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Dissipation kinetics and dietary risk assessment of metrafenone in greenhouse-grown tomatoes and cucumbers using LC-MS/MS

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This study investigates the dissipation kinetics, terminal residues, and dietary risk assessment of metrafenone in tomatoes and cucumbers cultivated under greenhouse conditions in the Khubash governorate, Najran region, Saudi Arabia. Residue analysis was performed using a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) method with acetonitrile-based extraction. The method demonstrated excellent linearity (R^2 = 0.9981 and 0.9946 for tomatoes and cucumbers, respectively), low limits of detection (LOD: 0.0002 mg kg^{-1} and 0.0003 mg kg^{-1}, respectively), and limits of quantification (LOQ: 0.0025 mg kg^{-1} for both matrices). Recovery rates ranged from 93.6% to 98.1% and 92.7% to 99.7% for tomatoes and cucumbers, respectively, with relative standard deviations (RSDs) below 6%, ensuring method accuracy. Precision analysis demonstrated intra-day (RSD_r) and inter-day (RSD_R) repeatability below 16% for both matrices, confirming the method's repeatability. Matrix effects were minimal, with values of −6.71% and −4.15% for tomatoes and cucumbers, respectively, indicating negligible signal suppression. The dissipation followed first-order kinetics, with half-lives of 1.93–1.96 days and 1.61–1.67 days, respectively. The pre-harvest interval (PHI) was estimated at 1.18–1.56 days for tomatoes and 1.37–2.68 days for cucumbers. Terminal residues varied based on application rates and spray frequency, with some exceeding maximum residue limits (MRLs) at early intervals before declining to safe levels. Chronic dietary risk assessment confirmed that the chronic hazard quotient (HQc) values remained significantly below the safety threshold of 100%, indicating no significant health risks. These findings provide essential data for determining appropriate PHIs and ensuring food safety compliance in commercial crop production.

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1 Introduction

Tomatoes (*Solanum lycopersicum*) and cucumbers (*Cucumis sativus*) are among the most economically significant horticultural crops in Saudi Arabia, particularly under protected agriculture systems. In 2023, open-field vegetable production reached approximately 4.78 million metric tons, while greenhouse production accounted for about 613.6 thousand metric tons. Tomatoes and cucumbers constitute nearly 83% of the total greenhouse cultivation area, underscoring their importance to national food security and agricultural sustainability.[1,2]

Powdery mildew is one of the most destructive fungal diseases affecting these crops during the vegetative and early fruiting stages. Characterized by white, powdery lesions on leaves, stems, and fruits, it reduces photosynthetic efficiency, weakens plants, and leads to substantial yield losses. Greenhouse conditions—warm temperatures and high humidity—further promote the spread of the disease, making its control particularly challenging.[3–7] Management strategies include the use of resistant cultivars, optimized airflow, and the application of fungicides as needed.[8]

Metrafenone (3′-bromo-2,3,4,6′-tetramethoxy-2′,6-dimethylbenzophenone) (Fig. 1) is a benzophenone-class fungicide with both protective and curative activities, widely used to combat powdery mildew in various crops.[9,10] Although its precise biochemical mode of action remains unclear, studies have confirmed its morphological impact on fungi by inhibiting mycelial growth and preventing disease establishment.[11–13]

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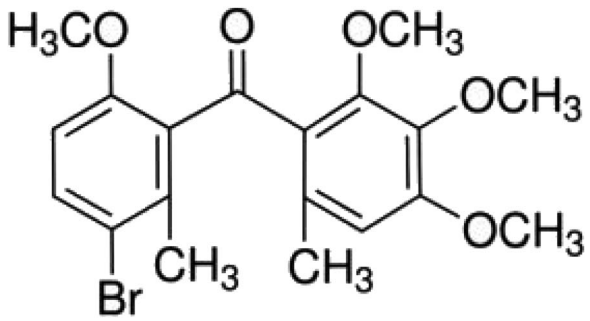

Fig. 1 Chemical structure of metrafenone.

Despite its efficacy, concerns persist regarding the persistence and accumulation of metrafenone residues in edible crops. Such residues pose potential health risks when they exceed the established safety thresholds.[14] Therefore, assessing the dissipation behavior of metrafenone is essential to determine appropriate pre-harvest intervals (PHIs), ensure compliance with maximum residue limits (MRLs), and minimize dietary exposure.[15–17]

Reliable quantification of pesticide residues in plant matrices requires analytical methods to address matrix complexity, particularly interference from pigments and waxes. This necessitates efficient sample preparation and robust detection systems to ensure high recovery and accuracy. Modern residue analysis relies heavily on validated techniques with demonstrated sensitivity, selectivity, and reproducibility.[18] Although studies on metrafenone efficacy are available,[11,13,19,20] information on its dissipation and residue behavior in tomato and cucumber crops remains scarce.

Recent advances have highlighted the effectiveness of sample preparation techniques such as QuEChERS (quick, easy, cheap, effective, rugged, and safe), in conjunction with LC-MS/MS, for multi-residue analysis.[21–23] Although gas chromatography with electron capture detection (GC-ECD) has been employed, it remains time-consuming and solvent-intensive.[24,25] The QuEChERS-UHPLC-MS/MS approach adopted by Baker *et al.* (2013) confirmed the method's utility in detecting metrafenone among 210 pesticide residues.[26]

This study aims to fill the existing knowledge gap by evaluating the dissipation kinetics of metrafenone in tomatoes and cucumbers grown under greenhouse conditions. A QuEChERS-based method using acetonitrile extraction and LC-MS/MS quantification will be employed for residue analysis. The study will assess the dissipation rate, half-life, and PHI of metrafenone at both recommended and double application rates. Furthermore, terminal residue levels and dietary exposure indicators—including national estimated daily intake (NEDI) and chronic hazard quotient (HQc)—will be analyzed to inform food safety assessments and regulatory decisions.

2 Materials and methods

2.1. Chemicals and reagents

A Metrafenone reference standard with 99.5% purity was obtained from Chem Service Inc., West Chester, PA, USA. Vivando® 500 SC, a commercial pesticide, was acquired from BASF in France. Fisher Scientific (Loughborough, UK) supplied the HPLC-grade acetonitrile and methanol. Chem-Lab NV (Zedelgem, Belgium) provided LC-MS grade formic acid, ammonium formate, analytical-grade sodium chloride (NaCl), and anhydrous magnesium sulfate ($MgSO_4$). Chrom Tech, Inc. (Apple Valley, MN, USA) supplied the Copure® ceramic homogenizer. An Evoqua Ultra Clear system, manufactured by Evoqua Water Technologies LLC (Günzburg, Germany), was used to obtain ultrapure water.

2.2. Pesticide standard preparation

A stock solution of metrafenone (1000 mg L^{-1}) was prepared by dissolving 0.0503 g in 50 mL of acetonitrile. A 100 mg per L intermediate solution was then prepared by diluting the stock solution with HPLC-grade acetonitrile, followed by further dilution to obtain a 10 mg per L working standard solution. Standard calibration solutions ranging from 0.001 to 0.50 mg L^{-1} were also prepared in acetonitrile. The proposed extraction method was applied to process tomato and cucumber samples, generating matrix blank extracts. For quantitation, matrix-matched calibration solutions were prepared using the final extracts. All standard solutions were stored at −20 °C.

2.3. LC-MS/MS

The analysis utilized a Dionex Ultimate 3000 RS UHPLC system, interfaced with a TSQ Altis Triple Stage Quadrupole (TSQ) tandem mass spectrometer (Thermo Fisher Scientific, Austin, TX, USA). Chromatographic separation was carried out using an Accucore (RP-MS) C18 column (2.6 μm, 2.1 × 100 mm) at a controlled temperature of 40 °C. The mobile phase consisted of two solvent mixtures: phase A, composed of methanol and water (95 : 5 v/v) with 0.1% formic acid and 5 mM ammonium formate, and phase B, consisting of water and methanol (95 : 5 v/v) with identical additives. The separation was performed at a flow rate of 0.3 mL min^{-1}, with each sample injection set at 2 μL. The gradient elution followed this sequence: 0–1 min at 2% B, increasing to 35% A from 1–5 min, transitioning to 98% B between 5–10 min, remaining at 98% B until 14 min, and finally re-equilibrating back to 2% B from 14.1 to 20 min.

The electrospray ionization (ESI) interface operated in selective reaction monitoring (SRM) mode for MS/MS analysis. The capillary voltage was set to 3.8 kV, with a source temperature of 300 °C and a desolvation temperature of 325 °C. Sheath and auxiliary gas flow rates were maintained at 40 and 10 Arb, respectively. For metrafenone detection, the monitored SRM transitions were m/z 409 → 209 (collision energy: 12 V) and m/z 409 → 226.9 (collision energy: 19 V), selected based on the product ion scan. These transitions were optimized to ensure maximum sensitivity and specificity. Data acquisition and analysis were performed using Trace Finder software v4.1 (Thermo Fisher Scientific Inc., Waltham, MA, USA).

2.4. Field experiment

The experiment was conducted in January 2025 in the Khubash governorate, Najran Region, southern Saudi Arabia. The study occurred in four greenhouses (10 m × 40 m each), with two

dedicated to tomato cultivation and the other two to cucumbers. Each greenhouse was subdivided into five subplots (10 m × 8 m), consisting of three plots for treatments and two as buffers. Plants were spaced 0.5 m × 0.5 m apart and grown under controlled greenhouse conditions with a drip irrigation system. Throughout the experiment, the temperature ranged from 16 to 28 °C, with humidity between 70% and 85%. Metrafenone (50% SC, Vivando®) was applied at two concentration levels: the recommended dose of 100 g a. i. per ha and a higher dose of 200 g a. i. per ha during the fruiting stage of both crops, a period characterized by active fruit growth and vulnerability to powdery mildew infection. This dose follows the registered use of metrafenone for both open-field and greenhouse cultivation, as per the manufacturer's label. Although the dose remains constant, the greenhouse environment provides a distinct setting for studying pesticide behavior due to reduced airflow and higher humidity, which may affect residue persistence. The formulation was diluted to 1000 L ha^{-1}, within the recommended spray volume range (200–1000 L ha^{-1}) specified by the manufacturer. This volume was chosen to ensure optimal spray coverage in the dense canopy structure typical of greenhouse cultivation, and applied using a knapsack sprayer. Samples (2–3 kg, $n = 3$) were randomly collected at 0 (2 h), 1, 3, 5, 7, and 10 days post-application to evaluate the dissipation pattern. For the terminal residue experiment, the pesticide applications were conducted either twice or three times at 10-day intervals. After the final application, samples were taken for laboratory analysis on days 3 and 7. All collected samples were immediately transported under controlled temperature conditions, cut into small pieces (2–3 cm), and stored at −20 °C overnight for further treatments.

2.5. Analytical procedure

A 10 ± 0.1 g portion of the homogenized frozen sample, prepared using a Stephan Universal UMS (Stephan Machinery GmbH, Hameln, Germany), was weighed into a 50 mL centrifuge tube. Then, 10 mL of acetonitrile and a ceramic homogenizer were added, and the mixture was vortexed for 2 minutes. Subsequently, 4 g of anhydrous $MgSO_4$ and 1 g of NaCl were added, followed by vortexing for 30 seconds and centrifugation at 5000 rpm for 5 minutes. A portion of the upper supernatant was filtered through a 0.22 μm syringe filter and transferred into an LC-MS/MS vial for analysis. Samples with residue concentrations exceeding the validated calibration range (0.1 mg kg^{-1}) were diluted with the corresponding blank matrix extract to fall within the 0.001–0.1 mg kg^{-1} linearity range.

2.6. Method validation

The method was validated according to the SANTE/11312/2021 guideline for linearity, limits of detection (LOD), limits of quantification (LOQ), recovery, and precision. Blank samples from untreated tomato and cucumber plots were used for validation. Linearity was assessed using a six-point calibration curve (0.001–0.1 mg kg^{-1}) by plotting detector response against concentration. The LOD was determined based on a signal-to-noise ratio of 3 : 1, while the LOQ was set at 3.3 times the LOD and confirmed through recovery (70–120%) and repeatability (<20%).[27] Method recovery was evaluated at three spiking levels (0.01, 0.1, and 1 mg kg^{-1}) with six replicates. Repeatability was determined by calculating the relative standard deviation (RSD%) at the LOQ level, with intra-day (RSD_r, $n = 6$) and inter-day (RSD_R, $n = 18$) precision measurements. Matrix effects (ME) were evaluated by comparing calibration curve slopes in pure solvent and matrix-matched solutions using eqn (1):

$$\mathrm{ME}\ (\%) = ((S_{\mathrm{matrix}} - S_{\mathrm{solvent}})/S_{\mathrm{solvent}}) \times 100. \quad (1)$$

where S_{matrix} is the slope of the matrix-matched calibration, and S_{solvent} is the slope of the in-solvent-standard calibration, ME values ranging from −20% to 20% indicate negligible matrix effects. Values between −20% and −50% or 20% and 50% suggest moderate interference. Values exceeding ±50% indicate strong matrix effects.[28]

2.7. Dissipation kinetics

A first-order kinetic model described the dissipation kinetics of metrafenone residues in tomato and cucumber. This model is represented by eqn (2):

$$C_t = C_0 \times \exp^{-kt} \quad (2)$$

where C_t represents the concentration (mg kg^{-1}) of metrafenone at time t (days), C_0 is the initial concentration (mg kg^{-1}), and k is the dissipation rate constant (per day). The goodness of fit was assessed using the correlation coefficient (R^2). The half-life ($t_{0.5}$) was calculated using eqn (3).[29] The pre-harvest interval (PHI), or the safe waiting period, was determined using eqn (4).[30–32]

$$t_{0.5} = \ln(2)/k \quad (3)$$

$$\mathrm{PHI} = (\ln C_0 - \ln \mathrm{MRL})/k \quad (4)$$

All data were expressed as mean ± standard deviation (SD). Descriptive statistical analysis, including the calculation of mean and SD, was performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA).

2.8. Chronic dietary risk assessment

The chronic dietary risk of metrafenone intake was evaluated by calculating the national estimated daily intake (NEDI) and the chronic hazard quotient (HQc) using eqn (5) and (6).[33,34]

$$\mathrm{NEDI} = \Sigma(\mathrm{STMR}_i \times F_i) \quad (5)$$

$$\mathrm{HQc} = \mathrm{NEDI}/(\mathrm{ADI} \times \mathrm{bw}) \quad (6)$$

In these equations, $STMR_i$ represents the median residue from supervised trials, while F_i denotes the average daily intake of tomato (82.87 g per day) and cucumber (19.84 g per day).[35] The term bw refers to the average adult body weight (60 kg).[36] The acceptable daily intake (ADI) for metrafenone is 0.25 mg per kg bw per day.[37]

3 Results and discussion

3.1. MS/MS optimization

An infusion-based optimization approach was utilized to achieve optimal MS/MS conditions. Initially, a precursor ion scan was performed to identify the parent ion of Metrafenone, which was observed at *m*/*z* 409.000. A Harvard infusion pump (Harvard Apparatus, South Natick, MA, USA) was used to introduce metrafenone at a concentration of 0.5 mg L^{-1}, dissolved in a 50 : 50 v/v methanol : water solution, with a constant flow rate of 5 μL min^{-1}, ensuring stable ionization and signal acquisition. The product ion spectrum revealed that the most intense fragment ions were observed at *m*/*z* 209 and 226.9, which were subsequently selected as the primary transitions for further analysis. The breakdown curve analysis demonstrated that the optimal collision energies for these transitions were 12 V for *m*/*z* 209 and 19 V for *m*/*z* 226.9, ensuring maximum fragmentation efficiency and signal intensity. Additionally, RF lens voltage optimization was performed to enhance ion transmission. The results indicated that an optimal RF lens voltage of 58 V yielded the highest signal intensity. As illustrated in Fig. 2, these optimized conditions were applied in targeted MS/MS experiments to achieve enhanced sensitivity and specificity for metrafenone detection.

3.2. Method validation

The analytical method was validated in accordance with the SANTE/11312/2021 guidelines, which require the evaluation of parameters such as linearity, matrix effects, limit of detection (LOD), limit of quantification (LOQ), recovery, precision including the relative standard deviation of intra-day repeatability (RSD_r) and inter-day reproducibility (RSD_R), selectivity, ion ratio, and retention time.

3.2.1. Sensitivity and selectivity. Sensitivity was confirmed by low LOQs and consistent detection at those levels. Selectivity was verified by analyzing blank tomato and cucumber extracts. As shown in Fig. 3, no interfering peaks were observed at the retention time of metrafenone, confirming method specificity. The method employed two selected reaction monitoring (SRM) transitions: *m*/*z* 409 → 209 (quantifier) and *m*/*z* 409 → 226.9 (qualifier). The measured ion ratio was 44.5%, which falls within the acceptable ±30% tolerance per SANTE/11312/2021 guidelines. The retention time of metrafenone was consistently 13.63 minutes (Fig. 3), with variation of less than 2% across all injections, satisfying the criteria for reliable compound identification.

3.2.2. Linearity and matrix effect. Matrix-matched calibration curves were constructed using blank tomato and cucumber extracts spiked with metrafenone at six concentration levels ranging from 0.001 to 0.1 mg kg^{-1}. The linearity of the method within this range was excellent, with R^2 values of 0.9981 and 0.9946 for tomato and cucumber, respectively (Table 1 and Fig. 3). This indicates a strong correlation between analyte concentration and detector response. The matrix effect was calculated to assess the potential influence of the sample matrix on analyte quantification. The matrix effect values were −6.71% for tomato and −4.15% for cucumber (Table 1), suggesting a minor signal suppression effect in both matrices. As demonstrated in Fig. 4, the representative chromatograms of blank and spiked samples confirm the method's reliability, showing clear peaks for metrafenone with minimal interference from the matrix.

3.2.3. LOD and LOQ. The LOD and LOQ were determined to evaluate the sensitivity and reliability of the analytical method for metrafenone residue analysis in tomato and cucumber (Table 1). The LOD values were 0.0002 mg kg^{-1} for tomato and 0.0003 mg kg^{-1} for cucumber, representing the lowest concentration at which metrafenone could be detected but not reliably quantified. The LOQ was established at 0.0025 mg kg^{-1} for both matrices, at which the recovery rates were 86.4 ± 13.4% for tomato and 84.7 ± 14.2% for cucumber, both of which fall within the acceptable recovery range of 70–120%, and the relative standard deviations (RSDs) were <20%. These results demonstrate sufficient sensitivity for detecting and quantifying metrafenone residues in tomato and cucumber samples.

3.2.4. Precision. The precision of the analytical method was evaluated at the limit of quantification (LOQ) level of 0.0025 mg kg^{-1} based on intra-day repeatability (RSD_t) and inter-day repeatability (RSD_R), as shown in Table 1. The relative standard deviations for intra-day precision (RSD_t) were 13.4% for tomato and 14.2% for cucumber, indicating a high level of repeatability within the same day. The inter-day precision (RSD_R), assessed over multiple days (3 different days with 7-day intervals), showed values of 15.2% for tomato and 15.8% for

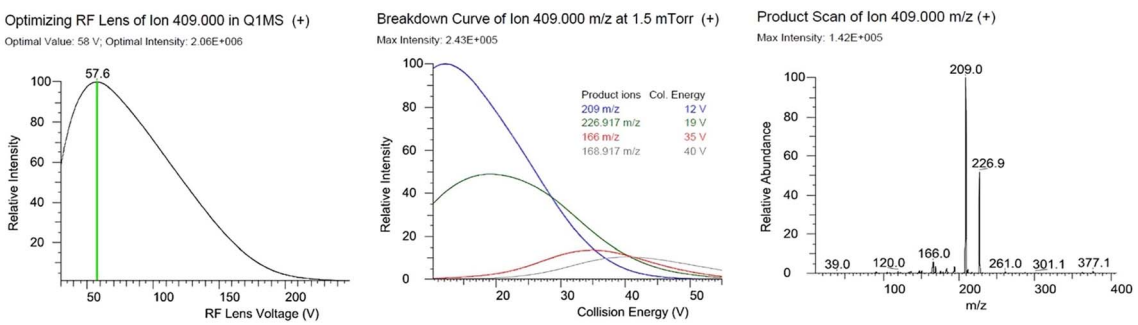

Fig. 2 Optimization of metrafenone MS/MS parameters.

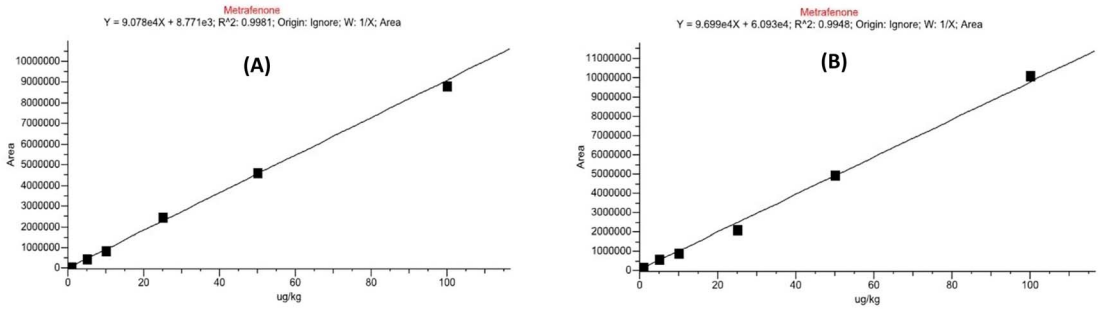

Fig. 3 Matrix matched calibration of metrafenone in tomato (A) and cucumber (B) sample extracts.

Table 1 Validation results

	Tomato	Cucumber
Range (mg kg^{-1})	0.001–0.1	0.001–0.1
R^2	0.9981	0.9946
ME (%)	−6.71	−4.15
LOD (mg kg^{-1})	0.0002	0.0003
LOQ (mg kg^{-1})	0.0025	0.0025
RSD_r ($n = 6$)[a]	13.4	14.2
RSD_R ($n = 18$)[b]	15.2	15.8
Average recoveries ($n = 6$)(%$R \pm$ RSD)		
Spiking levels (mg kg^{-1})		
0.01	93.6 ± 2.9	92.7 ± 5.4
0.1	97.5 ± 4.8	98.4 ± 3.9
1	98.1 ± 5.7	99.7 ± 2.6

[a] RSD_r: the relative standard deviation (intra-day repeatability) tested at 0.0025 mg kg^{-1}. [b] RSD_R: the relative standard deviation (inter-days repeatability) tested at 0.0025 mg kg^{-1}.

cucumber. Both RSD_t and RSD_R values were within the acceptable limit of ≤20%, confirming that the method provides reliable and reproducible results for metrafenone residue analysis in both matrices.

3.2.5. Recovery. The recovery of metrafenone from tomato and cucumber samples was evaluated at three different spiking levels (0.01, 0.1, and 1 mg kg^{-1}) to assess the accuracy and precision of the analytical method. As shown in Table 1, the recovery percentages (%R) for tomato samples ranged from 93.6% to 98.1%, while those for cucumber samples ranged from 92.7% to 99.7%, which fall within the acceptable range of 70–120%.[27] The relative standard deviations (RSDs%) were also within acceptable limits, ranging from 2.9% to 5.7% in tomatoes and 2.6% to 5.4% in cucumbers, remaining well below 20%.[27]

These results confirm that the analytical method provides reliable and accurate quantification of metrafenone residues in tomato and cucumber samples, meeting the validation criteria of the SANTE/11312/2021 guideline.

3.3. Comparative evaluation of method performance with published LC-MS/MS studies

To further validate the robustness and applicability of our analytical method, a comparative evaluation was conducted with previously published studies reporting LC-MS/MS-based methods for pesticide residue analysis in vegetables. Table 2 summarizes key figures of merit, including limits of detection (LOD), limits of quantification (LOQ), recovery rates, relative standard deviations (RSD), and matrix effects. Our method demonstrated superior sensitivity, with LOQ values of 0.0025 mg kg^{-1} for both tomato and cucumber, and high recovery rates (92.7–99.7%) with low RSD values (<6%), indicating excellent precision and accuracy. Compared to Ko *et al.* (2016), Kabir *et al.* (2015), and Kim *et al.* (2021), the performance of our method is comparable or better in most parameters.[38–40] Additionally, matrix effects were negligible (−6.71% for tomato and −4.15% for cucumber), falling within the acceptable range, confirming minimal ion suppression or enhancement. These comparisons further substantiate the method's suitability for routine monitoring of metrafenone residues in complex food matrices under greenhouse conditions.

3.4. Dissipation behaviour of metrafenone residues in tomato and cucumber

The initial pesticide deposits on tomatoes were 0.407 ± 0.134 mg kg^{-1} for the recommended dose (100 g a. i. per ha) and 0.853 ± 0.126 mg kg^{-1} for the double recommended dose (200 g a. i. per ha). Over time, the dissipation percentage increased steadily, indicating a reduction in residue levels. After one day, 26.78% of the pesticide had dissipated from the recommended dose, while 21.10% had dissipated from the double dose. By the third day, dissipation rose to 49.88% and 46.54%, signifying that nearly half of the pesticide had broken down. A sharp decline was observed by seven days, with dissipation reaching 85.75% for the recommended dose and 82.88% for the double dose. By ten days, dissipation was nearly complete, with 94.59% and 94.26% of the pesticide degraded from the respective doses (Fig. 5). The initial pesticide deposits on cucumbers were 0.819 ± 0.346 mg kg^{-1} for the recommended dose (100 g a. i. per ha) and 1.441 ± 0.421 mg kg^{-1} for the double recommended dose (200 g a. i per ha). Over time, the dissipation percentage increased, indicating a rapid reduction in residue levels. After one day, 34.19% of the pesticide had dissipated from the recommended dose, while 36.09% had dissipated from the double dose. By three days, dissipation rose to 67.40% and 70.09%, respectively, demonstrating that over two-thirds of the initial

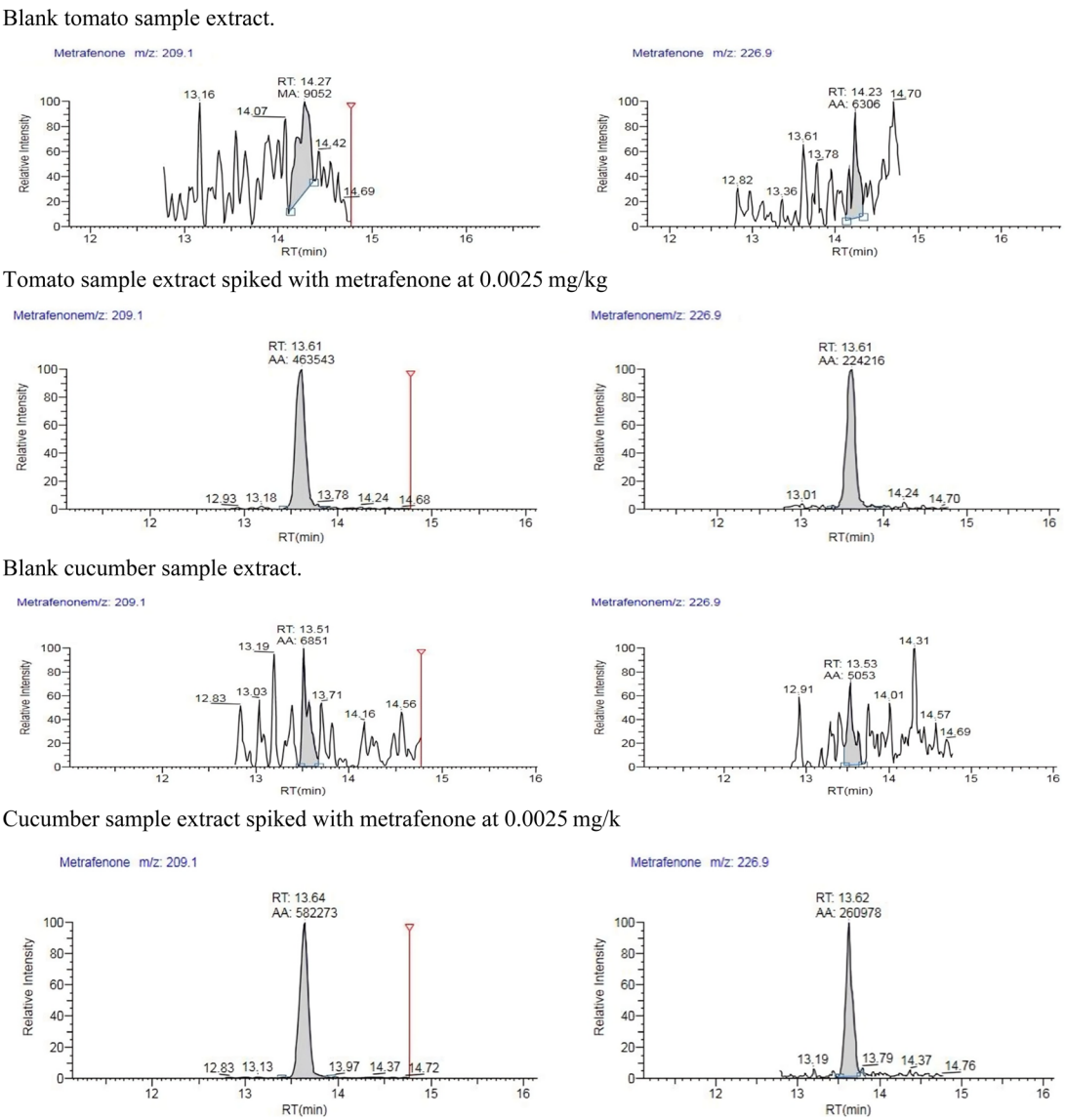

Fig. 4 Representative LC-MS/MS chromatograms of metrafenone in blank and spiked tomato and cucumber sample extracts.

pesticide had degraded. A sharp decline was observed by seven days, with dissipation reaching 89.99% for the recommended dose and 92.02% for the double dose. By ten days, the dissipation was nearly complete, with 98.05% and 98.40% of the pesticide breaking down from the respective doses. The dissipation kinetics of metrafenone in cucumbers and tomatoes followed first-order kinetics, as evidenced by the high regression coefficient (R^2) values ranging from 0.9863 to 0.9951 (Table 2), confirming a firm fit to the first-order kinetic model. The dissipation rate was faster in cucumbers, with a shorter half-life (1.61–1.67 days) compared to tomatoes (1.93–1.96 days) and a higher dissipation rate constant (k) of 0.3755–0.3983 in cucumbers *versus* 0.2825–0.2903 in tomatoes (Table 3).

Fantke *et al.* emphasized that dissipation variability is not only compound-specific but also crop-dependent, influenced by a combination of physiological (*e.g.*, water content, surface-to-

Table 2 Comparative performance metrics of the developed LC-MS/MS method *versus* published studies in vegetable matrices

Matrix	LOD (mg kg^{-1})	LOQ (mg kg^{-1})	Recovery (%)	RSD (%)	Matrix effect (%)	Study
Tomato/cucumber	0.0002/0.0003	0.0025	92.7–99.7	<6	−6.71/−4.15	This study
Green pepper	0.002	0.006	89.4–95.2	<10	−13.2	Ko *et al.*, 2016 (ref. 38)
Lettuce	0.001	0.005	88.1–94.7	<15	−12.6	Kabir *et al.*, 2015 (ref. 39)
Tomato	0.003	0.010	86.3–91.9	<12	−8.4	Kim *et al.*, 2021 (ref. 40)

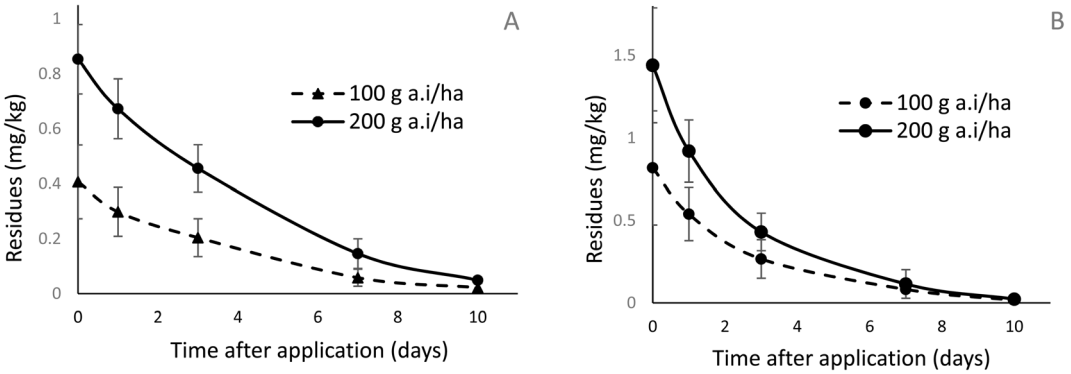

Fig. 5 Dissipation of metrafenone in tomato (A) and cucumber (B) at 100 and 200 g a. i. per ha, ($n = 3$, error bars represent ± standard deviation).

volume ratio), morphological (*e.g.*, wax layer thickness), and environmental factors (*e.g.*, temperature, relative humidity, and light exposure). Crops like cucumbers with high moisture content and thin cuticle layers show faster dissipation due to enhanced diffusion and metabolic breakdown. In contrast, depending on cultivar structure, crops like lettuce or tomatoes may exhibit slower degradation rates due to protective surface characteristics.[41] These mechanisms directly support our findings and explain the observed difference in half-life between cucumbers and tomatoes in this study.

Recent studies have provided insights into the dissipation behavior of metrafenone in various crops. Hur *et al.* (2015) reported that metrafenone exhibited a half-life of approximately 2.5 days in cherry tomatoes, adhering to first-order kinetic models.[42] Similarly, Shin *et al.* (2021) observed that in sweet peppers, the dissipation rate of metrafenone varied among different cultivars, emphasizing the influence of plant variety on pesticide residue dynamics.[43] These findings align with our observations in tomatoes and cucumbers, where metrafenone demonstrated rapid degradation, ensuring residue levels decline below established Maximum Residue Levels (MRLs) within a short period. Furthermore, EFSA's comprehensive assessment (2013) corroborates these results, confirming that metrafenone residues in tomatoes and cucumbers dissipate effectively, posing minimal risk to consumers when used according to recommended guidelines.[44]

The physicochemical properties of metrafenone play a critical role in its dissipation behavior. With a water solubility of 0.492 mg L^{-1} at 20 °C, a log *P* value of 4.3, a vapor pressure of 0.153 mPa, and a Henry's law constant of 1.32×10^{-1} at 25 °C,[45] metrafenone exhibits moderate hydrophobicity and low volatility. This suggests that dissipation is primarily governed by plant absorption, enzymatic degradation, and environmental interactions rather than volatilization. The observed differences in dissipation rates between cucumbers and tomatoes highlight the influence of both crop-specific morphological characteristics and the physicochemical nature of metrafenone on pesticide residue behavior. Kabir *et al.* (2015) reported that metrafenone residues in lettuce followed first-order kinetics, with half-lives ranging from 2.3 to 5.0 days, depending on seasonal variations.[39] In this study, the dissipation half-lives in tomatoes (1.93–1.96 days) and cucumbers (1.61–1.67 days) were shorter, indicating a faster degradation rate in these crops. The differences in dissipation rates can be attributed to crop-specific factors, such as surface morphology, water content, and enzymatic activity.[41,46] Lettuce may retain pesticide residues longer with a denser leaf structure and lower surface-to-volume ratio.[47] In contrast, cucumbers exhibit more rapid dissipation with their high water content and thin cuticles. The PHI values were determined using eqn (4), which accounts for the relationship between the MRL, initial residue concentration, and dissipation rate constant. Based on this calculation, the PHI values were 1.18–1.56 days for tomatoes and 1.37–2.68 days for cucumbers (Table 3), aligning with the observed data and confirming the need for a longer PHI in cucumbers despite their faster dissipation. This discrepancy is likely due to regulatory safety margins that ensure residues fall below the MRL before harvest. Additionally, the MRL for metrafenone is lower in cucumbers (0.5 mg kg^{-1}) than in tomatoes (0.6 mg kg^{-1}), which may be influenced by multiple factors. Dietary consumption patterns play an essential role, as cucumbers are typically eaten fresh with the skin, increasing potential pesticide exposure, whereas tomatoes are often peeled or processed, reducing residue intake.

Table 3 Dissipation kinetics and PHI of metrafenone in tomato and cucumber at different application rates

	Tomato		Cucumber	
	100 g a. i. per ha	200 g a. i. per ha	100 g a. i. per ha	200 g a. i. per ha
$t_{0.5}$ (days)	1.93	1.96	1.67	1.61
R^2	0.9951	0.9901	0.9863	0.9917
K (per day)	0.2903	0.2825	0.3755	0.3983
C_0 (mg kg^{-1})	0.4259	0.9329	0.8371	1.4534
PHI (days)	1.18	1.56	1.37	2.68

3.5. Terminal residues

The terminal residue concentrations of metrafenone in tomatoes and cucumbers were influenced by the applied dosage, number of

applications, and time elapsed after spraying. As shown in Table 4, residue levels followed a dissipation pattern consistent with first-order kinetics, gradually decreasing over time. In tomatoes, residues at 100 g a. i. per ha ranged from 0.306–0.624 mg kg^{-1} at 3 days, decreasing to 0.093–0.154 mg kg^{-1} at 7 days, depending on the number of applications. At 200 g a. i. per ha, residues varied between 0.681–0.781 mg kg^{-1} at 3 days, declining to 0.208–0.401 mg kg^{-1} at 7 days. Similarly, in cucumbers, residues at 100 g a. i. per ha ranged from 0.413–0.769 mg kg^{-1} at 3 days, reducing to 0.152–0.234 mg kg^{-1} at 7 days. At 200 g a. i. per ha, residues were recorded between 0.717–0.833 mg kg^{-1} at 3 days, dropping to 0.314–0.568 mg kg^{-1} at 7 days. Some residue levels initially exceeded the maximum residue limits (MRLs) of 0.6 mg kg^{-1} for tomatoes and 0.5 mg kg^{-1} for cucumbers, particularly under higher dosage and multiple applications.

3.6. Risk assessment

The risk assessment of metrafenone residues was evaluated based on the National Estimated Daily Intake (NEDI) and the Hazard Quotient (HQc) (Table 4), which measure the potential dietary risk associated with residue consumption. Across all treatments, NEDI values ranged from 0.423 to 1.08 μg per kg bw in tomatoes and 0.137 to 0.275 μg per kg bw in cucumbers, reflecting dosage and spray frequency variations. The HQc values remained below the regulatory safety threshold of 100%, with tomatoes ranging from 0.169–0.431% and cucumbers from 0.055–0.110%. Metrafenone residues in cucumbers were higher than in tomatoes at corresponding time points, particularly at higher application rates and multiple sprays. This suggests that cucumbers retained more pesticide, which may be attributed to higher initial deposits (C_0) and differences in surface properties, including wax composition and cuticle structure. Despite cucumbers exhibiting a faster dissipation rate, the higher initial residues sometimes resulted in elevated terminal concentrations. However, residue concentrations declined over time due to the growth dilution effect, eventually reducing dietary exposure. Although some terminal residue levels exceeded the MRLs of 0.6 mg kg^{-1} for tomatoes and 0.5 mg kg^{-1} for cucumbers, the HQc values remained within the safe limit, indicating negligible dietary risk even at the highest application scenarios.

4 Conclusion

This study presents a comprehensive assessment of metrafenone residues in greenhouse-grown tomatoes and cucumbers, with a focus on dissipation kinetics, terminal residues, and dietary risk evaluation. The LC-MS/MS method employed, based on acetonitrile extraction, was rigorously validated, demonstrating excellent sensitivity, accuracy, and precision, thereby confirming its suitability for routine pesticide residue monitoring. Dissipation followed first-order kinetics, with notably shorter half-lives in cucumbers (1.61–1.67 days) compared to tomatoes (1.93–1.96 days), reflecting a faster degradation rate in cucumbers. Pre-harvest intervals (PHIs) were estimated at 1.18–1.56 days for tomatoes and 1.37–2.68 days for cucumbers, ensuring compliance with food safety standards before harvest. While some residue concentrations initially exceeded maximum residue limits (MRLs), they declined to acceptable levels over time. Chronic dietary risk assessment confirmed that hazard quotient (HQc) values remained substantially below the 100% safety threshold, indicating no significant health risk to consumers. These findings provide essential evidence to inform PHI recommendations and regulatory decisions, reinforcing food safety assurance in commercial tomato and cucumber production. Nevertheless, certain limitations warrant consideration. The study was conducted in a single agro-climatic zone (Khubash, Saudi Arabia), which may constrain the broader applicability of the results to other environmental conditions. Moreover, potential degradation products and the environmental fate of metrafenone were not evaluated. Future research should expand the geographic scope of field trials and include metabolite profiling to enable a more comprehensive and regionally relevant risk assessment framework.

Table 4 Terminal residues and dietary risk assessment of metrafenone in tomato and cucumber

Commodity	Dosage (g a. i. per ha)	Number of times sprayed	Days after spraying	Mean residues (mg kg^{-1})	SD	NEDI (μg per kg bw)	HQc (%)
Tomato	100	2	3	0.306	0.088	0.423	0.169
			7	0.093	0.026	0.128	0.051
		3	3	0.624	0.146	0.862	0.345
			7	0.154	0.021	0.213	0.085
	200	2	3	0.681	0.241	0.941	0.376
			7	0.208	0.053	0.287	0.115
		3	3	0.781	0.203	1.080	0.431
			7	0.401	0.133	0.554	0.222
Cucumber	100	2	3	0.413	0.171	0.137	0.055
			7	0.152	0.063	0.050	0.020
		3	3	0.769	0.151	0.254	0.102
			7	0.234	0.061	0.077	0.031
	200	2	3	0.717	0.191	0.237	0.095
			7	0.314	0.076	0.104	0.042
		3	3	0.833	0.257	0.275	0.110
			7	0.568	0.111	0.188	0.075

Abbreviations

QuEChERS	Quick, easy, cheap, effective, rugged, and safe
MRL	Maximum residue limit
ADI	Acceptable daily intake
NEDI	National Estimated Daily Intake
LOQ	The limit of quantitation
ME%	Matrix effect percent
$STMR_i$	The median final residue obtained from the supervised trials (mg kg^{-1})
F_i	The average daily per capita consumption (kg per day)
SRM	Selective reaction monitoring
SC	Suspension concentrate
PHI	Pre-harvest interval
HQc	Chronic hazard quotient

Data availability

The data associated with this article have been included in the manuscript.

Author contributions

Osama I. Abdallah and Jari S. Algethami: conceptualization, methodology, and investigation. Osama I. Abdallah, Mohamed F. Ramadan, and Eid H. Alosaimi: formal analysis, data curation, writing – original draft. Jari S. Algethami and Abdulhadi H. Al-Marri: editing and visualization. Mohsen A. M. Alhamami: supervision, project administration, and funding acquisition.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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