusions

A new and comprehensive multiresidue method for the determination of 76 pesticides and nine veterinary drugs in agricultural soil by UHPLC–MS/MS was successfully validated using a modified QuEChERS method associated with a shaker. In addition, the proposed method has the advantage of being simple to carry out, low-cost, and environmentally friendly, since it uses a small amount of solvent. The absence of a cleaning step makes it possible to use the proposed method for routine analysis in different laboratories. Agricultural soil samples were used to verify the applicability of the validated method, where 24 of the 60 samples contained residues of the pesticides and four samples contained the veterinary drug chloramphenicol. It can be concluded that the method is suitable for multiresidue determination of pesticides and veterinary drugs in agricultural soil and can be applied in routine analysis.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/separations11060188/s1, Table S1: Retention time (tR), precursor and products ions monitored, and collision energies (CE) used for the UHPLC-MS/MS analysis.

Author Contributions: Conceptualization, R.Z. and O.D.P.; methodology, M.C.V., J.F.F. and S.C.P.; validation, M.C.V., J.F.F. and S.C.P.; formal analysis, M.C.V., J.F.F. and S.C.P.; writing—original draft preparation, M.C.V., J.F.F. and S.C.P.; writing—review and editing, G.S.d.C., L.F. and M.B.A.; visualization, G.S.d.C. and L.F.; supervision, O.D.P.; project administration, R.Z.; funding acquisition, R.Z., O.D.P. and M.B.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), grant number 315515/2023-6.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: All related data and methods are presented in this paper. Additional inquiries should be addressed to the corresponding author.

Acknowledgments: The authors gratefully acknowledge the support of the Brazilian agencies CNPq and CAPES.

Conflicts of Interest: The authors declare no conflicts of interest. The funder had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Silva, V.; Mol, H.; Zomer, P.; Tienstra, M.; Ritsema, C.; Geissen, V. Pesticide residues in European agricultural soils—A hidden reality unfolded. *Sci. Total Environ.* **2019**, *653*, 1532–1545. [CrossRef]
2. Bobkov, M.; Zbinden, P. Occurrence of veterinary drug residues in poultry and products thereof. A review. *Chimia* **2018**, *72*, 707–712. [CrossRef]
3. Bao, Y.; Zhou, Q.; Guan, L.; Wang, Y. Depletion of chlortetracycline during composting of aged and spiked manures. *Waste Manag.* **2009**, *29*, 1416–1423. [CrossRef]
4. Caneschi, A.; Bardhi, A.; Barbarossa, A.; Zaghini, A. The Use of Antibiotics and Antimicrobial Resistance in Veterinary Medicine, a Complex Phenomenon: A Narrative Review. *Antibiotics* **2023**, *12*, 487. [CrossRef] [PubMed]
5. Quaik, S.; Embrandiri, A.; Ravindran, B.; Hossain, K.; Al-Dhabi, N.A.; Arasu, M.V.; Ignacimuthu, S.; Ismail, N. Veterinary antibiotics in animal manure and manure laden soil: Scenario and challenges in Asian countries. *J. King Saud Univ. Sci.* **2020**, *32*, 1300–1305. [CrossRef]
6. Menz, J.; Olsson, O.; Kümmerer, K. Antibiotic residues in livestock manure: Does the EU risk assessment sufficiently protect against microbial toxicity and selection of resistant bacteria in the environment? *J. Hazard. Mater.* **2019**, *379*, 120807. [CrossRef]
7. Mahmood, I.; Imadi, S.R.; Shazadi, K.; Gul, A.; Hakeem, K.R. Effects of Pesticides on Environment. In *Plant, Soil and Microbes*; Hakeem, K., Akhtar, M., Abdullah, S., Eds.; Springer: Cham, Switzerland, 2016. [CrossRef]
8. Hamscher, G.; Sczesny, S.; Höper, H.; Nau, H. Determination of Persistent Tetracycline Residues in Soil Fertilized with Liquid Manure by High-Performance Liquid Chromatography with Electrospray Ionization Tandem Mass Spectrometry. *Anal. Chem.* **2002**, *74*, 1509–1518. [CrossRef] [PubMed]
9. Ministry of Natural Resource and Environment. QCVN15 (2008)/BTNMT: National Technical Regulation on the Pesticide Residues in the Soils. Available online: https://aigavn.com.vn/wp-content/uploads/2021/06/16_2008_QD-BTNMT_PROMULGATION-OF-NATIONAL-TECHNICAL-REGULATION-ON-ENVIRONMENT-E.pdf (accessed on 15 December 2023).
10. Li, Z.; Niu, S. Improving screening model of pesticide risk assessment in surface soils: Addressing regional specific human exposure risks and regulatory management. *Ecotoxicol. Environ. Saf.* **2021**, *227*, 112894. [CrossRef] [PubMed]
11. Zhang, X.; Li, Z. Generalizable consistency of soil quality standards for pesticides: Modeling perspectives. *Soil Environ. Health* **2023**, *1*, 100031. [CrossRef]
12. Chaudhari, Y.S.; Kumar, P.; Soni, S.; Gacem, A.; Kumar, V.; Singh, S.; Yadav, V.K.; Dawane, V.; Piplode, S.; Jeon, B.-H.; et al. An inclusive outlook on the fate and persistence of pesticides in the environment and integrated eco-technologies for their degradation. *Toxicol. Appl. Pharmacol.* **2023**, *466*, 116449. [CrossRef]
13. Ghimpeteanu, O.; Pogurschi, E.; Popa, D.; Dragomir, N.; Dragotoiu, T.; Mihai, O.; Pectu, C. Antibiotic Use in Livestock and Residues in Food—A Public Health Threat: A Review. *Foods* **2022**, *11*, 1430. [CrossRef]
14. Litskas, V.D.; Paraskevas, C.G.; Karamanlis, X.N.; Batzias, G.C. Assessing the mobility of veterinary drugs with column experiments using different soils and under controlled flow conditions. *Chemosphere* **2021**, *277*, 130329. [CrossRef] [PubMed]
15. Rösch, A.; Wettstein, F.E.; Wächter, D.; Reininger, V.; Meuli, R.G.; Bucheli, T.D. A multi-residue method for trace analysis of pesticides in soils with special emphasis on rigorous quality control. *Anal. Bioanal. Chem.* **2023**, *415*, 6009–6025. [CrossRef]
16. Golovko, O.; Koba, O.; Kodesova, R.; Fedorova, G.; Kummar, V.; Grabic, R. Development of fast and robust multiresidual LC-MS/MS method for determination of pharmaceuticals in soils. *Environ. Sci. Pollut. Res.* **2016**, *23*, 14068–14077. [CrossRef] [PubMed]
17. González-Curbelo, M.Á.; Varela-Martínez, D.A.; Riaño-Herrera, D.A. Pesticide-Residue Analysis in Soils by the QuEChERS Method: A Review. *Molecules* **2022**, *27*, 4323. [CrossRef]
18. Jagirani, M.S.; Ozalp, O.; Soylak, M. New Trend in the Extraction of Pesticides from the Environmental and Food Samples Applying Microextraction Based Green Chemistry Scenario: A Review. *Crit. Rev. Anal. Chem.* **2022**, *52*, 1343–1369. [CrossRef]
19. Brinco, J.; Guedes, P.; da Silva, M.G.; Mateus, E.P.; Ribeiro, A.B. Analysis of pesticide residues in soil: A review and comparison of methodologies. *Microchem. J.* **2023**, *195*, 109465. [CrossRef]
20. Wong, F.; Bidleman, T.F. Hydroxypropyl-β-cyclodextrin as non-exhaustive extractant for organochlorine pesticides and polychlorinated biphenyls in muck soil. *Environ. Pollut.* **2010**, *158*, 1303–1310. [CrossRef] [PubMed]

21. Qin, B.; Yu, B.; Zhang, Y.; Lin, X. Residual Analysis of Organochlorine Pesticides in Soil by Gas Chromatograph–Electron Capture Detector (GC-ECD) and Gas Chromatograph–Negative Chemical Ionization Mass Spectrometry (GC-NCI-MS). *Environ. Forensics* **2009**, *10*, 331–335.
22. Nishina, T.; Kien, C.N.; Noi, N.V.; Ngoc, H.M.; Kim, C.S.; Tanaka, S.; Iwasaki, K. Pesticide residues in soils, sediments, and vegetables in the Red River Delta, northern Vietnam. *Environ. Monit. Assess.* **2010**, *169*, 285–297. [CrossRef]
23. Diez, C.; Barrado, E.; Marinero, P.; Sanz, M. Orthogonal array optimization of a multiresidue method for cereal herbicides in soils. *J. Chromatogr. A* **2008**, *1180*, 10–13. [CrossRef] [PubMed]
24. Pareja, L.; Niell, S.; Asteggiante, L.G.; Roehrs, R.; Pizzutti, I.R.; Garcia, C.; Heinzen, H.; Cesio, V. Development of methods for multiresidue analysis of rice post-emergence herbicides in loam soil and their possible applications to soils of different composition. *J. AOAC Int.* **2010**, *93*, 425–431.
25. Colazzo, M.; Pareja, L.; Cesio, M.V.; Heinzen, H. Multi-residue method for trace pesticide analysis in soils by LC-QQQ-MS/MS and its application to real samples. *Int. J. Environ. Anal. Chem.* **2018**, *98*, 1292–1308. [CrossRef]
26. Shi, X.; Zhang, S.; Zhang, Y.; Geng, Y.; Wang, L.; Peng, Y.; He, Z. Novel and simple analytical method for simultaneous determination of sulfonamide, quinolone, tetracycline, macrolide, and chloramphenicol antibiotics in soil. *Anal. Bioanal. Chem.* **2022**, *414*, 6497–6506. [CrossRef] [PubMed]
27. Hang, L.; Zhao, Y.; Liu, C.; Yu, Y.; He, Y.; Xu, J.; Lu, Z. Determine Multiple Classes of Veterinary Antibiotics in Soil: Comparing Dispersive and Solid-Phase Extraction for Sample Cleanup. *Chromatographia* **2021**, *84*, 833–844. [CrossRef]
28. Sanchez-Brunete, C.; Albero, B.; Tadeo, J.L. Multiresidue determination of pesticides in soil by gas chromatography-mass spectrometry detection. *J. Agric. Food Chem.* **2004**, *526*, 1445–1450. [CrossRef] [PubMed]
29. Martínez-Parreño, M.; Llorca-Pórcel, J.; Valor, I. Analysis of 51 persistent organic pollutants in soil by means of ultrasonic solvent extraction and stir bar sorptive extraction GC-MS. *J. Sep. Sci.* **2008**, *31*, 3620–3629. [CrossRef]
30. Fenoll, J.; Hellin, P.; Martinez, C.M.; Flores, P. Multiresidue analysis of pesticides in soil by high-performance liquid chromatography with tandem mass spectrometry. *J. AOAC Int.* **2009**, *92*, 1566–1575. [CrossRef] [PubMed]
31. Ho, Y.B.; Zakaria, M.P.; Latif, P.A.; Saari, N. Simultaneous determination of veterinary antibiotics and hormone in broiler manure, soil and manure compost by liquid chromatography-tandem mass spectrometry. *J. Chromatogr. A* **2012**, *1262*, 160–168. [CrossRef]
32. Liu, X.; Xu, J.; Li, Y.; Dong, F.; Li, J.; Song, W.; Zheng, Y. Rapid residue analysis of four triazolopyrimidine herbicides in soil, water, and wheat by ultra performance liquid chromatography coupled to tandem mass spectrometry. *Anal. Bioanal. Chem.* **2011**, *399*, 2539–2547. [CrossRef]
33. Tor, A.; Aydin, M.E.; Ozcan, S. Ultrasonic solvent extraction of organochlorine pesticides in soil. *Anal. Chim. Acta* **2006**, mboxemph559, 173–180. [CrossRef]
34. Bian, K.; Liu, Y.; Wang, Z.; Zhou, T.; Song, X.; Zhang, F.; He, L. Determination of multi-class antimicrobial residues in soil by liquid chromatography-tandem mass spectrometry. *RSC Adv.* **2015**, *5*, 27584–27593. [CrossRef]
35. Castiñeira-Landeira, A.; Vazquez, L.; Gonzalez-Leirado, H.; Llompart, M.; Dagnac, T. Ultrasound-assisted extraction followed by liquid chromatography coupled to tandem mass spectrometry for the simultaneous determination of multiclass herbicides in soil. *Anal. Bioanal. Chem.* **2023**, *415*, 7197–7209. [CrossRef]
36. Wang, W.; Meng, B.; Lu, X.; Liu, Y.; Tao, S. Extraction of polycyclic aromatic hydrocarbons and organochlorine pesticides from soils: A comparison between Soxhlet extraction, microwave-assisted extraction and accelerated solvent extraction techniques. *Anal. Chim. Acta* **2007**, *602*, 211–222. [CrossRef] [PubMed]
37. Fuentes, E.; Baez, M.; Labrea, R.J. Parameters affecting microwave-assisted extraction of organophosphorus pesticides from agricultural soil. *J. Chromatogr. A* **2007**, *1169*, 40–46. [CrossRef] [PubMed]
38. Łukaszewicz, P.; Białk-Bielińska, A.; Dołżonek, J.; Kumirska, J.; Caban, M.; Stepnowski, P. A new approach for the extraction of tetracyclines from soil matrices: Application of the microwave-extraction technique. *Anal. Bioanal. Chem.* **2018**, *410*, 1697–1707. [CrossRef] [PubMed]
39. Hildebrandt, A.; Lacorte, S.; Barceló, D. Assessment of priority pesticides, degradation products, and pesticide adjuvants in groundwaters and top soils and pesticide adjuvants in groundwaters and top soils from agricultural areas of the Ebro river basin. *Anal. Bioanal. Chem.* **2007**, *387*, 1459–1468. [CrossRef] [PubMed]
40. Martinez-Vidal, J.L.; Padilla-Sanchez, J.A.; Plaza-Bolanos, P.; Garrido-Frenich, A.; Romero-Gonzalez, R. Use of pressurized liquid extraction for the simultaneous analysis of 28 polar and 94 non-polar pesticides in agricultural soils by GC/QqQ-MS/MS and UPLC/QqQ-MS/MS. *J. Assoc. Off. Anal. Chem. Int.* **2010**, *93*, 1715–1731.
41. Lesueur, C.; Gartner, M.; Mentler, A.; Fuerhacker, M. Comparison of four extraction methods for the analysis of 24 pesticides in soil samples with gas chromatography-mass spectrometry and liquid chromatography-ion trap-mass spectrometry. *Talanta* **2008**, *75*, 284–293. [CrossRef]
42. Gros, M.; Rodríguez-Mozaz, S.; Barceló, D. Rapid analysis of multiclass antibiotic residues and some of their metabolites in hospital, urban wastewater and river water by ultra-high-performance liquid chromatography coupled to quadrupole-linear ion trap tandem mass spectrometry. *J. Chromatogr. A* **2013**, *1292*, 173–188. [CrossRef]
43. Zhao, R.; Wang, X.; Fu, S.; Yuan, J.; Jiang, T.; Xu, X. A Novel Headspace Solid-Phase Microextraction Method for the Exact Determination of Organochlorine Pesticides in Environmental Soil Samples. *Anal. Bioanal. Chem.* **2006**, *384*, 1584–1589. [CrossRef] [PubMed]

44. Đurović-Pejčev, R.D.; Umiljendić, J.; Svjetlana, R.; Ljubiša, I. Solid Phase Microextraction as an Efficient Method for Characterization of the Interaction of Pesticides with Different Soil Types. *J. Braz. Chem. Soc.* **2010**, *21*, 985–994.
45. Fernández-Álvarez, M.; Llompart, M.; Lamas, J.P.; Lores, M.; García-Jares, C.; Cela, R.; Dagnac, T. Simultaneous determination of traces of pyrethroids, organochlorines and other main plant protection agents in agricultural soils by headspace solid-phase microextraction-gas chromatography. *J. Chromatogr. A* **2008**, *1188*, 154–163. [CrossRef] [PubMed]
46. Forero-Mendieta, J.R.; Castro-Vargas, H.I.; Parada-Alfonso, F.; Guerrero-Dallos, J.A. Extraction of pesticides from soil using supercritical carbon dioxide added with methanol as co-solvent. *J. Supercrit. Fluids* **2012**, *68*, 64–70. [CrossRef]
47. Koeber, R.; Niessner, R. Screening of pesticide-contaminated soil by supercritical fluid extraction (SFE) and high-performance thin-layer chromatography with automated multiple development (HPTLC/AMD). *Fresenius J. Anal. Chem.* **1996**, *354*, 464–469. [CrossRef] [PubMed]
48. Santalad, A.; Zhou, L.; Shang, F.; Fitzpatrick, D.; Burakham, R.; Srijaranai, S.; Glennon, J.D.; Luong, J.H.T. Micellar electrokinetic chromatography with amperometric detection and off-line solid-phase extraction for analysis of carbamate insecticides. *J. Chromatogr. A* **2010**, *1217*, 5288–5297. [CrossRef] [PubMed]
49. Dong, F.; Liu, X.; Chen, W.; Li, J.; Qin, D.; Zheng, Y. Determination of metaflumizone residues in cabbage and soil using ultra-performance liquid chromatography/ESI-MS/MS. *J. Sep. Sci.* **2009**, *32*, 3692–3697. [CrossRef] [PubMed]
50. Chen, L.; Li, X.S.; Wang, Z.Q.; Pan, C.P.; Jin, R.C. Residue dynamics of procymidone in leek sand soil in greenhouses by smoke generator application. *Ecotoxicol. Environ. Saf.* **2010**, *73*, 73–77. [CrossRef] [PubMed]
51. Shi, C.; Gui, W.; Chen, J.; Zhu, G. Determination of Oxadiargyl Residues in Environmental Samples and Rice Samples. *Bull. Environ. Contam. Toxicol.* **2010**, *84*, 236–239. [CrossRef]
52. Ramasubramanian, T.; Paramasivam, M.; Jayanthi, R. Rapid and Sensitive Analytical Method for Simultaneous Determination of Imidacloprid and Thiamethoxam Residues in Soils of Sugarcane Ecosystem by Reversed-Phase HPLC. *Water Air Soil Pollut.* **2012**, *223*, 6045–6050. [CrossRef]
53. Feng, X.; He, Z.; Wang, L.; Peng, Y.; Luo, M.; Liu, X. Multiresidue analysis of 36 pesticides in soil using a modified quick, easy, cheap, effective, rugged, and safe method by liquid chromatography with tandem quadrupole linear ion trap mass spectrometry. *J. Sep. Sci.* **2015**, *38*, 3047–3054. [CrossRef] [PubMed]
54. Rashid, A.; Nawaz, S.; Barker, H.; Ahmad, I.; Ashra, M. Development of a simple extraction and clean-up procedure for determination of organochlorine pesticides in soil using gas chromatography–tandem mass spectrometry. *J. Chromatogr. A* **2010**, *1217*, 2933–2939. [CrossRef]
55. Mahdavi, V.; Heris, M.E.S.; Dastranj, M.; Farimani, M.M.; Eslami, Z.; Aboul-Enein, H.Y. Assessment of Pesticide Residues in Soils Using a QuEChERS Extraction Procedure and LC-MS/MS. *Water Air Soil Pollut.* **2021**, *232*, 159. [CrossRef]
56. Yang, X.B.; Ying, G.G.; Kookana, R.S. Rapid multiresidue determination for currently used pesticides in agricultural drainage waters and soils using gas chromatography-mass spectrometry. *J. Environ. Sci. Health Part B* **2010**, *45*, 152–161. [CrossRef] [PubMed]
57. Ramos, M.A.; Borges, J.H.; Pérez, L.M.R.; Delgado, M.A.R. Evaluation of a modified QuEChERS method for the extraction of pesticides from agricultural, ornamental and forestal soils. *Anal. Bioanal. Chem.* **2010**, *396*, 2307–2319. [CrossRef] [PubMed]
58. Correia-Sá, L.; Fernandes, V.C.; Carvalho, M.; Calhau, C.; Domingues, V.; Delerue-Matos, C. Optimization of QuEChERS method for the analysis of organochlorine pesticides in soils with diverse organic matter. *J. Sep. Sci.* **2012**, *35*, 1521–1530. [CrossRef] [PubMed]
59. Drozdzynski, D.; Kowalska, J. Rapid analysis of organic farming insecticides in soil and produce using ultra-performance liquid chromatography/tandem mass spectrometry. *Anal. Bioanal. Chem.* **2009**, *394*, 2241–2247. [CrossRef] [PubMed]
60. Łozowicka, B.; Rutkowska, E.; Jankowska, M. Influence of QuEChERS modifications on recovery and matrix effect during the multi-residue pesticide analysis in soil by GC/MS/MS and GC/ECD/NPD. *Environ. Sci. Pollut. Res.* **2017**, *24*, 7124–7138. [CrossRef] [PubMed]
61. Martins, G.; Friggi, C.; Prestes, O.; Vicari, M.; Friggi, D.; Adaime, M.; Zanella, R. Simultaneous LC-MS/MS Determination of Imidazolinone Herbicides Together with Other Multiclass Pesticide Residues in Soil. *CLEAN Soil Air Water* **2014**, *42*, 1441–1449. [CrossRef]
62. Arias, J.; Rombaldi, C.; Caldas, S.; Primel, E. Alternative sorbents for the dispersive solid-phase extraction step in quick, easy, cheap, effective, rugged and safe method for extraction of pesticides from rice paddy soils with determination by liquid chromatography tandem mass spectrometry. *J. Chromatogr. A* **2014**, *1360*, 66–75. [CrossRef]
63. Kaczynski, P.; Lozowicka, B.; Jankowska, M.; Hrynko, I. Rapid determination of acid herbicides in soil by liquid chromatography with tandem mass spectrometric detection based on dispersive solid phase extraction. *Talanta* **2016**, *152*, 127–136. [CrossRef] [PubMed]
64. Zaidon, S.Z.; Ho, Y.B.; Hamsan, H.; Hashim, Z.; Saari, N.; Praveena, S.M. Improved QuEChERS and solid phase extraction for multi-residue analysis of pesticides in paddy soil and water using ultra-high performance liquid chromatography tandem mass spectrometry. *Microchem. J.* **2019**, *145*, 614–621. [CrossRef]
65. Lee, Y.; Choi, J.; El-Aty, A.; Chung, H.; Lee, H.; Kim, S.; Rahman, M.; Park, B.; Kim, J.; Shin, H.; et al. Development of a single-run analytical method for the detection of ten multiclass emerging contaminants in agricultural soil using an acetate-buffered QuEChERS method coupled with LC-MS/MS. *J. Sep. Sci.* **2016**, *40*, 415–423. [CrossRef] [PubMed]

66. Yu, Y.; Liu, X.; He, Z.; Wang, L.; Luo, M.; Peng, Y.; Zhou, Q. Development of a multi-residue method for 58 pesticides in soil using QuEChERS and gas chromatography-tandem mass spectrometry. *Anal. Methods* **2016**, *11*, 2463–2470. [CrossRef]
67. Đurović-Pejčev, R.D.; Bursíc, V.P.; Zeremski, T.M. Comparison of QuEChERS with Traditional Sample Preparation Methods in the Determination of Multiclass Pesticides in Soil. *J. Assoc. Off. Anal. Chem.* **2019**, *102*, 46–51. [CrossRef] [PubMed]
68. Ninga, E.; Sapozhnikova, Y.; Lehotay, S.J.; Lightfield, A.R.; Monteiro, S.H. High-Throughput Mega-Method for the Analysis of Pesticides, Veterinary Drugs, and Environmental Contaminants by Ultra-High-Performance Liquid Chromatography-Tandem Mass Spectrometry and Robotic Mini-Solid-Phase Extraction Cleanup + Low-Pressure Gas Chromatography-Tandem Mass Spectrometry, Part 2: Catfish. *J. Agric. Food Chem.* **2021**, *69*, 1169–1174. [CrossRef] [PubMed]
69. Anastassiades, M.; Lehotay, S.J.; Stajnbaher, D.; Schenk, F.J. Fast and easy multiresidue method employing acetonitrile extraction/partitioning and "dispersive solid-phase extraction" for the determination of pesticide residues in produce. *J. Assoc. Off. Anal. Chem.* **2003**, *86*, 412–431. [CrossRef]
70. Lehotay, S.J.; Hiemstra, M.; Bodegraven, P.; Kok, A. Validation of a Fast and Easy Method for the Determination of Residues from 229 Pesticides in Fruits and Vegetables Using Gas and Liquid Chromatography and Mass Spectrometric Detection. *J. Assoc. Off. Anal. Chem.* **2005**, *88*, 595. [CrossRef]
71. Anastassiades, M.; Scherbaum, E.; Tasdelen, B.; Stajnbaher, D. *Crop Protection, Public Health, Environmental Safety*; Wiley-VCH: Weinheim, Germany, 2007; p. 439.
72. Sante (European Commission). Guidance Document on Analytical Quality Control and Method Validation Procedures for Pesticides Residues Analysis in Food and Feed; Document SANTE/11312/2021. Available online: https://food.ec.europa.eu/system/files/2023-11/pesticides_mrl_guidelines_wrkdoc_2021-11312.pdf (accessed on 9 August 2022).
73. Nieto-Garcia, A.J.; Romero-Gonzalez, R.; Frenich, A.G. Multi-pesticide residue analysis in nutraceuticals from grape seed extracts by gas chromatography coupled to triple quadrupole mass spectrometry. *Food Control* **2015**, *47*, 369–380. [CrossRef]
74. Prestes, O.D.; Padilla-Sánchez, J.A.; Romero-González, R.; Grio, S.L.; Garrido-Frenich, A.; Martínez-Vidal, J.L. Comparison of several extraction procedures for the determination of biopesticides in soil samples by ultrahigh pressure LC-MS/MS. *J. Sep. Sci.* **2012**, *35*, 861–868. [CrossRef]
75. Koesukwiwat, U.; Sanguankaew, K.; Leepipatpiboon, N. Rapid determination of phenoxy acid residues in rice by modified QuEChERS extraction and liquid chromatography–tandem mass spectrometry. *Anal. Chim. Acta* **2008**, *626*, 10–20. [CrossRef] [PubMed]
76. Bragança, I.; Plácido, A.; Paíga, P.; Domingues, V.F.; Delerue-Matos, C. QuEChERS: A new sample preparation approach for the determination of ibuprofen and its metabolites in soils. *Sci. Total Environ.* **2012**, *433*, 281–289. [CrossRef] [PubMed]
77. Kruve, A.; Künnapas, A.; Leito, I. Matrix effects in pesticide multi-residue analysis by liquid chromatography-mass spectrometry. *J. Chromatogr. A* **2008**, *1187*, 58–66. [CrossRef] [PubMed]