Egypt. J. Chem. **Vol.** 68, SI: Z. M. Nofal, pp. 1277- 1290(2025)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Residual Behavior and Consumer Safety Evaluation of Flometoquin, Flupyradifurone, and Flonicamid in Tomatoes Using QuEChERS–HPLC/DAD

Mohammed A. Bayoumi[1*], Sayed A. El-Mahy[1], Dalia A. Barakat[1], and Dalia E. Elhafny[2]

[1]*Department of Economic Entomology and Pesticides, Faculty of Agriculture, Cairo University, Egypt*

[2]*Pesticides Residues and Environmental Pollution Dept., Central Agricultural Pesticides Laboratory, Agricultural Research Center, Giza, Egypt*

Abstract

An effective analytical technique for the simultaneous determination of flometoquin, flupyradifurone, and flonicamid residues was assessed in the tomato fruit, which were randomly collected at intervals of 0, 1, 3, 5, 7, 10, 15, and 21 days following treatment. The residue levels were conducted by employing the QuEChERS (quick, easy, cheap, effective, rugged, and safe) methodology as a pre-treatment procedure, along with solid phase extraction (SPE) for clean-up, followed by analysis with high-performance liquid chromatography equipped with diode-array detection (HPLC/DAD). The method showed good recoveries (93.74–102.44% for flometoquin, 92.30–105.90% for flupyradifurone, and 94.94–108.11% for flonicamid) at 0.1, 0.5, and 1 mg/kg, with RSDs below 20%. Calibration curves displayed excellent linearity ($R^2 > 0.99$). The residual half-life (RL_{50}) of the evaluated pesticides on tomato fruits was 4.85, 0.8, and 5.16 days for flometoquin, flupyradifurone, and flonicamid, in that order. In line with the maximum residue level (MRL) of 1, 1, and 0.5 mg/kg, respectively. The pre-harvest interval (PHI) was set at 3, 5, and 7 days, respectively. The hazard quotients (HQs) for all three insecticides remained below 1 throughout the monitoring period, with maximum values of 0.59 for flometoquin, 0.17 for flupyradifurone, and 0.08 for flonicamid at day 0. These values gradually declined over time, indicating a decreasing exposure risk. As all HQ values were significantly less than 1, the estimated dietary intake of treated tomato fruits poses no significant health risk to consumers.

Keywords: Flometoquin, Flupyradifurone, Flonicamid, HPLC-DAD, QuEChERS, Risk assessment.

1. Introduction

Global food systems face growing challenges related to food safety, food security, and environmental sustainability. As the demand for high-quality, residue-free fruits and vegetables continues to rise, maintaining safe levels of pesticide residues in food has become a central focus of public health policy and international trade regulation [1]. The presence of pesticide residues above maximum residue limits (MRLs) not only compromises consumer health but also jeopardizes market access and food supply chain integrity. In this context, effective residue monitoring is essential to support the pillars of food security, which include food availability, access, utilization, and stability [2].

Tomatoes (*Solanum lycopersicum*) play a pivotal role in Egypt's agricultural sector, serving as both a staple in domestic consumption and a significant export commodity. In 2023, Egypt exported approximately 25,000 tons of tomatoes, worth $53.2 million, reflecting a 62% increase from the previous year. underscoring the growing importance of tomato exports within the nation's economy. Notably, tomatoes exports constituted 14% of Egypt's total vegetable exports in 2023, highlighting their critical role in the agricultural export portfolio. Egypt's tomatoes reached 39 international markets during this period, with Saudi Arabia, Turkey, and Russia emerging as the top importers. Given this expansive reach and economic significance, ensuring the quality and safety of exported tomatoes is paramount to maintain and enhance Egypt's position in the global market [3].

Tomatoes plants are frequently treated with pesticides to control a variety of insect pests that threaten both yield and quality. Among the newer-generation systemic insecticides, flonicamid, flometoquin, and flupyradifurone are widely used in integrated pest management (IPM) programs. These compounds exhibit strong systemic activity and are particularly effective against sap-feeding insects such as leafhoppers, aphids, and whiteflies [4-5]. Despite their targeted efficacy and favourable toxicological profiles, residues of these compounds may persist in edible tissues, necessitating robust analytical methods for their detection.

Flonicamid, N-cyanomethyl-4-(trifluoromethyl)nicotinamide is a pyridinecarboxamide insecticide with systemic and translaminar activity. It acts by disrupting feeding behavior in sap-sucking pests such as aphids, whiteflies, and thrips. Flonicamid is categorized by the Insecticide Resistance Action Committee (IRAC) as belonging to Group 29. It is rapidly

*Corresponding author e-mail: mohammedabdallah851@agr.cu.edu.eg.;(Mohammed. A. Bayoumi).

Received date 01 June 2025; Revised date 24 August 2025; Accepted date 28 August 2025

DOI: 10.21608/ejchem.2025.391228.11855

absorbed and translocated through xylem and phloem tissues, making it effective against pests on both the upper and lower leaf surfaces [6-7].

Flonicamid and its metabolites are moderately persistent in crops. Regulatory agencies typically require the monitoring of both parent compound and key metabolites, such as TFNA (2-trifluoromethyl nicotinic acid) and TFNG (it's glucoside), as part of the total residue definition [8].

Flupyradifurone, 4-((6-chloro-3-pyridylmethyl)(2,2-difluoroethyl)amino)furan-2(5H)-one is a butenolide insecticide structurally distinct from neonicotinoids but shares a similar mechanism of action [9]. Classified in IRAC Group 4D, flupyradifurone has a unique structure that reduces the risk of cross-resistance with traditional neonicotinoids.

It is highly systemic, with both upward and downward translocation in the plant vascular system. This allows flupyradifurone to protect new plant growth and effectively control pests that feed on the phloem. Its relatively low acute mammalian toxicity and rapid dissipation make it an attractive option for integrated pest management (IPM), but its residues still require careful quantification due to its widespread use and potential environmental concerns [10].

Flometoquin 2-ethyl-3,7-dimethyl-6-(4-(trifluoromethoxy)phenoxy)-4-quinolyl methyl carbonate is a relatively new acaricide and insecticide belonging to the quinoline-based chemical class. Although primarily developed for mite control, it has also shown activity against various insects, especially in fruits and vegetables [11].

Unlike flonicamid and flupyradifurone, flometoquin is less extensively studied, and residue data are still being established in many jurisdictions. Due to its lipophilic nature, it tends to accumulate in plant tissues, which raises concerns about its potential persistence and accumulation in fruits. As a result, the monitoring of flometoquin residues in crops like tomatoes is crucial for establishing MRLs and risk assessments.

In many agricultural settings, particularly where there is high demand for produce and limited awareness of pesticide risks, farmers may harvest crops too soon after pesticide application, without allowing sufficient time for residues to degrade. This practice, coupled with the growing reliance on chemical pest control, increases the likelihood of pesticide residues entering the food chain.

From a food safety perspective, this raises a critical question: Are the pesticide residues remaining in tomatoes after application within safe levels for human consumption?

Addressing this question requires not only sensitive and validated analytical methods but also robust dietary risk assessments. Health-based guidance values such as the Acceptable Daily Intake (ADI), combined with Estimated Daily Intake (EDI) calculations and Hazard Quotients (HQs), provide a quantitative framework for evaluating consumer exposure and potential health risks [12].

To meet this need, analytical methods must be not only accurate and sensitive but also practical for routine application in regulatory and food safety laboratories. The QuEChERS approach, which stands for (Quick, Easy, Cheap, Effective, Rugged, and Safe), was first presented by Anastassiades et al. 2003 [13], has revolutionized pesticide residue analysis due to its simplicity, high extraction efficiency, and adaptability across a wide range of food matrices. QuEChERS involves an initial acetonitrile extraction followed by partitioning and dispersive solid-phase extraction (d-SPE), making it particularly effective for high-water-content samples such as tomatoes. This technique minimizes matrix effects and has been successfully applied in numerous multiresidue methods.[14]

Following extraction, High-Performance Liquid Chromatography with Diode Array Detection (HPLC-DAD) serves as a reliable tool for residue determination. HPLC-DAD provides high selectivity and sensitivity for non-volatile, thermally labile, and UV-absorbing compounds.[15] The diode array detector allows simultaneous multi-wavelength monitoring, facilitating the identification and quantification of structurally diverse analytes in complex matrices. [16-17]

Several analytical methods have been developed for the determination of flonicamid, flupyradifurone, and their metabolites in various crops using advanced chromatographic techniques. For instance, Fang et al. (2020, 2022) [18-19] and Feng et al. (2022) [20] employed HPLC–MS/MS methods combined with modified QuEChERS for analyzing flupyradifurone in ginseng and pepper, achieving high recovery rates (71–98%) and low LOQs (0.01–0.1 mg/kg). Similarly, validated methods evaluated by JMPR and EFSA (2016, 2015) [21-22] confirm the suitability of MS-based techniques for enforcement purposes. However, the current study adopts a cost-effective HPLC–DAD method with recoveries of 92–106%, RSDs below 7%, and LOQs comparable to MS/MS methods. These findings demonstrate that our approach offers reliable and practical performance, particularly in routine monitoring settings where high-end instrumentation may not be available. Additionally, the inclusion of flometoquin—an emerging insecticide with limited residue data—adds value to the existing literature, especially under Egyptian agro-climatic conditions where such data are scarce.

This study focuses on evaluating the residual behavior and dietary safety of flonicamid, flometoquin, and flupyradifurone in tomato fruits under open-field conditions. An analytical method combining QuEChERS extraction with HPLC-DAD detection was applied for the simultaneous determination of these insecticides. By integrating this analytical approach with dietary risk assessment models—including Estimated Daily Intake (EDI) and Hazard Quotient (HQ) calculations—the study aims to ensure the safety of tomato consumption, establish scientifically informed pre-harvest intervals (PHIs), and support safe agricultural practices. These efforts contribute to broader food safety objectives, consumer health protection, and the promotion of sustainable food systems in line with national and international regulatory standards.

2. Materials and methods

2.1. Chemicals and Reagents

Certified reference standards of flometoquin, flupyradifurone, and flonicamid (Fig. 1), each with a purity of > 98%. All solvents were of HPLC-grade. Sodium chloride and anhydrous magnesium sulfate were obtained from Merck, while the bulk primary secondary amine (PSA) sorbent (Bondesil-PSA, 40 µm) was supplied by (Supelco). Before being used, sodium chloride and anhydrous magnesium sulfate were activated by heating at 250ºC for four hours and then stored in desiccators. For field experiments, pesticide technical formulations Kagura 10%SC (Flometoquin) and Teppeki 50%WG (Flonicamid) were supplied by Shoura Company, Egypt; Sivanto 20%SL (Flupyradifurone) was supplied by Bayer, Egypt.

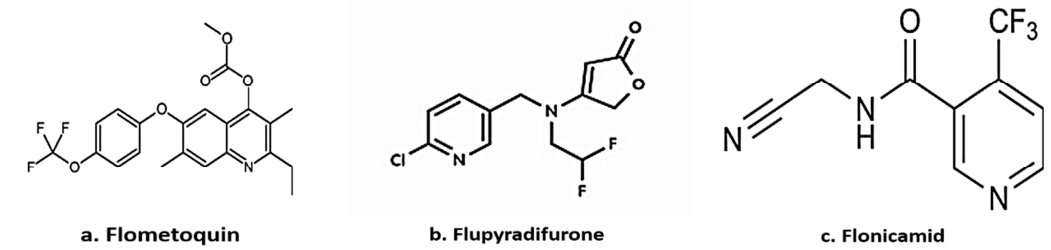

Figure 1: Chemical structures of the investigated insecticides

2.2. Apparatus

The HPLC system (Agilent HPLC 1260 infinite series; Agilent Technologies) included a quaternary pump, a variable wavelength diode array detector, and an autosampler with an electric sample valve. The HPLC system employed a 150 mm × 4.6 mm × 5 m octadecyl-silica analytical column. The mobile phases (acetonitrile 90% + water 10%, acetonitrile 60% + water 40%, and acetonitrile 65% + water 35%) had flow rates of 0.8, 0.8, and 1 ml/min for flometoquin, flupyradifurone, and flonicamid, respectively. The injection volume for each sample was 20 µl, and the wavelengths for detection were maintained at 210, 254, and 254 nm. Flupyradifurone, flonicamid, and flometoquin had retention durations of 3.88, 3.32, and 4.51 minutes, respectively.

2.3. Standard preparation

10 mg of the analytes were dissolved in 100 ml of ethyl acetate and methanol, to prepare stock solutions of flometoquin, flupyradifurone, and flonicamid at a concentration of 0.1 mg/ml. The stock solutions were diluted with methanol to provide working standard solutions of 10, 5, 2, 1, 0.5, 0.1, and 0.01 µg/ml. All solutions were meticulously stored in the refrigerator at -20 °C, ensuring their integrity and efficacy, and shielded from light with aluminum foil for optimal protection. Working standard solutions were stored in the dark at 4 °C when not in use to ensure maximum stability and reliability.

2.4. Field experiment

During the 2023 season, in Al Ayat City, Giza, Egypt, a field experiment was conducted, and tomato plants were sprayed with flometoquin (Kagura 10% SC), flupyradifurone (Sivanto 20% SL), and flonicamid (Teppeki 50% WG) at 200 ml, 50 ml, and 40 g / 200 L water, respectively. Via foliar application. Samples of tomatoes were randomly collected after 0, 1, 3, 5, 7, 10, 15, and 21 days from the treatment of the plants.

2.5. Sampling and storage

Tomato fruit samples were collected according to the principles of Good Harvesting Practice (GHP) to ensure representative, uncontaminated, and reliable sampling for pesticide residue analysis. For each treatment and the control group, 2 kilograms of tomatoes were randomly harvested from different locations within the field, ensuring coverage of all treated plants. The samples included fruits from different parts of the plant canopy (upper, middle, and lower) and from multiple rows, to maintain representativeness. Harvesting was performed manually using clean, pesticide-free gloves and stainless steel scissors. Each sample was immediately placed in pre-labeled, sterile polyethylene bags, which were then stored in insulated iceboxes at approximately 4 °C to minimize any post-harvest degradation or volatilization of pesticide residues. Samples were promptly transported to the laboratory and stored at -20 °C until analysis. Control samples (untreated) were collected prior to pesticide application (from untreated plots) to confirm the absence of background residues. All procedures for sampling, handling, and storage were conducted in compliance with the guidelines outlined in the FAO Manual on Pesticide Residue Data. [23]

2.6. Extraction and clean up

10.0 mL acetonitrile with 1% formic acid was added to a 50.0 mL Teflon centrifuge tube containing 10.0 g of a homogenised tomato sample. After vortexing the tube for 1.0 min, 1.0 g of sodium chloride (NaCl) and 4.0 g of magnesium sulfate anhydrous ($MgSO_4$) were added, and the tube was centrifuged for five minutes at ≥3000 rpm. Then, 1.0 mL of the supernatant was removed to a 2.0 mL centrifuge tube with the sorbent, (150 mg of anhydrous $MgSO_4$, and 25.0 mg of PSA). The tube was vortexed for 30 seconds and centrifuged for 5.0 minutes at ≥ 3000 rpm. A 0.22 µm nylon syringe filter was then used to filter the supernatant into a 2.0 mL vial for HPLC–DAD analysis.

2.7. Method validation

The main validation parameters testes; accuracy, precision, LOD, LOQ, and Linearity ensured the reliability of the method. Individual amounts of standard solutions at different concentrations were: 10, 5, 2, 1, 0.5, 0.1 and 0.01 mg/kg. The experiments demonstrated a positive linear association between the pesticides and were conducted three times at each concentration.

The residual matrix effects were adjusted for using matrix-matched calibration (MMC). The impact of one or more co-extracted components from the samples on the determination of flometoquin, flupyradifurone, and flonicamid concentrations was referred to as the matrix effects. By contrasting the responses generated by flometoquin, flupyradifurone, and flonicamid, the existence of these effects is shown. Following the extraction of the materials in a neat solvent solution, flometoquin, flupyradifurone, and flonicamid were added at the same concentration levels (10, 5, 2, 1, 0.5, 0.1, and 0.01 mg/kg) in the same solvent.

Matrix effects (%ME) for each analyte were calculated by using the following equation:[24]

$$\text{ME }\% = \frac{\text{M matrix} - \text{M solvent}}{\text{M solvent}} X100\%$$

From the previous equation:

M matrix: the calibration curve's slope in the matrix.

M solvent: the calibration curve's slope in the neat solvent.

The approved lowest residue concentration that can be measured by routine monitoring using validated control procedures is known as the limit of detection (LOD), and it is defined as a signal-to-noise ratio (S/N) of 3:1. LOQ, is the lowest concentration of the analyte that has been verified using the whole analytical method with acceptable trueness (70–120%) and precision (RSD ≤ 20%). Dg-sanco (2013) [25] states that the limit of quantification need to be ≤ maximum residue level (MRL) [25].

The trueness of a method was assesed from the determination of recovery results,[25] where the samples were spiked with all certified analytes at concentrations ranging from (0.01-1 mg/kg), and five replicates were used for each level to verify the recovery at acceptable mean recoveries, which are within the acceptable range of 70-120%.

The following equation was used to calculate trueness:

$$\%R = \frac{X}{\mu} \times 100$$

From the previous equation: %R: recovery percentage, X: flometoquin, flupyradifurone, or flonicamid experimental concentrations in mg/kg, and µ: flometoquin, flupyradifurone or flonicamid calculated concentrations in mg/kg

The precision of the measurements was assessed using five replicates at each recovery level (ranging from 0.01 to 1 mg/kg) over three separate days. A limit of ≤ 20% was established for the relative standard deviation (RSD) to evaluate the precision of the results.

$$\%RSD = \frac{Sd}{M} \times 100$$

From the previous equation: SD: represents the replicates' standard deviation, and M: represents the mean concentration of replicates.

2.8. Data processing and Statistical analysis

Flometoquin, flupyradifurone and flonicamid residues in tomato was determined by plotting residue concentration against elapsed time after application. Data fitting and statistical analyses were performed using OriginPro 2023 (OriginLab Corporation, USA). Equations of best fit were selected based on the maximum coefficient of determination (R^2), residual analysis, and Akaike Information Criterion (AICc). For dissipation of flometoquin, flupyradifurone and flonicamid in tomato, exponential relationships were found to be applicable corresponding to the general first-order kinetics equation**:**

$$C_t = C_0 e^{-kt}$$

Where: C_t = concentration at time t, C_0 = initial concentration, e = base e, k = rate constant of decline 1/days, and t = time. From this equation, the dissipation half-life periods ($t_{1/2}$=ln 2/k), for the flometoquin, flupyradifurone and flonicamid in tomato fruits were investigated. [26, 27, 28]

The pre-harvest interval (PHI) for each pesticide was determined based on the dissipation curve of residue concentrations over time. Specifically, PHI was defined as the time point at which the pesticide residue levels fell below the maximum residue limit (MRL) established by the Codex Alimentarius Commission. This approach does not rely on the calculated half-life (RL_{50}) but rather ensures that residues are within acceptable safety limits at harvest. The methodology aligns with guidelines provided by the FAO for estimating PHI in supervised residue trials. [23]

2.9. Risk Assessment:

Dietary exposure assessment plays a critical role in evaluating the potential health risks associated with pesticide residues in food commodities. To estimate consumer risk, an exposure evaluation was conducted using residue levels obtained from field trials. The dietary risk was assessed by comparing the Estimated Daily Intake (EDI) with the Acceptable Daily Intake (ADI) established by international regulatory authorities.

The EDI for each pesticide was calculated using the following equation:

$$\mathrm{EDI} = \frac{\mathrm{C} \times \mathrm{F}}{\mathrm{BW}}$$

Where: C is the mean pesticide residue concentration in the food (mg/kg), F is the average daily tomato consumption (0.115 kg/day per capita for Egypt, based on WHO/FAO GEMS/Food Consumption Cluster Diets, 2012 [29]), BW is the average body weight of an adult (assumed to be 60 kg).

A dietary risk is considered acceptable when the ratio of EDI to ADI (i.e., the Hazard Quotient, HQ) is less than 1. Values above 1 indicate a potential health concern.

The National Estimated Daily Intake (NEDI) was calculated using the following formula:

$$\mathrm{NEDI} = \frac{\mathrm{C} \times \mathrm{F}}{\mathrm{BW}}$$

Where: C is the concentration of pesticide residue in the food (mg/kg), F is the average daily food consumption (kg/day), BW is the average adult body weight (assumed to be 60 kg).

The National Acceptable Daily Intake (NADI) refers to the estimated acceptable daily intake for an average adult, also assuming a body weight of 60 kg, in accordance with the guidelines provided by the WHO/Global Environment Monitoring System – Food (GEMS/Food, 2012).[29]

All maximum residue limits (MRLs) and acceptable daily intake (ADI) values were obtained from the EU Pesticides Database. Food consumption data were sourced from the GEMS/Food, 2012. [29]

The long-term dietary risk assessment was conducted by calculating the Estimated Daily Intake (EDI) as a percentage of the ADI. This was expressed using the Health Risk Index (HRI), calculated as follows:

$$\mathrm{HRI} = \frac{\mathrm{EDI}}{\mathrm{ADI}}$$

An HRI value > 1 indicates that the pesticide residue level may pose a potential health risk to consumers, whereas an HRI < 1 suggests that the exposure is within acceptable safety limits.

3. Results and discussion

3.1. Method Validation

To evaluate the linearity of the calibration curves for flometoquin, flupyradifurone, and flonicamid, standard working solutions were prepared in methanol at various concentrations: 10, 5, 2, 1, 0.5, 0.1, and 0.01 mg/kg. Each concentration level was then injected into the HPLC-DAD system for analysis.

The concentrations of the analytes were plotted against their corresponding peak areas to create standard calibration curves for flometoquin, flupyradifurone, and flonicamid. The correlation coefficients (R^2) for these curves were found to be 0.99, indicating a strong linear relationship. This approach allowed for accurate assessment of the relationship between concentration and signal response, facilitating the quantification of these compounds in subsequent analyses.

The investigation of the matrix effect involved a detailed comparison of the slopes of calibration curves at several concentrations (10, 5, 2, 1, 0.5, 0.1, and 0.01 mg/kg) for flometoquin, flupyradifurone, and flonicamid in both tomato matrix and pure solvent. This analysis is crucial as it identifies any potential enhancements or suppressions in signal response caused by the tomato matrix, thereby allowing for a more precise quantification of these compounds in the presence of complex matrices. Understanding these effects can significantly improve the reliability of analytical results and enhance the overall accuracy of the methods used.

The % matrix effect can be either negative or positive and is categorized into three distinct classifications: no matrix effect (ranging from -20% to 20%), medium matrix effect (spanning from -50% to -20% or from 20% to 50%), and strong matrix effect (defined as below -50% or above 50%) [16, 17]. In this analysis study, the results indicated a positive medium matrix effect, with values of 33.76%, 48.66%, and 40.42% for flometoquin, flupyradifurone, and flonicamid, respectively. These findings suggest that, there were no interfering endogenous peaks that could significantly suppress or enhance the instrument's response, thereby affirming the reliability of the detection method in the tomato matrix. This conclusion is further supported by the chromatographic profiles obtained for each analyte, which showed well-resolved peaks with minimal matrix interference (Figure 2).

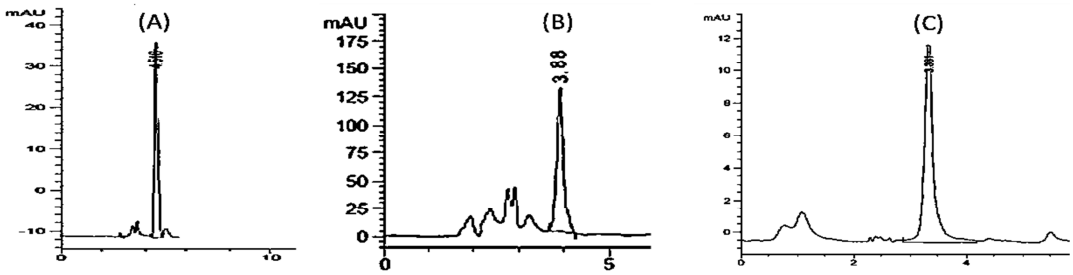

Figure 2: Representative chromatograms of the three studied insecticides in tomato matrix: (A) flometoquin, (B) flupyradifurone, and (C) flonicamid, obtained using the QuEChERS–HPLC–DAD method. All analytes were clearly resolved with minimal matrix interference, demonstrating good selectivity and suitability of the analytical procedure.

The lowest validated levels of flometoquin, flupyradifurone, and flonicamid, which demonstrated acceptable precision and trueness for HPLC analysis in tomato samples, were determined to be 0.2, 0.1, and 0.1 mg/kg, respectively. These values represent the limit of quantification (LOQ) and are significant in ensuring reliable detection of these compounds. These LOQ values are acceptable as they fall below or equal to the maximum residue limits (MRLs) established for these substances, which are set at 1, 1, and 0.5 mg/kg for flometoquin, flupyradifurone, and flonicamid, respectively [25]. This compliance underscores the effectiveness and robustness of the analytical method employed, ensuring that it can be reliably used for monitoring pesticide residues in tomato, contributing to food safety and regulatory adherence.

The assessment of trueness, bias, or mean recovery (as presented in Table 1) was conducted through five replicates at three fortification levels (1, 0.5, and 0.1 mg/kg) by spiking 10 g of blank samples with a standard solution. The mean recovery rates obtained were 93.74-102.44% for flometoquin, 92.30-105.90% for flupyradifurone, and 94.94-108.11% for flonicamid, indicating strong performance across all compounds. The relative standard deviation (%RSD) for the analysis demonstrated good precision, with values ranging from 2.09 to 3.32% for flometoquin, 2.61 to 3.49% for flupyradifurone, and 3.44 to 7.27% for flonicamid. Reports that these mean recovery values fall within the acceptable range of 70-120% [25]. This further supports the conclusion that the method is both sensitive and suitable for determining residues of flometoquin, flupyradifurone, and flonicamid in tomato, thereby ensuring reliable monitoring of pesticide levels in food products.

Table 1: Recovery of flupyradifurone, flometoquin and flonicamid residues from Tomato fruits

Spiked Level	Flupyradifurone		Flometoquin		Flonicamid	
	Recovery %	RSD	Recovery %	RSD	Recovery %	RSD
0.1	92.30	2.61	93.74	2.09	94.94	3.44
0.5	100.42	3.50	96.57	2.35	97.91	3.18
1	105.90	3.49	102.44	3.32	108.11	7.27

The recovery values and RSDs presented in Table 1 clearly demonstrate that the method provides high trueness and precision across all tested concentration levels. These results not only fulfill international method validation criteria but also indicate that the QuEChERS–SPE–HPLC/DAD approach is robust enough for routine pesticide residue monitoring. To further contextualize these findings, Table 2. Compares the present method with previously reported analytical approaches, highlighting its comparable analytical performance despite relying on a simpler and more cost-effective detection platform.

3.2. Comparison with previously reported analytical methods

As shown in Table 2, most previous studies on flonicamid and flupyradifurone relied on advanced LC–MS/MS or UPLC–MS/MS platforms, with recoveries generally ranging from 70–114%, LOQs at or below 0.01 mg/kg, and RSDs below 15%. In contrast, our QuEChERS–HPLC/DAD method achieved comparable recovery (91–103%) and precision, while requiring simpler and more cost-effective instrumentation. This demonstrates that reliable residue quantification can be achieved without high-end mass spectrometry, thus extending analytical accessibility to laboratories in resource-limited settings. Importantly, this is the first study to simultaneously determine flometoquin, flupyradifurone, and flonicamid in tomatoes using this approach, supporting both regulatory compliance and dietary risk assessment.

Table 2: Comparison between the current method and previously reported analytical methods for determination of flonicamid, flupyradifurone, and flometoquin residues

Study	Matrix	Pesticide(s)	Instrument	Extraction Method	LOQ (mg/Kg)	Recovery (%)	RSD (%)
Xu et al., 2011 [30]	Cucumber	Flonicamid	LC-MS/MS	QuEChERS	0.01	81-95	-
Abdel-Ghany et al., 2016 [31]	Cucumber	Flonicamid	LC- MS/MS	QuEChERS	0.01	99.75	<2
JMPR 2016 [21]	Various	Flonicamid, metabolites	LC-MS/MS	QuEChERS	0.01	75-105	<15
Rabie et al., 2018 [32]	Pepper	Dinotefuran and Thiamethoxam	HPLC-DAD	QuEChERS	0.01	77-112	<3
Wang et al., 2018 [33]	Cabbage	Flonicamid, metabolites	LC-MS/MS	QuEChERS	0.02	88-100	<8
Xu et al., 2021[34]	peach	Flonicamid and Dinotefuran	UPLC-MS/MS	QuEChERS	0.02	94-108	<9
Xu and Hu 2023 [35]	Cucumber	Flonicamid	HPLC-MS/MS	QuEChERS	0.01	80-101	≤9
Fang et al., 2020 [18]	herbal medicines	Flupyradifurone, metabolites	LC-MS/MS	QuEChERS	0.01	71-102	<14
Fang et al., 2022 [19]	Ginseng	Flupyradifurone, metabolite	HPLC-MS/MS	QuEChERS	0.01	73-97	<8
Feng et al., 2022 [20]	Pepper	Flupyradifurone, metabolites	LC-MS/MS	QuEChERS	0.01	71-94	<8
Hu et al., 2025 [36]	Animal products	Flupyradifurone, metabolites	UPLC-MS/MS	QuEChERS	0.001–0.025	70-114	<10
Yanqiu et al., 2024 [37]	Milk	Flupyradifurone, metabolites	UPLC-MS/MS	QuEChERS	-	70-98	<5
Current Study	Tomato	Flonicamid, Flupyradifurone, Flometoquin	HPLC-DAD	QuEChERS	0.01	92-108	<7

3.3. Dissipation of insecticide flometoquin, flupyradifurone and flonicamid in tomato fruits

Building on the validated analytical performance, the developed QuEChERS–HPLC-DAD method was applied to investigate the dissipation dynamics of flometoquin, flupyradifurone, and flonicamid in tomato fruits under field conditions. The observed residue decline patterns reflected the interplay between the compounds' physicochemical properties, plant metabolism, and prevailing environmental conditions. Understanding these degradation dynamics is essential for elucidating their environmental fate, determining persistence, and assessing potential dietary risks to consumers. Such insights also contribute to establishing scientifically sound pre-harvest intervals and guiding regulatory measures for safe agricultural practices.

3.3.1. Flometoquin

Flometoquin residues in tomato fruits were monitored over a 21-day period at intervals of 0, 1, 3, 5, 7, 10, 15, and 21 days after application (Table 3, Figure 3). The initial deposit, recorded two hours post-treatment, was 1.27 ± 0.11 mg/kg. Residues declined rapidly following a first-order kinetic model, reaching 1.15 mg/kg (9.44% dissipation) after 1 day, 0.87 mg/kg (31.49%) after 3 days, 0.61 mg/kg (51.96%) after 5 days, and 0.33 mg/kg (74.01%) after 7 days. By day 10, residues had dropped to 0.03 mg/kg (97.63% reduction) and were below the detectable limit at days 15 and 21, indicating complete degradation.

Table 3: Dissipation of flometoquin residue in tomato fruits

Time after application	Residues ±SD (mg/kg)	% Dissipation	RSD%
Initial	1.27±0.11	00.00	0.11
1day	1.15±0.10	09.44	0.10
3 days	0.87±0.08	31.49	0.08
5 days	0.61±0.10	51.96	0.10
7 days	0.33±0.08	74.01	0.08
10 days	0.03±0.01	97.63	0.01
15 days	ND	---	---
21 days	ND	---	---
RL_{50}(days)		4.85	
MRL		1	
PHI (days)		3	

*MRL values are based on the Codex Alimentarius Commission (FAO, 2009) [38].

Flometoquin is a relatively new quinoline-type insecticide for which residue data remain limited in several jurisdictions. Its reported partition coefficient (logP ≈ 5.4–6.3) indicates high lipophilicity [39], a property that generally promotes sorption into and accumulation within plant tissues. Consequently, the potential for persistence and storage of flometoquin in edible parts particularly fruits has been raised as a concern and justifies targeted residue monitoring in crops such as tomato. Nevertheless, our field results showed a moderate half-life (RL_{50} ≈ 4.85 days) and rapid decline below the MRL 1.0 mg/kg [38], within 24 h, suggesting that under the tested conditions environmental degradation processes and plant metabolic activity may offset the lipophilic tendency to some extent [28, 40]. Given the limited and emerging nature of residue datasets for flometoquin, we recommend cautious interpretation and advocate for additional crop- and region-specific residue studies to confirm accumulation risks and to support MRL setting.

Based on plant metabolism studies conducted by regulatory authorities such as the Food Safety Commission of Japan (FSCJ), flometoquin is shown to remain largely un metabolized in various crops. The parent compound was identified as the only residue of toxicological relevance, with no significant accumulation of degradation or metabolic products. This finding supports the analytical focus on the unchanged flometoquin molecule when determining residue levels in tomato fruits and other plant matrices. Accordingly, our method targeted the parent compound, aligning with international residue definition standards and ensuring accurate dietary risk assessment [41].

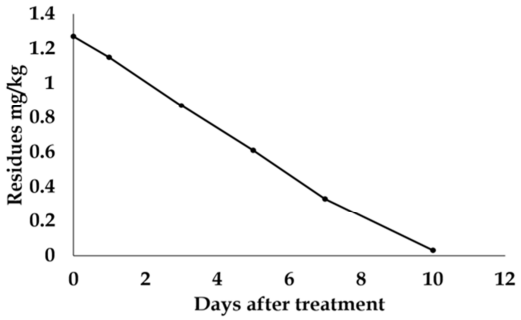

Figure 3: Dissipation curve of flometoquin in tomato fruits

3.3.2. Flupyradifurone

Table 4 and Figure 4 show the initial residue levels and dissipation behavior of flupyradifurone in tomato fruits. Two hours after application, the concentration was 3.60 mg/kg, which declined sharply to 1.26 mg/kg within 24 hours (65% loss) and to 1.07 mg/kg by the third day (70.27% loss). The degradation continued steadily, reaching 0.23 mg/kg (93.61% loss) after 7 days, 0.10 mg/kg (97.22% loss) after 10 days, and 0.04 mg/kg (98.88% loss) by day 15. No detectable residues remained by day 21. The calculated half-life (RL_{50}) was 0.8 days, indicating rapid dissipation. Based on the Codex Alimentarius Commission [38], the MRL for flupyradifurone in tomatoes is 1 mg/kg, the fruits would be considered safe for consumption five days after application.

Table 4: Dissipation of flupyradifurone residue in tomato fruits

Time after application	Residues ±SD (mg/kg)	% Dissipation	RSD%
Initial	3.60±0.35	00.00	0.35
1day	1.26±0.11	65.00	0.11
3 days	1.07±0.09	70.27	0.09
5 days	0.76±0.08	78.88	0.08
7 days	0.23±0.03	93.61	0.03
10 days	0.10±0.02	97.22	0.02
15 days	0.04±0.01	98.88	0.01
21 days	ND	---	---
RL_{50}(days)		0.8	
MRL		1	
PHI		5	

*MRL values are based on the Codex Alimentarius Commission (FAO, 2009) [38].

From a physico-chemical perspective, flupyradifurone is highly soluble in water (3.2 g/L at 20 °C), exhibits negligible volatility from moist soil or aquatic surfaces under field conditions, and demonstrates low potential for long-range atmospheric transport. These properties limit environmental dispersion via volatilization while facilitating systemic uptake and translocation within plant tissues, likely contributing to the initial rapid dissipation observed on fruit surfaces (Health Canada PMRA, 2015) [42].

Consistent with previous field studies, flupyradifurone dissipation followed a biphasic pattern an initial rapid phase with approximately 78% residue loss, followed by a slower decline of the remaining residues (Health Canada PMRA, 2015) [42]. The present results reflect this trend, with a marked reduction in the first three days, followed by gradual degradation until complete dissipation by day 21.

The rate of decline may also be accelerated by a dilution effect associated with fruit growth [28]. Under controlled laboratory conditions, flupyradifurone undergoes rapid photodegradation, with a reported half-life of 5 minutes and complete breakdown within 30 minutes [43]. In aqueous systems, the photolysis half-life is approximately 2.5 days [44]. Field dissipation trials across different crops have reported RL_{50} values ranging from 8 to 251 days, suggesting the potential for residue carry-over under certain agronomic conditions [23]. However, no prior field studies have quantified its dissipation kinetics in tomato fruits, underscoring the novelty and significance of the present findings [45].

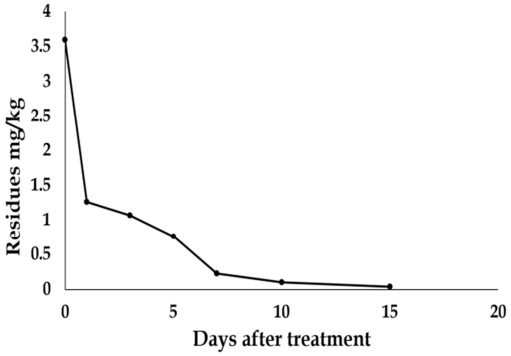

Figure 4: Dissipation curve of flupyradifurone in tomato fruits

3.3.3. Flonicamid

The data shown in Table 5 and Figure 5 reveal both the initial residue levels and the residual behavior of flonicamid in tomato fruits. Two hours after application, the initial residue of flonicamid in the tomatoes was 1.55 mg/kg. Within the first 24 hours, this amount decreased to 1.03 mg/kg, representing a 33.54% reduction. By the third day, the residue level further dropped to 0.91 mg/kg, with a notable 41.29% decrease.

Table 5: Dissipation of flonicamid residue in tomato fruits

Time after application	Residues ±SD (mg/kg)	% Dissipation	RSD%
Initial	1.55±0.11	0.00	0.11
1day	1.03±0.18	33.54	0.18
3 days	0.91±0.06	41.29	0.06
5 days	0.62±0.09	60.00	0.09
7 days	0.48±0.04	69.03	0.04
10 days	0.37±0.12	76.12	0.12
15 days	0.18±0.04	88.37	0.04
21 days	ND	---	---
RL_{50}(days)		5.16	
MRL		0.5	
PHI		7	

*MRL values are based on the Codex Alimentarius Commission (FAO, 2009) [38].

Over time, the residues of flonicamid continued to decline, reaching 0.62 mg/kg (60% reduction), 0.48 mg/kg (69.03% reduction), 0.37 mg/kg (76.12% reduction), and 0.18 mg/kg (88.37% reduction) on the 5th, 7th, 10th, and 15th days, respectively. No flonicamid residues were detectable by the 21st day from the application. Based on these findings, the RL_{50} of flonicamid in tomato fruits was 5.16 days. According to the Codex Alimentarius Commission, the MRL for flonicamid in tomato fruits is set at 0.5 mg/kg, indicating that the fruits can be safely consumed after 7 days post-application [38].

Flonicamid, is prone to photolytic degradation and microbial breakdown under favorable environmental conditions [46, 47].Overall, these findings reinforce the importance of considering environmental dissipation mechanisms including photodegradation, volatilization, hydrolysis, and biological metabolism when assessing pesticide safety in food crops. It is essential to tailor pesticide application protocols to local climatic conditions and growth stages to ensure compliance with food safety standards and minimize consumer exposure [32].

The findings of the present study align well with several previously published investigations regarding the behavior and risk profile of flonicamid and related insecticides in various crops. Similar dissipation dynamics of flonicamid in cherry tomatoes under greenhouse conditions, with a half-life of 4.25 days and recoveries ranging from 92.8% to 106.0%, closely match the current study's values (half-life = 5.16 days; recovery = 92–106%) [48]. Likewise, rapid degradation of flonicamid and imidacloprid in strawberries and green beans, with half-lives around 2–3 days [49, 50].

Evidence from studies on cabbage [33, 51] supports this behavior, reporting fast dissipation with half-lives of 1.49–4.99 days and terminal residues below MRLs. These studies predominantly utilized modified QuEChERS extraction coupled with LC-MS/MS; however, our adoption of HPLC-DAD still achieved high recovery and precision demonstrating that reliable residue analysis is attainable even with simpler detection platforms when properly validated.

Comparable findings were also reported for flonicamid in Sichuan pepper across multiple sites, with half-lives ranging from 3.7 to 6.5 days and a proposed MRL of 1 mg/kg for dried samples values consistent with our tomato MRL reference (0.5 mg/kg) [52]. Notably, this study observed increased residue levels after processing, underscoring the need for further evaluation of processing factors in tomato products.

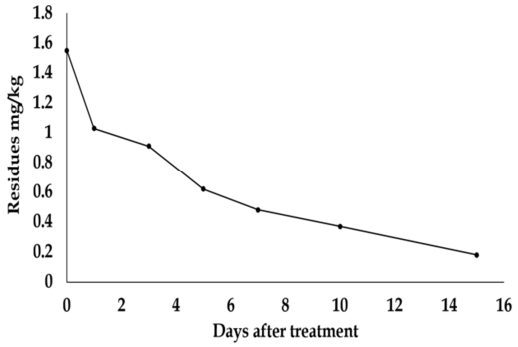

Figure 5: Dissipation curve of flonicamid in tomato fruits

Taken together, these findings validate the robustness of the QuEChERS–SPE–HPLC/DAD approach used in this study and confirm that the dissipation and residue patterns of flonicamid, flupyradifurone, and flometoquin in tomato fruit align with reports from other crops and regions. This strengthens the evidence base for establishing pre-harvest intervals (PHIs) and supports the safe application of these insecticides under local agricultural practices.

3.4. Risk evaluation

According to Table 6, the National Estimated Daily Intake (NEDI) and corresponding Hazard Quotients (HQ) for flometoquin, flupyradifurone, and flonicamid were calculated based on residue levels over the dissipation period. All HQ values were consistently below the threshold of 1, indicating that none of the tested insecticides pose a potential dietary risk under the current application regime. The highest HQ values were recorded on the day of application (0.59 for flometoquin, 0.17 for flupyradifurone, and 0.08 for flonicamid), and decreased sharply with time, reflecting the rapid dissipation and reduced consumer exposure risk.

Table 6: National estimated daily intake (NEDI) and risk quotient (RQ) of flometoquin, flupyradifurone and flonicamid residues in tomato fruits

Days after treatment	Flometoquin			Flupyradifurone			Flonicamid		
	Residues mg/kg	NEDI mg/kg.bw /day	RQ	Residues mg/kg	NEDI mg/kg.bw /day	RQ	Residues mg/kg	NEDI mg/kg.bw /day	RQ
0	1.27	4.8×10^{-3}	0.59	3.6	1.3×10^{-2}	0.17	1.55	5.8×10^{-3}	0.08
1	1.15	4.3×10^{-3}	0.54	1.26	4.7×10^{-3}	0.06	1.03	3.9×10^{-3}	0.06
3	0.87	3.3×10^{-3}	0.41	1.07	4.0×10^{-3}	0.05	0.91	3.4×10^{-3}	0.05
5	0.61	2.3×10^{-3}	0.29	0.76	2.8×10^{-3}	0.04	0.62	2.3×10^{-3}	0.03
7	0.33	1.2×10^{-3}	0.15	0.23	8.6×10^{-4}	0.01	0.48	1.8×10^{-3}	0.03
10	0.03	1.1×10^{-4}	0.01	0.1	3.7×10^{-4}	0.004	0.37	1.4×10^{-3}	0.02
15	---	---	---	0.04	1.5×10^{-4}	0.001	0.18	6.7×10^{-4}	0.01

Rapid degradation of flonicamid and imidacloprid in strawberries and green beans, with half-lives around 2–3 days and negligible dietary risks (HQ < 1), corroborates our current risk assessment outcomes (HQ < 0.59 for all compounds at day 0) [49,50]. Our findings are consistent with previous studies that reported low dietary risks associated with pesticide residues in fruits and vegetables. A hazard quotient of 26.59% was reported for pyriproxyfen, indicating minimal risk to consumer health [53]. Similarly, sulfoxaflor residues in squash posed no substantial health concern, with HQ values ≤ 0.0102 [54]. Malhat et al. Dietary risk levels below 1 were also observed across various crops, with HQs ranging from 0.01 to 0.52 in eggplant, 0.002 to 0.10 in guava, and 0.004 to 0.41 in orange [55]. Moreover, recoveries of 80–101% and RSD ≤9.1% were reported in cucumbers for flonicamid and its metabolites, with negligible dietary risks (HQ <1), supporting our data on analytical method performance and consumer safety [35]. Similarly, the current dissipation kinetics of flupyradifurone (half-life = 0.8 days) and flometoquin (4.85 days) are consistent with their physicochemical properties, and their HQ values <1 throughout the monitoring period confirm that their use in tomato cultivation is unlikely to pose health hazards when applied according to GAP.

These findings align with our results, reinforcing that the long-term dietary intake of flometoquin, flupyradifurone, and flonicamid residues poses no significant health risk to Egyptian consumers and remains within acceptable exposure limits under the tested conditions.

4. Conclusion

An HPLC-DAD method combined with QuEChERS extraction was successfully employed for the simultaneous determination of flometoquin, flupyradifurone, and flonicamid residues in tomato fruits. The analytical method demonstrated strong performance, with mean recovery rates ranging from 92.30–108.11% and relative standard deviations (RSDs) below 20%, confirming its accuracy, precision, and suitability for routine pesticide residue monitoring. The dissipation kinetics of the three insecticides followed first-order models, with half-lives (RL_{50}) calculated as 4.85 days for flometoquin, 0.8 days for flupyradifurone, and 5.16 days for flonicamid. These results indicate that the compounds degrade effectively under field conditions. Accordingly, pre-harvest intervals (PHIs) of 3, 5, and 7 days were recommended for flupyradifurone, flometoquin, and flonicamid, respectively, provide practical guidance for Egyptian tomato farmers and exporters. Strict adherence to these intervals can help ensure compliance with international MRLs, thereby safeguarding market access and supporting the competitiveness of Egyptian tomato exports.

The dietary risk assessment, based on Estimated Daily Intake (EDI) and Acceptable Daily Intake (ADI), showed that all Hazard Quotient (HQ) values were well below 1. The highest HQs were observed on the day of application but declined rapidly during the dissipation period, reflecting minimal long-term consumer exposure. These findings confirm that, when used in accordance with good agricultural practices, the studied insecticides pose no significant health risk and are safe for human consumption. By promoting food safety and protecting consumer health, the findings of this study also align with Sustainable Development Goal (SDG) 2 (Zero Hunger) and SDG 3 (Good Health and Well-being).

In conclusion, the tested insecticides are suitable for integrated pest management (IPM) in tomato cultivation. Their rapid dissipation, low residue levels, and minimal dietary risk support their continued use, provided adherence to recommended application intervals is maintained. Future studies should also investigate the influence of common processing practices, such as washing, peeling, juicing, and paste production, on residue levels. Such work would provide additional insights into consumer exposure from processed tomato products and further strengthen food safety assessments.

5. Conflict of interest

The authors affirm that this study was carried out without commercial or financial interests that could be interpreted as potential conflicts of interest.

6. Acknowledgements

This research was supported by the Faculty of Agriculture, Cairo University, Egypt.

7. References

1. FAO/WO. International Code of Conduct on Pesticide Management– Guidelines on Pesticide Residue Monitoring. Rome: Food and Agriculture Organization of the United Nations and World Health Organization, 2020.
2. FAO. The State of Food Security and Nutrition in the World. Rome: FAO, IFAD, UNICEF, WFP and WHO, 2021.
3. https://oec.world/en/profile/bilateral-product/tomatoes/reporter/egy.
4. Nauen, R., Jeschke, P., Velten, R., Beck, M. E., Ebbinghaus-Kintscher, U., Thielert, W., and Elbert, A. Flupyradifurone: a brief profile of a new butenolide insecticide. Pest Management Science, 2015; 71(6):850-862.
5. Sparks, T. C., Crossthwaite, A. J., Nauen, R., Banba, S., Cordova, D., Earley, F., and Wessels, F. J. Insecticides, biologics and nematicides: Updates to IRAC's mode of action classification-a tool for resistance management. Pesticide Biochemistry and Physiology, 2020; 167:104587-104597.
6. Nauen, R., Elbert, A., and Jeschke, P. Overview of the status and global strategy for neonicotinoids. Pest Management Science, 2008; 64(11):1084–1088.
7. IRAC. Insecticide Resistance Action Committee MoA Classification., 2023; https://irac-online.org.
8. EFSA. Reasoned opinion on the review of the existing maximum residue levels for flonicamid according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal, 2021; 19(8): e06892.
9. Jeschke, P., Nauen, R., Gutbrod, O., Beck, M. E., Matthiesen, S., Haas, M., and Velten, R. Flupyradifurone (Sivanto™) and its novel butenolide pharmacophore: Structural considerations. Pesticide biochemistry and physiology, 2015; 121: 31-38.
10. Jeschke, P. Current trends in the design of fluorine-containing agrochemicals. Organofluorine chemistry: Synthesis, modeling, and applications, 2021; 363-395.
11. Mitchell, P., Browne, S. E., and Osborn, M. J. Quinoline derivatives as inhibitors of mitochondrial respiration. Pesticide Biochemistry and Physiology, 2018; 146: 22–29.
12. World Health Organization (WHO). Principles and methods for the risk assessment of chemicals in food (Environmental Health Criteria 240). Geneva: WHO Press, 2009; https://www.who.int/publications/i/item/9789241572408.
13. Anastassiades, M., Lehotay, S. J., Štajnbaher, D., and Schenck, F.J. Fast and easy multiresidue method employing acetonitrile extraction/partitioning and "dispersive solid-phase extraction" for the determination of pesticide residues in produce. Journal of AOAC international, 2003; 86(2): 412-431
14. Lehotay, S. J., Maštovská, K., and Lightfield, A. R. Use of buffering and other means to improve results of problematic pesticides in a fast and easy method for residue analysis of fruits and vegetables. Journal of AOAC International, 2010; 93(4): 1161–1187.
15. Carbonell-Rozas, L., Lara, F. J., and García-Campaña, A. M. Analytical methods based on liquid chromatography and capillary electrophoresis to determine neonicotinoid residues in complex matrices. A comprehensive review. Critical Reviews in Analytical Chemistry, 2024; 54(7): 2554-2582.
16. Pico, Y., Blasco, C., and Font, G. Environmental and food applications of LC-tandem mass spectrometry in pesticide-residue analysis: An overview. Mass Spectrometry Reviews, 2007; 26(6): 917–960.
17. Goulas, V., Georgiou, C. A., and Mavromoustakos, T. Chromatographic and spectroscopic techniques in the analysis of pesticide residues in food and environment. In Analytical Methods in the Determination of Bioactive Compounds and Elements in Food, 2021; 115–135.

18. Fang, N., Lu, Z., Zhang, Z., Hou, Z., Liang, S., Wang, B., and Lu, Z. Determination of the novel insecticide flupyradifurone and its two metabolites in traditional Chinese herbal medicines using modified QuEChERS and high-performance liquid chromatography-tandem mass spectrometry. International Journal of Analytical Chemistry, 2020; (1): 8812797.
19. Fang, N., Zhang, C., Lu, Z., Lu, Z., Zhang, Z., Wang, B., and Zhao, X. Dissipation, processing factors and dietary risk assessment for flupyradifurone residues in ginseng. Molecules, 2022; 27 (17): 5473.
20. Feng, Y., Zhang, A., Bian, Y., Liang, L., and Zuo, B. Determination, residue analysis, dietary risk assessment, and processing of flupyradifurone and its metabolites in pepper under field conditions using LC–MS/MS. Biomedical Chromatography, 2022;36(4): e5312.
21. JMPR (Joint FAO/WHO Meeting on Pesticide Residues). (2016). Flupyradifurone. In: Pesticide Residues in Food – 2016 Evaluations. FAO Plant Production and Protection Paper 227. Rome, FAO. (Based on data submitted by Rzepka, S., 2014; Method 01330/M002)
22. EFSA (European Food Safety Authority). (2015). Conclusion on the peer review of the pesticide risk assessment of the active substance flupyradifurone (EFSA Journal, 13(8), 4192). https://doi.org/10.2903/j.efsa.2015.4192.
23. FAO (Food and Agriculture Organization of the United Nations). Submission and evaluation of pesticide residues data for the estimation of maximum residue levels in food and feed. FAO Plant Production and Protection Paper 197. Rome, Italy, 2009; https://www.fao.org/3/i0526e/i0526e00.htm
24. Wang, H., Kong, W., Yang, M., He, Y., & Hu, Y. (2012). Validation and uncertainty evaluation of a method for the determination of neonicotinoid pesticide residues in vegetables using LC–MS/MS. Journal of Separation Science, 35(11), 1376–1383. https://doi.org/10.1002/jssc.201100932
25. Dg-sanco, E. C., Guidance document on analytical quality control and validation procedures for pesticide residues analysis in food and feed., 2013; SANCO/12571.http://www.eurl-pesticides.eu/library/docs/allcrl/AqcGuidance_Sanco_2013_12571.pdf
26. Hoskins, W. M., Mathematical treatment of loss of pesticide residues. Plant Protection Bulletin, (FAO), 1961; 9:163-168.
27. Moye, H. A., Malagodi, M. H., Yoh, J., Leibee, G. L., Ku, C. C., and Wislocki, P. G., Residues of avermectin B1a in rotational crops and soils following soil treatment with (14C) avermectin B a. Journal of agricultural and food chemistry, 1987; 35(6): 859-864. DOI:10.1021/jf00078a003
28. Fantke, P. and Juraske, R. Variability of pesticide dissipation half-lives in plants. Environmental Science & Technology, 2013; 47(8):3548-3562.
29. GEMS/Food (2012). Consumption Cluster Diets WHO database.
30. Xu, Y., Shou, L. F., and Wu, Y. L., Simultaneous determination of flonicamid and its metabolites in vegetables using QuEChERS and reverse-phase liquid chromatography–tandem mass spectrometry. Journal of Chromatography A, 2011; 1218(38):6663-6666.
31. Abdel-Ghany, M. F., Hussein, L. A., El Azab, N. F., El-Khatib, A. H., and Linscheid, M. W., Simultaneous determination of eight neonicotinoid insecticide residues and two primary metabolites in cucumbers and soil by liquid chromatography–tandem mass spectrometry coupled with QuEChERS. Journal of Chromatography B, 2016; 1031:15-28.
32. Rabie, M., Ibrahim, E. D. S., Elhafny, D., and Bayoumi, M. Determination of dinotefuran and thiamethoxam residues in pepper fruits under greenhouse conditions using the QuEChERS method and HPLC/DAD. Egyptian Journal of Chemistry, 2018; 61(2): 249-257.
33. Wang, S., Jin, F., Cao, X., Shao, Y., Wang, J., She, Y., and Zheng, L. Residue behaviors and risk assessment of flonicamid and its metabolites in the cabbage field ecosystem. Ecotoxicology and Environmental Safety, 2018; 161: 420–429. https://doi.org/10.1016/j.ecoenv.2018.06.042
34. Xu, F., Du, G., Xu, D., Chen, L., Zha, X., and Guo, Z., Residual behavior and dietary intake risk assessment of flonicamid, dinotefuran and its metabolites on peach trees. Journal of the Science of Food and Agriculture, 2021; 101(14): 5842-5850.
35. Xu, M., and Hu, J. Residue analysis and dietary risk assessment of thiamethoxam, flonicamid and their metabolites in cucumber under field conditions in China. Environmental Science and Pollution Research, 2023; 30(19): 55471-55484. https://doi.org/10.1007/s11356-023-28345-3
36. Hu, X., Mei, Y., Li, X., and Chen, Y, Simultaneous Determination of Flupyradifurone and Its Metabolites in Animal-Derived Foods Using QuEChERS-UPLC-MS/MS. Food Analytical Methods, 2025; 1-9.
37. Yanqiu, C. H. E. N., Hao, L. I. N., Quanwei, X. I. A. O., Juan, S. O. N. G., Chuan, L. I. U., and Qin, D. A. I., Determination of flupyradifurone and its metabolites in milk using QuEChERS and ultra-high performance liquid chromatography-tandem mass spectrometry. Food Science, 2024; 45(12): 285-291.
38. Codex Alimentarius Commission for Pesticide Residues (CAC/PR). . List of maximum residue limits for pesticides in food and animal feeds, 2009; http://www.codexalimentarius.net.
39. Lewis, K. A., Tzilivakis, J., Warner, D. J., and Green, A., An international database for pesticide risk assessments and management. Human and ecological risk assessment: An International Journal, 2016; 22(4): 1050-1064.

40. Kaushik, G., Satya, S., and Naik, S. N. Food processing a tool to pesticide residue dissipation–A review. Food Research International, 2009; 42(1): 26-40. https://doi.org/10.1016/j.foodres.2008.09.009
41. Food Safety Commission of Japan. (2017). Risk assessment report: Flometoquin (CAS No. 875775 74 9). Food Safety, 5(3), 114–117. https://doi.org/10.14252/foodsafetyfscj.2017008s
42. Health Canada, Pest Management Regulatory Agency (PMRA). Proposed Registration Decision PRD2014-20: Flupyradifurone Technical Product and End-Use Products. Ottawa, Canada; 2015. https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/cps-spc/alt_formats/pdf/pubs/pest/_decisions/rd2015-24/rd2015-24-eng.pdf
43. Dal Bello, F., Medana, C., Guarino, B., Dioni, A., Fabbri, D., and Calza, P., Investigation of sulfoxaflor, flupyradifurone and their transformation products in plant-based food matrices. Food Control, 2022; 132, 108537.
44. Reynolds, D., Groups eye suit over new pesticide, Broadening Push For ESA Reviews. Inside EPA's Risk Policy Report, 2015; 22(11):16-16.
45. Jacobsen, R. E., Fantke, P., and Trapp, S., Analysing half-lives for pesticide dissipation in plants. SAR and QSAR in Environmental Research, 2015; 26(4): 325-342.
46. Mansour, H., El-Dars, F., and Radwan, O. Thermal and forced hydrolytic degradation studies of flonicamid and its photolysis in Egyptian clay-loam soil. Egyptian Journal of Chemistry, 2024; 67(1): 563-580.
47. Sun, S., Guo, J., Zhu, Z., and Zhou, J. Microbial degradation mechanisms of the neonicotinoids acetamiprid and flonicamid and the associated toxicity assessments. Frontiers in Microbiology, 2024; 15:1500401-1500408.
48. Moustafa, M. A., El Hefny, D. E., Alfuhaid, N. A., Helmy, R. M., El-Said, N. A. and Ibrahim, E. D. S. Effectiveness and biochemical impact of flubendiamide and flonicamid insecticides against bemisia tabaci (Hemiptera: Aleyrodidae) and residue dissipation in cherry tomato plants and soil under greenhouse conditions1. Journal of Entomological Science, 2024; 59(3): 289-310.
49. Malhat, F., Bakery, M., Anagnostopoulos, C., Youssef, M., Abd El-Ghany, W., Abdallah, A., and Abd el-salam, S. Investigation of the dissipation behaviour and exposure of spitotetramat, flonicamid, imidacloprid and pymetrozine in open field strawberries in Egypt. Food Additives & Contaminants: Part A, 2021; 38(12): 2128–2136. https://doi.org/10.1080/19440049.2021.1973113
50. Malhat, F., Anagnostopoulos, C., Bakery, M., Youssef, M., El-Sayed, W., Abdallah, A., Purnama, I., and Abd El-Salam Shokr, S. Investigation of the dissipation behaviour and exposure of flonicamid and imidacloprid in open field green beans under dry climatic conditions. International Journal of Environmental Analytical Chemistry, 2024; 104(19): 7824–7836.
51. Cao, J., Lv, Y., Qi, Y., Qin, S., Wang, X., and Li, J. Dissipation, terminal residue and dietary risk assessment of flonicamid in cabbage. International Journal of Environmental Analytical Chemistry, 2022; 104(18): 6886–6897. https://doi.org/10.1080/03067319.2022.2155050
52. Lin, H., Yang, Y., Liu, S., Liu, L., Li, Z., Li, H., and Zhang, Y. Unveiling the residual characteristic, processing, and dietary risk of flonicamid and acetamiprid in sichuan pepper production: a multisite field trial research. ACS Agricultural Science & Technology, 2024; 4(10): 980–987. https://doi.org/10.1021/acsagscitech.3c00292
53. Qin, S., and Hu, J. Fate and dietary risk assessment of pyriproxyfen, dinotefuran, and its metabolites residues in tomato across different regions in China. Environmental Science and Pollution Research, 2023; 30(3):7030-7039. doi: 10.1007/s11356-022- 22129-2.
54. Abdallah, O., Soliman, H., El-Hefny, D., Abd El-Hamid, R., and Malhat, F. Dissipation profile of sulfoxaflor on squash under Egyptian field conditions: a prelude to risk assessment. International Journal of Environmental Analytical Chemistry, 2021; 103(16): 3820-3834. https://doi.org/10.1080/03067319.2021.1915297.
55. Malhat, F., Abdallah, O., Anagnostopoulos, C., Hussien, M., Purnama, I., Helmy, RMA., Soliman, H., and El-Hefny, D. Residue, dissipation, and dietary intake evaluation of fenpyroximate acaricide in/on guava, orange, and eggplant under open field condition. Frontiers in nutrition, 2022; 9:939012. doi: 10.3389/fnut.2022.939012.