Original Research Article

Residue analysis and dissipation study of dinotefuran in paddy field using a UHPLC-MS/MS method and risk assessment

Abstract: Dinotefuran is widely utilized to control sucking insect pests in rice crops due to its high efficiency and relatively low hazard potential. However, repeated applications within a single crop season raise concerns about residue deposition in plants and surrounding environment. Therefore, thecurrent study was executed tounderstand the degradation of foliar sprayed dinotefuran in paddyfield after one, two and three application frequenciesin a modified QuEChERS method and analysis using UHPLC-MS/MS. The method was linear with corresponding correlation coefficient (R^2) > 0.99.The method achieved recovery rates of 78.11-109.30% in plant matrices and 70.93-75.50% in soil matrices at spiking concentrations of 0.01, 0.05 and 0.10 µg g^{-1}. Precision, expressed as repeatability (RSD_r), ranged from 1.99-6.99% in plant matrices and 1.09-4.06% in soil matrices and intra-laboratory precision expressed as Horwitz ratio (HorRat) was within 0.3. In the field trial, dinotefuran showed rapid dissipation rates in rice, with half-lives ranging from 1.62 to 2.21 days in leaves and 7.05 days in grains after different application frequencies. No residues were detected in the soil samples regardless of the application frequencies from the 0th day itself.Significant differences in residue levels were not observed amongdifferent application frequencies attributed to similar environmental conditions during the growing period. As residues in leaves were below the maximum residue limit on the initial day of application, no waiting period is recommended.All harvested samples were free of residues. Dietary risk assessment indicated that the risk quotient values were below 1, suggesting low risks for consumers.

Keywords: Dinotefuran, rice, soil, repeated applications, dissipation, half-lives, risk assessment

1. INTRODUCTION

Neonicotinoids have emerged as one of the most extensively utilized categories of insecticides, capturing over 25% of the global market and is considered rapidly growing pesticide group[1]. Dinotefuran is a third-generation nitroguanidine neonicotinoid insecticide belonging to the furanicotinyl sub-class discovered and commercialized by Mitsui Chemicals Inc., Japan [2]. It acts as a competitive modulator of nicotinic acetylcholine receptors (nAChRs) of the central nervous system causing receptor blockage, paralysis and death of insects [3,4]. The pesticide properties database (PPDB) has confirmed that dinotefuran is highly mobile with moderate persistence in soil due to very high water solubility of 39.83 g l^{-1}, low vapour pressure of 0. 0017 mPa, Henry's law constant of 8.63 x 10^{-14}atm m^3 mol^{-1} and octanol water-partition coefficient (K_{ow}) of -0.549. It has very low toxicity to natural enemies like spiders, mirid bugs and coccinellids [5], moderately toxic to sediment organisms [6]but highly toxic to honey bees[7] and earthworms[8]. The compound has proven to be the best alternative to conventional insecticide products of carbamates, organophosphates and synthetic pyrethroids. It is widely adopted for controlling disease vectors like mosquitoes besides being utilised primarily for agricultural sucking insects [9]. In India, Central Insecticide Board and Registration Committee (CIBRC) have registered dinotefuran for managing brown plant hopper (BPH) in rice as well as

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whitefly, jassids, aphids and thrips in cotton [10].Rice is attacked by monophagous BPH at different life stages leading to burned appearance of the plant called 'hopper burn' which are visible only at the later stage[11].Insecticide becomes the sole dependable choice for urgent control when insect pest populations reach or exceed the economic threshold level. Dinotefuran is highly recommended for protecting the paddy crop from BPH due to their relatively safe nature [5]. However, inappropriate and repeated application of dinotefuran in rice cultivation has led to residual accumulation in the environment and cereal grains, posing significant risks to human health and quality of life. Moreover, it adversely impacts biodiversity by harming beneficial organisms and reducing the efficacy of natural pest enemies [12,13,14].However, studies on dinotefuran dissipation behaviour and risk assessment in paddy field ecosystem are very less under Indian climatic conditions [15]. Hence, a thorough understanding of the dissipation kinetics of dinotefuran and assessing the dietary intake risk is crucial for ensuring food safety and maintaining ecological balance in paddy fields. Therefore, the present study was conducted to determine the dissipation pattern of dinotefuran in paddy plants and soil as well as to assess the risk to the general Indian population.

2. MATERIALS AND METHODS

2.1 Chemicals and solvents

Dinotefuran standard ($C_7H_{14}N_4O_3$)with a purity of 99.25 % was obtained from Biostadt India Limited, Mumbai. Acetonitrile (ACN), methanol and sodium chlorideof HPLC grade, sodium sulfate of GR grade and magnesium sulfate heptahydrate of AR grade were supplied by Merck Specialities Pvt. Ltd, Mumbai. The procured salts were activated in a muffle furnace at 400°C for 4 hours before use. Primary Secondary Amine (PSA) was bought from Agilent Technologies, USA. Distilled water was obtained from an Elga water purification system. Commercial formulation of dinotefuran available as Token 20% soluble granules (SG), was provided by a retail shop. Standard stock solution of dinotefuranwas prepared at a concentration of 400 µg ml^{-1} in methanol. Intermediate standard solution of 100 µg $ml^{-1}$was prepared from stock solution and working standard solutions of 0.1-10 µg ml^{-1} were prepared from intermediate standard by serial dilution with methanol.Matrix-matched standards were prepared by incorporating extracts from untreated rice leaves, straw, grains and soil into each serially diluted standards.The standards were stored at -20°C.

2.2 Field trials

Experiments on the residue determination and dissipation kinetics of dinotefuran were conducted in 2022 at the Integrated Farming Systems Research Station in Karamana, Kerala. The initial soil properties were determined before conduction of the experiment which included texture, bulk density (BD), particle density (PD), porosity, pH, electrical conductivity (EC) andorganic matter (OM)[16,17,18,19]. The study included four treatments: three different application frequencies (25, 50 and 75 DAT) of dinotefuran and one control treatment. Each treatment was implemented in four 20 m² plots, separated by buffer zones and all plots received standard care. Dinotefuran, in a 20 % soluble powder form was uniformly applied at a rate of 30 g ha^{-1} using a knapsack sprayer on the rice plants at 25, 50 and 75 days after transplanting. The control plots were sprayed with water. Plant samples were collected at intervals of 2 hours, 1, 3, 5, 7, 10, 15, 20 and 25 days post-application to analyse the pesticide's dissipation pattern.

2.3 Sample preparation

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The pretreatment was performed following a QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe) method with slight modifications [20]. A 10-g sample of soil was weighed into a 50-ml polypropylene centrifuge tube, 20 ml of ACN was added and the mixture was vortexed for a min. To this, 4 g of anhydrous magnesium sulfate and 1 g of sodium chloride were added, vortexed for a min and centrifuged at 3300 rpm for 4 min. A 10-ml aliquot of the supernatant was transferred to a 15-ml centrifuge tube prefilled with 0.25 g PSA and 1.5 g anhydrous magnesium sulphate, vortexed for a min and centrifuged at 4400 rpm for 10 min. Afterwards, 4 ml of the aliquot was transferred to a turbo tube and evaporated in nitrogen stream in turbovap at 40 °C. The dry residues were rehydrated to 1 ml in methanol and filtered through 0.22 µm microporous filter before LC-MS/MS analysis.

Dinotefuran was extracted from blended leaf sample by adding 30 ml of ACN and 6 g of sodium chloride to 15 g of leaf sample in 250-ml centrifuge bottle. The bottles were shaken and centrifuged at 4500 rpm for 5 min. Aliquots obtained were decanted to 50-ml centrifuge tube readily loaded with 6 g of sodium sulphate and vortexed for 1 min followed by further decantation to 15-ml centrifuge tube having0.2 g of PSA and 1.2 g of magnesium sulphate. The tubes were then centrifuged at 8000 rpm for 8 minutes. To grain (25 g) sample, 25 ml of distilled water, 50 ml of ACN and 12 g of sodium chloride were added. The components were shaken for 30 min and subjected to centrifugation. Aliquot (16 ml) from this was decanted to 50-ml tube having 2 g each of magnesium and sodium sulphate, vortexed and centrifuged. The contents were further pipetted to 15-ml tube prepacked with 0.1 g PSA and 0.75 g magnesium sulphate and centrifuged.In the case of straw, to 5 g of sample, 40 and 50 ml of distilled water and ACN, respectively were added to 250-ml bottle followed by 10 g of sodium chloride and the mixture was shaken for 5 min and centrifuged. The decanted liquid to about 25 ml was transferred to 50 ml tube containing 5 g of sodium sulphate, vortexed and centrifuged. A 10 ml liquid from this was poured to 15-ml tube preloaded with 2 g of anhydrous magnesium sulphate and 0.125 g of PSA. The samples were vortexed and centrifuged. All centrifugation was done at 8000 rpm for 8 min.A 3 ml of centrifuged extracts of leaf, grain and straw samples were concentrated using turbovap and rehydrated with methanol to 1 ml for analysis.

2.4 LC-MS/MS conditions

The chromatographic determination was performed with a Dionex Ultimate 3000 UHPLC system (Thermo Scientific, Germany) equipped with aThermo Scientific, AccucoreaQ (100 mm x 2.1 mm, 2.6 µ particle size) column and TSQ Quantiva mass spectrometer (Thermo Scientific, US). The mobile phase was operated in binary mode which consisted of 5 mM ammonium formate and 0.1% formic acid (v/v) in water (A) and in methanol (B) with a flow rate of 0.3 ml min^{-1}. The elution was performed using a gradient method with the following steps: from 0 to 0.5 minutes, eluent B was maintained at 2%; from 0.5 to 2 minutes, eluent B was increased to 60%; from 2 to 8 minutes, eluent B was further increased to 95%; from 8 to 9 minutes, eluent B was held at 95%; from 9 to 9.1 minutes, eluent B was decreased back to 2%; and from 9.1 to 10 minutes, eluent B was kept at 2%. The column temperature was set at 30°C, and the sample temperature was maintained at 10°C.The parameters of MS detection were as follows: ion transfer tube temperature of 350°C and vapourizer temperature of 450°C. Sheath gas, auxiliary gas and sweep gas were maintained at 60, 5 and 1 respectively, in arbitrary units with a dwell time of 158.06 milli seconds. The multiple reaction monitoring (MRM) model was selected with heated electrospray ionisation (H-ESI) in positive ionisation mode was used for quantification.

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The chromatogram and mass spectrum parameters of dinotefuran are portrayed in Table 1 and Fig. 1.

Table 1. LC-MS/MS conditions of dinotefuran

Target compound	Polarity	Precursor ion (m/z)	Daughter ion (m/z)	Collision energy (V)	Retention time (min)
Dinotefuran	Positive	203.085	129.186 (Q)	21.00	3.09
			112.238 (C)	15.00	

Q: Quantitative ion; C: Confirmatory ion.

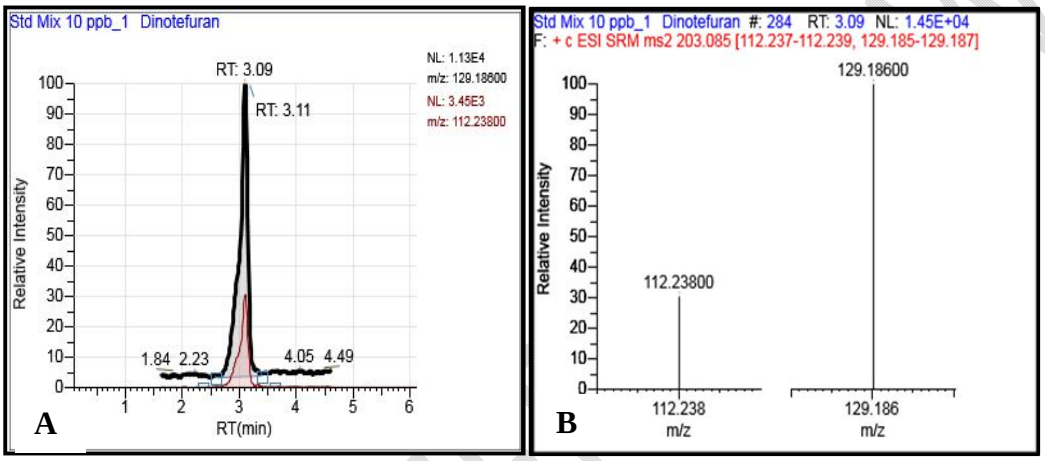

Fig. 1. A) LC chromatogram and B) Mass spectrum of dinotefuran

2.5 Method performance evaluation

The performance of the developed method was verified using the parameters of linearity, sensitivity, recovery and precision [21,22,23]. The linearity of the method was calculated by preparing calibration curves of dinotefuran in each matrices within the concentration range from 0.003-1µg g^{-1}.Sensitivity test was done by detecting LOD (limit of detection) and LOQ (limit of quantification). LOD is the lowest concentration of the chemical that can be detected in the experiment, whereas LOQ is the lowest concentration that can be detected with acceptable recovery (70-120%) and precision (≤20%). Fortified rice leaf, grain and soil samples were prepared using the standard solution of dinotefuran to afinal concentration of 0.01, 0.05 and 0.10 µg g^{-1}which were used for conducting recovery tests.Repeatability was evaluated through percent relative standard deviation (RSD) which was determined by comparison of standard deviation (SD) of recovery samples[21]. The horwitz ratio (HorRat), a measure of precision was determined as described by [22,23].

2.6 Statistics

Nonlinear regression was used for describing the degradation curves in each matrix. The kinetics of dinotefuran dissipation in rice leaf and grain were worked out using first-order kinetics model: $C_t = C_0e^{-kt}$, where C was the dinotefuran residual concentration (µg g^{-1}), C_0 was the dinotefuran residual concentration at the initial time (t) in daysand k is the first-order reaction rate constant [24]. The correlation coefficient (R^2) illustrates the extent of fitness between data and kinetic

equation. The half-life ($t_{1/2}$) was obtained from the regression equation and is defined as thetime needed for dissipation of half of the initial resides [25].

Risk assessment of Indian population was determined by working out risk quotient (RQ). RQ was obtained as a ratio of estimated daily intake (EDI) and acceptable daily intake (ADI). ADI of dinotefuran was fixed at0.2 mg kg^{-1}bw[26] whereas EDI was obtained by dividing the highest residue levels found in paddy grains on specific days by the grain intake rate (300 g) and mean body weight of Indian adult (60 Kg) [27,28,29]. RQ values less than 1 signify acceptable risk, whereas values more than 1 depict unacceptable risk levels [30,31].

3. RESULTS AND DISCUSSIONS

3.1 Initial analysis of soil

The texture of the soil was determined to be sandy clay loam with sand, silt and clay percent of 56.28, 14.30 and 29.42, respectively. The BD and PD of the soil were 1.42 and 2.50 Mg m^{-3}. Porosity percent of the field soil was 43.20 %. The soil was strongly acidic with a pH of 5.05 and non-saline with an EC of 0.20 dS m^{-1}. The OM content of the soil was 1.59%.

3.2 Method performance evaluation

Satisfactory linearity was achieved with correlation coefficients (R^2) of 0.9953 for rice leaf, 0.9999 for grain, 0.9993 for straw and 0.9993 for soil matrices, based on the measurement of analyte peak areas. The LOD and LOQ of the developed method were 0.003 and 0.01 µg g^{-1}.This LOQ value meets the maximum residue limit requirements set by FSSAI for dinotefuran in rice crops and higher than the LOQs reported by [32]of 0.05 µg g^{-1}using HPLC-MS/MSas well as by [33]of 0.5 µg g^{-1}using HPLC in rice for dinotefuran. Recovery rates within permissible limits were obtained for dinotefuran in the ranges of 87.61-109.30, 78.11-108.82, 95.81-109.21, and 70.93-75.50% with associated RSDs of 1.99-3.86, 2.12-6.99, 2.44-6.61 and 1.09-4.06% respectively in rice leaf, straw, grain and soil matrices. TheHorRat values were below 0.3 at all spiking levels.Since the repeatability was performed over a shorter period, not all variability parameters were accounted for. This could explain the very low HorRat values [23].The results of the method performance were demonstrated in Table 2.

Table 2. Method validation parameters of dinotefuran in rice and soil matrices

Matrix	Accuracy and Precision (n = 5)				Linearity		Sensitivity
	Spiked level (µg g^{-1})	Recovery(%) ± SD	RSD (%)	Horwitz ratio	Equation	R^2	LOQ (µg g^{-1})
Leaf	0.01	78.11 ± 5.23	6.99	0.21	Y = 2.156x + 9.947	0.9953	0.01
	0.05	108.82 ± 5.70	5.24	0.21			
	0.10	87.95 ± 1.87	2.12	0.09			
Grain	0.01	109.21 ± 7.22	6.61	0.21	Y =1.769x – 7.609	0.9999	0.01
	0.05	95.81 ± 2.34	2.44	0.10			
	0.10	105.10 ± 5.75	5.47	0.25			
Straw	0.01	109.30 ± 2.71	2.48	0.08	Y = 1.949x+ 6.353	0.9993	0.01
	0.05	87.61 ± 1.74	1.99	0.08			
	0.10	90.77 ± 3.50	3.86	0.17			
Soil	0.01	75.50 ± 2.72	3.61	0.11	Y = 2.369x + 6.302	0.9993	0.01
	0.05	70.93 ± 0.77	1.09	0.04			

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0.10	72.84 ± 2.96	4.06	0.17

SD: Standard deviation; RSD: Relative standard deviation; R2: Correlation coefficient; LOQ: Limit of quantification.

3.3Field experiment

3.3.1 Dissipation kinetics

Dinotefuran applied at the field recommended concentration produced maximum residues in the range of 2.56-3.48 µg g^{-1} after 2 hours. Similarly, [13]reported initial residues in the range of 2.84 – 3.12in paddy plants. The dissipation rates were about 30 and 90 % on the 1st and 10th day after spray, respectively. Residues were not detected on the subsequent days. The nature of dissipation kinetics were consistent with first-order reaction with DT_{50} of 1.62-2.21 days after three sprays (Table 3 and Fig. 2). In previous literatures, similar DT_{50} of around 2 days were recorded for dinotefuran in rice plants [13,15,34]. Dinotefuran sprayed samples were found suitable for fodder purpose immediately after spraying as the residue levels on 0th day itself were less than the MRL value. Following the harvest, there were no traces of residues found in the straw samples from any of the treatment groups.

In soils, residues were not detected on any sampling days irrespective of different application frequencies (Table 3). Insecticides were given toward the closely spaced rice plants as foliar spray, so much of the residues were found concentrated in the plant system during the initial days. [35] reported dinotefuran applied to grapevine was not found during the first day in soil, however, residual concentration increased later on by leaching of residue from plants.In the present study, residues were not detected in the soil even after the first day. This can be attributed to the highly soluble and systemic properties of dinotefuran as well as very low K_{ow} values resulting in poor adsorption to soil components which can increase the mobility and leaching of dinotefuran to deeper soil depths [36]. This characteristic likely leads to quicker movement and degradation of dinotefuran in flooded paddy soil.[35] reported dinotefuran exhibited more rapid degradation in acid soil than in alkaline soil. Thus, strongly acidic pH and sandy nature of soils of the studied soil facilitated a more rapid movement and dissipation of chemicals. This shows that along withinsecticide nature, the soil propertieslike soil type, moisture content, drainage, pH, soil organic matter (SOM) and humus play dominant role in determining the persistence of dinotefuran in soils [37-41].

Table 3 Residue dissipation and reaction rate parameters of flonicamid in rice leaf and soil at different frequencies of application

DAS	Residues (µg g^{-1}) ± SD in leaf (n = 4)			Residues (µg g^{-1}) ± SD in soil (n = 4)		
	Single spray	Double spray	Triple spray	Single spray	Double spray	Triple spray
0	2.56 ± 0.07	3.06 ± 0.07	3.48 ± 0.54	BLQ	BLQ	BLQ
1	1.95 ± 0.17	2.13 ± 0.08	2.22 ± 0.37	BLQ	BLQ	BLQ
3	0.74 ± 0.06	1.48 ± 0.08	1.02 ± 0.12	BLQ	BLQ	BLQ
5	0.33 ± 0.03	0.80 ± 0.14	0.43 ± 0.07	BLQ	BLQ	BLQ
7	0.12 ± 0.01	0.42 ± 0.04	0.17 ± 0.03	BLQ	BLQ	BLQ
10	0.04 ± 0.02	0.12 ± 0.02	0.08 ± 0.01	BLQ	BLQ	BLQ
15	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
20	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
25	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ

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Harvest	BLQ	BLQ	BLQ	BLQ	BLQ	BLQ
DT_{50}	1.62	2.21	1.79	-	-	-
SWP	-	-	-	NA	NA	NA

DAS: Days after spray; SD: Standard deviation; BLQ: Below limit of quantification (0.01 µg g-1); DT50: Half-life; SWP: Safe waiting period; NA: Not applicable

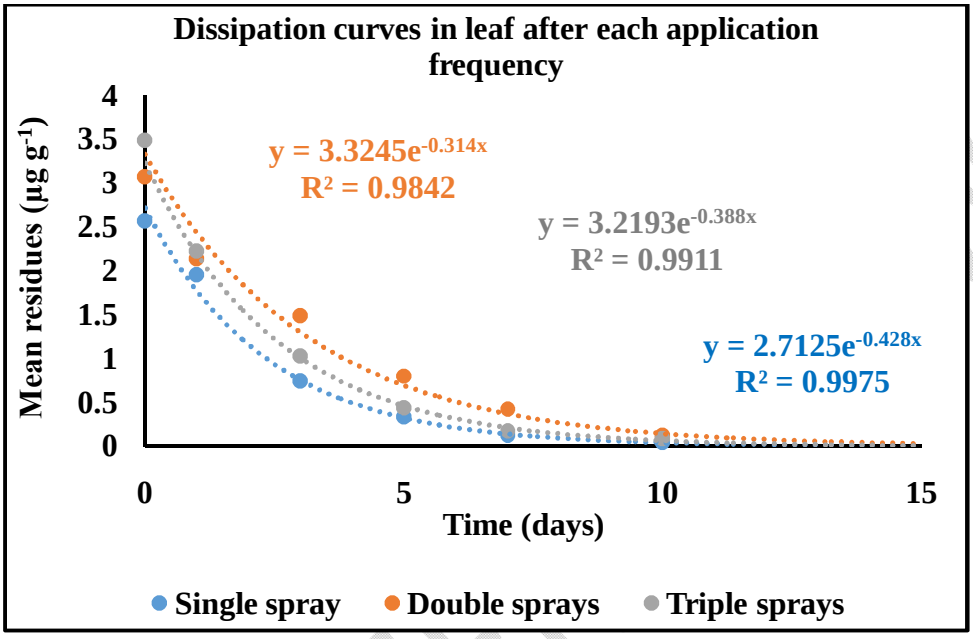

Fig 2. Dissipation curve of dinotefuran in paddy leaf

The matured rice grains from thethree times sprayed plots were sampled and residues were determinedwhich are presented in Table 4. The mean initial residues were found to be 1.13 µg g^{-1}. Half of the residues degraded on the 7th day and the residues become undetected on the 25th day. Dissipation curve of dinotefuran in grains are portrayed in Fig. 3. The residues in rice grains were significantly lower than in leaves which may be attributed to less translocation to grains. By the time of harvest, dinotefuran residues were below quantifiable limit.

Table 4 Residue degradation and half-life of flonicamid in rice grain after triple application.

DAS	Residues (µg g^{-1}) ± SD (n = 4)	Dissipation (%)
0	1.13 ± 0.19	0.00
1	0.88 ± 0.11	22.12
3	0.84 ± 0.09	25.66
5	0.61 ± 0.09	46.02
7	0.49 ± 0.08	56.64
10	0.39 ± 0.06	65.49
15	0.24 ± 0.04	78.76
20	0.15 ± 0.03	86.73
25	BLQ	-

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Harvest	BLQ	-
DT_{50}	7.05	

DAS: Days after spraying; SD: Standard deviation; BLQ: Below limit of quantification (0.01 µg g-1); DT50: Half-life.

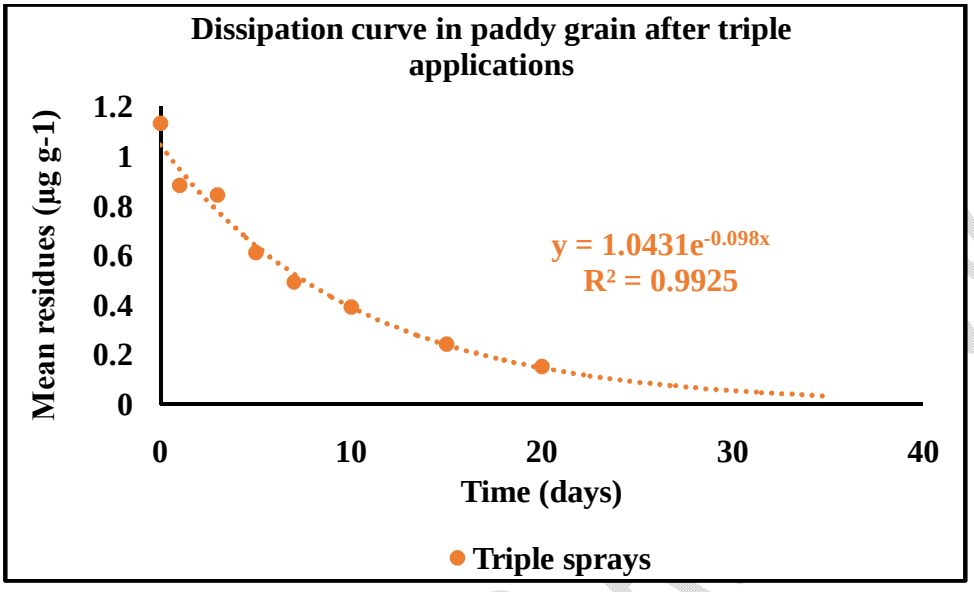

Fig 3. Dissipation curve of dinotefuran in paddy grain

3.4 Risk assessment

The dissipation study results were used to evaluate the dietary risk of rice crops. The maximum residue values from the four replicates recorded on specific days during the field study were used to determine the RQ values. These RQ values remained consistently below 1 as showed in Table 5. This demonstrates that applying dinotefuran to rice crops at three different intervals is considered to be under acceptable for consumption.Likewise, acceptable risks of dinotefuran in rice were disclosed by [13,32]. Low risk of dinotefuran were also documented by [42] in apples, [43,44] in wolfberry, [45] in tea and [46] in tomato.

Table 5 Dietary risk assessment of flonicamid residues in grain

DAS	Maximum residues in grain (µg g^{-1})	EDI	RQ
0	1.33	0.007	0.04
1	1.08	0.006	0.03
3	0.95	0.005	0.03
5	0.83	0.004	0.02
7	0.60	0.003	0.02
10	0.47	0.003	0.02
15	0.34	0.002	0.01
20	0.17	0.0009	0.005
25	-	-	-
Harvest	-	-	-

DAS: Days after spraying; EDI: Estimated daily intake; RQ: Risk quotient

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4. CONCLUSION

In the study elaborated in this paper, a quick and simple LC-MS/MS method was developed and validated for the determination of dinotefuran in rice leaf, grain, straw and soil samples. The assay method was linear over the entire concentration range (0.003-1 μg g^{-1}) and the average recoveries in rice and soil matrices were in the range of 70.93-109.30 % with a RSD of within 7 % and HorRat values within 0.3. The LOD and LOQ of dinotefuran in each matrices were 0.003 and 0.010 μg g^{-1}, respectively.This method is a useful tool to monitor residues in the rice field ecosystem. The half-lives of dinotefuran in rice leaf were in the range of 1.62-2.21 days after three application frequencies. In rice grain, the half-lives were around 7.05 days after the third application frequency. At the time of harvest, straw, grain and soil samples had residues below the detectable limit. The dietary risk assessment data depicted that RQ value were below 1 in grains immediately after spraying. The study shows that applying dinotefuran to paddy crop as foliar spray thrice is considered to be safe from consumer point of view.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts

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