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Dynamics and dietary risk assessment of thiamethoxam in wheat, lettuce and tomato using field experiments and computational simulation

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Abstract

Thiamethoxam is a widely used pesticide applied to different field crops. To inform risk assessment for this pesticide across relevant crops, we usually rely on field trials, which require time, cost and energy. For providing reliable data across crops and reduce experimental efforts, field trials should be complemented with dynamic modeling. In the present work, we hence focused on combining field trials with dynamic modeling to simulate mass evolutions of the pesticide-plant-system for thiamethoxam applied to wheat, lettuce and tomato as three major food crops. Field trials were conducted with QuEChERS (quick, easy, cheap, effective, rugged and safe) liquid chromatography-mass spectrometry, which gave consistent maximum residue concentrations for thiamethoxam in wheat, lettuce and tomato. We used these residues to evaluate the related dietary risk of humans consuming these food crops. Our results indicated that thiamethoxam did not provide any unacceptable dietary risk for humans across these three food crops, which was in line with other studies. Results for the studied crops could be extrapolated to other crops and with that, our study constituted a cost- and time-efficient way of providing reliable input for risk assessment of pesticides across crops, which was relevant for both practitioners and regulators.

Keywords: dietary risk assessment; dynamiCROP; liquid chromatography mass spectrometry; pesticide residue; thiamethoxam

20 1 Introduction

21 Pesticides are widely used to increase crop yields. However, it is also well known that pesticide
22 residues put burden on not only the environment but also on humans by pathways including wind,
23 rainfall, surface runoff, and especially food intake of treated cereals, fruits, vegetables, and other food
24 crops (Fantke, 2012a; Fantke and Jolliet, 2016). Thus, pesticide residue analysis and dietary risk
25 assessment have been a global focus for the management and control of not only environmental
26 protection but also food safety. Nowadays, pesticide residue analysis requires extensive field trials,
27 sample preparation and complex confirmatory techniques such as mass spectrometry (MS) (Hajslova et
28 al., 2011). Relying exclusively on field trials that are usually a representation of specific local soil,
29 weather and crop growth conditions at a specific point of time, however, is challenged to elucidate
30 general dissipation kinetics of pesticides in different plants under variable conditions (Fantke, 2013;
31 Fantke et al., 2014; Jacobsen, 2015). Thus, models have been developed to give deeper insights into the
32 whole system of pesticide-plant-environments (Fantke et al., 2011a). Among them, steady-state and
33 dynamic models have been developed, focusing on cereals (Fantke et al., 2011a, Rein et al., 2011),
34 vegetables (Juraske et al., 2011; Trapp et al., 2007), root crops (Fujisawa et al., 2002; Juraske et al.,
35 2009), and fruit trees (Paraíba, 2007). Both types of models require various input parameters to
36 accurately account for kinetics describing pesticide elimination as well as diverse transfer processes.
37 Dynamic models typically rely on solving a set of ordinary first order linear differential equations with
38 constant coefficients as function of time (between pesticide application and crop sampling or harvest),
39 yielding a multi-compartment mass balance problem. Either numerical or analytical methods can be
40 used to solve this problem, or the entire mass balance system can be linearized *via* model
41 parameterization (Fantke et al., 2012b). As an analytical approach, matrix decomposition (Fantke et al.,
42 2013) provides a convenient and transparent solution.

43 Using matrix decomposition in a dynamic modelling approach to assess pesticide mass distribution
44 dynamics in different crop-environment systems, the dynamiCROP model was developed as multi-crop

dynamic plant update model (Fantke and Jolliet, 2016; Fantke et al., 2011a, 2011b). This model has been evaluated against measured residues in wheat (Fantke et al., 2011a; Pang et al., 2016), passion fruit (Juraske et al., 2012), tomato (Fantke et al., 2011a; Feng et al., 2018), potato (Fantke et al., 2011a), rice (Fantke et al., 2011a), apple (Fantke et al., 2011a) and lettuce (Fantke et al., 2011a; Sevine-Itoiz et al., 2012). The dynamiCROP model describes the whole plant and environment system in a set of interconnected compartments. For example, pesticides distribute, bioaccumulate, translocate, transform, and degrade in soil and air, but also in crop leaf, stem, root and fruit components. This is described by first-order linear differential equations and solved by matrix algebra. Thus, model outputs of pesticide residues represent the plant-environment system at different times after pesticide application.

With the development of economy and education, public food safety incidents draw more and more attention. These incidents, especially pesticide residues in food, threaten consumers' well-being and furthermore undermine the corresponding food market. Such is the anxiety that not only technologies and methods to detect pesticide residues but also dietary risk assessment of pesticides have been called to be implemented worldwide.

There are two methods of assessment, namely, long-term and short-term (or acute) toxicological risk evaluation. Of these, short-term risk evaluation attracts more attention due to the immediate risk at which the short-term pesticide residue intake *via* food has put the public's health, demanding greater controls on quality of food (Harris et al., 2000). In a long-term evaluation, the estimated daily intake (EDI) of various pesticides is compared with the acceptable daily intake (ADI) issued by World Health Organization (WHO)/ Food and Agriculture Organization of the United Nations (FAO) Joint Meeting on Pesticide Residue (JMPR). Similarly, in short-term evaluations of dietary risk, the estimated short-term intake (ESTI) of pesticides is compared with acute reference doses (ARfD) to illustrate potential acute health risks for consumers.

Mainly, dietary risk evaluations rely on field trials. However, due to enormous labor, time, solvents and other materials use, field trials cannot provide efficient data for dietary risk assessments for pesticides applied across various crops under different environmental conditions. More importantly, the

low applied quantity of pesticides (usually in the range of mg/m^2) following good agricultural practice in field trials (Pang et al., 2016) results in low highest residue levels (HRs) in plants that are difficult to evaluate experimentally. Measured residues are often near or below the analytical detection limits, which greatly contributes to deviation and uncertainty (Pang et al., 2016). Thus, field trials cannot provide sufficient data for dietary risk assessment when comparing multiple pesticides or crops. In order to address this gap, we combined our field trials for three major food crops with the application of the dynamiCROP model, which could give the maximum HR through modelling simulation across various pesticide-crop combinations. Related model results can be used as input for screening-level dietary risk evaluation where field trials are difficult to obtain or lacking. However, there has been no such application yet for important staple crops which were treated with the pesticide of thiamethoxam (CAS: 153719-23-4), which is selected in the present study (chemical structure is given in Table 1). Thiamethoxam is a second-generation neonicotinoid insecticide. By binding to nicotinic acetylcholine receptors in the central nervous system, it is presently one of the most effective pesticides for the pest control of such aphids, whiteflies and thrips. It has been recommended for various agricultural crops with global soil, foliar and seed treatments. Its main metabolite is clothianidin (CAS: 210880-92-5) (Table S1) with a maximum occurrence fraction in soil of 35.6%. Liquid chromatography (LC) (Abd-Alrahman, 2014; Jyot and Singh, 2017; Ramasubramanian et al., 2012; Zhou et al., 2006) and LC-MS (Rahman et al., 2015; Valverde et al., 2016) have been widely used to determine residue and dissipation of thiamethoxam (Gupta et al., 2008; Karmakar and Kulshrestha, 2009; Li et al., 2007; Liu et al., 2009; Pareja et al., 2012; Singh and Kulshrestha, 2005). Efforts have also focused on understanding the degradation of thiamethoxam as well as its metabolites (Fan and Shi, 2017; Hilton et al., 2016; Yang et al., 2014). Besides, based on field trials, the dietary risk has been evaluated e.g. in mango (Bhattacharjee and Dikshit, 2016) and tomato (Malhat et al., 2014). However, despite various existing studies focusing on environmental distribution and residue kinetics of thiamethoxam, residue studies for various important food crops are currently still missing, highlighting the need for complementary experimental data and modelling in support of assessing related potential risks for consumers and the environment.

In the present work, field trials were combined with dynamic modelling to study the environmental fate and behavior of thiamethoxam in wheat, lettuce and tomato as example crops, among which only for tomato specific experimental residue studies are currently available in the scientific literature, while missing for the other two crops. Based on HRs from modelling and our own field trials, the acute dietary risk of thiamethoxam was evaluated in the three crops. This is the first dietary risk assessment based on not only on specific experimental data, but also evaluation in complementary computational simulation for this pesticide. This is in line with recommendations to complement and align experimental and modeling results to provide consistent decision support (Fantke et al., 2016).

CAS NO.	153719-23-4
Structure
Molecular weight (g/mol)	291.71
Octanol-water partition coefficient	0.74
Air-water partition coefficient	1.9×10^{-13}
$t_{1/2}^a$ soil (d) [1]	50
$t_{1/2}^a$ wheat (d) [2]	3.3
$t_{1/2}^a$ tomato (d) [2]	4.5
$t_{1/2}^a$ lettuce (d) [2]	2.6
M_{applied} in model and experiment (mg/m ²)	0.11 (wheat), 0.11 (lettuce), 1.98 (tomato)
The lowest MRL ^b (mg kg ⁻¹)	0.02 (wheat, China), 0.2 (tomato, Korea), 3 (lettuce, China)

^a half-lives used in model

[1] Pesticide Properties Database (<https://sitem.herts.ac.uk/aeru/ppdb>)

[2] Fantke et al. (2014)

^b MRL = maximum residue limits

Table 1. Physico-chemical properties, degradation half-lives and applied substance mass applied in model for thiamethoxam.

114 2 Materials and methods

115 2.1 Chemicals and solution preparation

116 Thiamethoxam and its main metabolite clothianidin were purchased from Beijing Qinchengyixin
117 Co. Ltd. (Beijing, China). Acetonitrile and formic acid (LC grade) were from Fisher Scientific (MA,
118 USA). Anhydrous magnesium sulphate (MgSO_4), sodium chloride (NaCl), and acetic acid of analytical
119 grade were purchased from Beijing Chemical Reagents Company (Beijing, China). C18 (50 μm , 60 $\text{\AA}$),
120 primary secondary amine (PSA) (40-60 μm) and graphitized carbon black (GCB) (120-400 mesh) were
121 purchased from Agela Technologies (Tianjin, China). The stock solutions of thiamethoxam and
122 clothianidin (1 mg/mL) were prepared and kept at $-20\text{ }^\circ\text{C}$ in the dark.

123

124 2.2 Field trials

125 Field trials were conducted according to NY/T 788-2004 (Guideline on pesticide residue trials)
126 (Ministry of Agriculture P.R. China). The field trials were carried out at three sites, namely site A of
127 Beijing (116.46°E, 39.92°N), site B of Shandong province (120.42°E, 36.58°N), and site C of Anhui
128 province (116.93°E, 34.19°N) in China. The characteristic properties of soil used in the field, such as pH
129 values were 6.73, 7.32 and 6.79 for site A, B and C, respectively. In addition, organic matter contents of
130 soil were 2.7%, 3.9% and 1.7% for site A, B and C, respectively. The average temperature of three sites
131 during the experimental period was in the range of 20 to 24 $^\circ\text{C}$ in the field trial years of 2016 and 2017.
132 The detailed field trials information were shown in Table S2.

133 For wheat, 0.1% granule of thiamethoxam was tested to investigate residue dynamics. The
134 recommended dosage was 450-750 grams active ingredient per hectare (g a.i./ha). Residue level trials
135 adopted the high dosage as well as 1.5 folds (1125 g a.i./ha) with one application before planting.
136 Representative wheat grains at the harvest time (53 d) were collected.

137 For lettuce, 25% water dispersion granule of thiamethoxam with recommended dosage of 15-30 g
138 a.i./ha was utilized. The high dosage as well as 1.5 folds (45 g a.i./ha) with two and three times of

application were adopted. Representative samples with pre-harvest intervals (PHIs) of 3, 5, 7 days after the last application were collected.

For tomato, 21% suspension concentrate of thiamethoxam with recommended dosage of 47.25-63 g a.i./ha was utilized. The high dosage as well as 1.5 folds (94.5 g a.i./ha) with three and four times application at the peak period of whitening diseases were adopted. Representative samples with PHIs of 1, 3, 5 days after the last application were collected.

All samples were stored in dark at -20 °C for further analysis.

2.3 Sample preparation by QuEChERS (quick, easy, cheap, effective, rugged and safe)

Homogenized wheat grain (5 g), lettuce (5 g) and tomato (5 g) were extracted by 10 mL acetonitrile by vortexing for 1 min. Additionally, water was added to maintain wetness, i.e. 3 mL to grain and tomato and 2 mL to lettuce. The salting out step used anhydrous NaCl (1 g) and MgSO₄ (4 g) with vortexing for 1 min. After centrifugation at 1,600 relative centrifugal force (rcf) for 3 min, 1.5 mL of the supernatant was transferred and purified by dispersive solid phase extraction and vortexing for 1 min. Different matrices adopted different combinations of sorbents, i.e. 100 mg PSA, 20 mg GCB and 150 mg MgSO₄ for wheat grain, 100 mg PSA, 100 mg C18, 10 mg GCB and 150 mg MgSO₄ for lettuce, and 150 mg PSA, 5 mg multi-walled nanotubes and 150 mg MgSO₄ for tomato.

2.4 LC-MS/MS analysis

All experiments were performed with Agilent 1260 infinity LC system (Agilent Technologies, USA) with a Poroshell 120 EC-C18 column (Agilent Technologies) (50 mm × 3.0 id, 2.7 μm). Two analytes were separated with a mobile phase consisting of 0.2% formic acid and acetonitrile (30:70). The injection volume for all samples was 5 μL and the column temperature was 40 °C.

Agilent 6420 triple quadrupole mass spectrometer (Agilent technologies) was operated in positive electrospray ionization multi-reaction monitoring mode (Table S3). Other operating conditions were as

164 follows: capillary voltage 4000 V, nebulizer pressure 45 psi, drying gas (N₂) flow rate 11 L/min, and dry
 165 gas temperature 350 °C.

166

167 2.5 Model application

168 The dynamic model of dynamiCROP (<http://dynamicrop.org>) developed by Fantke et al. (2011a)
 169 were used in this work. This model was extended to include six crop types covering a large fraction of
 170 the worldwide human consumption (Fantke et al., 2011b), and was applied in the present study for
 171 wheat, lettuce and tomato to evaluate the evolution, distribution and whereabouts of thiamethoxam
 172 between pesticide application and crop harvest. The input data included the selection of pesticide name
 173 and crop name as well as the applied amount. The output data included residues in different
 174 compartments.

175

176 2.6. Dietary risk assessment

177 EDI is calculated from supervised trials median residue levels (STMR) in field trials or modeling
 178 results as described in equation 1:

$$179 \quad EDI = \frac{\sum STMR \times Food \text{ intake}}{Body \text{ weight}} \quad (1)$$

180 ESTI is calculated from HR obtained in field trials (or highest theoretical residue levels obtained from
 181 dynamic modeling), the daily intake of the highest large portion of food (LP), and unit weight (Ue)
 182 following equations 2:

$$183 \quad ESTI = \begin{cases} \frac{HR \times LP}{Body \text{ weight}} & \text{if no } Ue \\ \frac{Ue \times HR \times \vartheta + (LP - Ue) \times HR}{Body \text{ weight}} & \text{if } Ue < LP \\ \frac{HR \times LP \times \vartheta}{Body \text{ weight}} & \text{if } Ue > LP \end{cases} \quad (2)$$

184 where ϑ is the variability factor.

185

186 3 Results and Discussion

3.1 Modelled evolution of thiamethoxam

The dynamiCROP model consists of source compartments (relevant for pesticide application) and receiving compartments (relevant for residues in harvest), i.e., air, soil, leaf surface, fruit surface and leaf, fruit, stem, root, respectively. According to the modelled processes, thiamethoxam firstly distributed among four source compartments according to the characteristic of plants and pesticides. Thiamethoxam then transferred, diffused, transformed and degraded in all included compartments. The modelled mass evolution of thiamethoxam in wheat, lettuce and tomato was shown in Figure 1. Mass evolutions included mainly two parts, the initial diffusion and transferring part, and the longer term decreasing trend driven by degradation. After application, thiamethoxam in air, soil, leaf surface and fruit surface decreased due to diffusion and transfer. Thiamethoxam started entering leaf, stem, root, and fruit quickly and then accumulated in these compartments over the first five days. More specifically, after initial distribution, the mass in the crops increased *via* gas exchange, root uptake, and translocation within the crops. Pesticide mass increased until a maximum was reached, e.g. for fruit, ranging from 16 g/kg in tomato to 300 g/kg in wheat (see Table 2). From the maximum levels, masses decreased more or less exponentially in all compartments, mainly driven by degradation processes, which was in line with other studies (Jacobsen et al., 2015). It was characteristic that the dynamics in lettuce were driven by soil processes, which was consistent with the longest residence time (40.77 d) in Table 2. The studied metabolite clothianidin generally also showed the initial diffusion and long term decreasing trend that was described for thiamethoxam (Figure S1). In dynamiCROP, any metabolite can be run by first identifying the fraction of this metabolite in relation to the parent compound mass applied and then run this fraction of metabolite as separate chemical in dynamiCROP.

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		wheat	lettuce	tomato
residence time t^b (d)	Air	0.08	0.07	0.08
	Soil	1.21	40.77	1.06
	Leaf surface	0.88	0.68	0.86
	Fruit surface	4.74	3.70	2.96
	Leaf	3.29	3.70	6.31
	Fruit	4.67	3.70	6.58
	Stem	0.12	0.01	0.19
	Root	0.09	0.01	0.05
residue max (mg/kg)	Leaf	1.0×10^6	1.4×10^5	
	Fruit	3.0×10^5		1.6×10^4
	Stem	2.6×10^5	33	
Harvest fraction max	Leaf	0.08	0.4	
	Fruit	0.39		0.04
	Stem	0.07	1.3×10^{-5}	

221 ^a $t_{m, \max}$ = maximal mass of pesticides occurring time in plants (d).

222 ^b t = residence time of pesticides in plants (d).

223 **Table 2.** Modelled parameters in spatial and temporal distribution of thiamethoxam in wheat, lettuce,
224 and tomato. (Data from DynamiCROP)

225

Figure 1. Evolution of masses of thiamethoxam with main driving compartment in wheat (a), soil for lettuce (b), and tomato (c). (Data from DynamiCROP)

3.2 Modelled contribution of source compartments to crop residue levels

After application, thiamethoxam distributed in four source compartments of air, soil, leaf surface and fruit surface. Herein, for lettuce, it was more convenient to recognize leaves and stem as edible crop parts. In field trials, residues in leaves and the edible crop parts have been paid great attention to considering two important parameters, namely the dissipation half-lives and maximum residue limits (MRLs). Thus, the contribution of the four source compartments on crop residues at different times were quantified by modelling simulation and shown in Figure 2. For residues in leaf, the largest

238 contribution came from leaf surface for wheat and tomato, and from soil for lettuce, respectively. This
 239 was mainly related to differences in crop characteristics, where different crops showed different
 240 contributions of pesticide translocation processes (Fantke et al., 2013). The evolution of pesticide
 241 residues in edible fruit was more complex. For wheat, residue in grain mainly came from leaf surface.
 242 For lettuce, residues in leaf mainly came from leaf surface initially and then from soil in the long term.
 243 For tomato, different compartments contributed at different points in time, with fruit surface in the
 244 initial term, then soil, and finally leaf surface in the longer term. Furthermore, residues in three crops
 245 decreased following more or less the same trend over time (Figure 2).

246

247 **Figure 2.** Evolution of contribution of initial thiamethoxam masses in air, soil, leaf surface, and grain
 248 surface to masses in leaf and fruit. (Line describing evolution of the harvest fractions in the edible crop
 249 parts) (Data from DynamiCROP)

250

251

252 3.3 Modelled whereabouts of thiamethoxam with soil and foliar application

253 Pesticides are usually applied by either foliar spray or soil spray. Different application methods
 254 resulted in different distribution, transfer, and degradation dynamics. To illustrate the fate of the
 255 pesticide relying on application method, Figure 3 illustrated the whereabouts of thiamethoxam with soil
 256 and foliar spray. The mass evolutions of thiamethoxam were different within different crops as well as

257 application methods. For soil spray, most thiamethoxam mass went to soil at first, then was transferred
 258 to leaf and fruit gradually in wheat and tomato. In lettuce, almost all the pesticide mass at a specific time
 259 point was retained in the leaf.

260 The distribution of thiamethoxam with foliar spray was different. Thiamethoxam quickly
 261 transferred from leaf surface to leaf at first. In the longer term (100 d), thiamethoxam migrated to fruit
 262 for wheat and tomato, and to soil for lettuce. The pesticide fraction in fruit in wheat and lettuce
 263 increased and followed a long time decrease, with a maximum of 0.84 at 30 d in wheat, and 0.97 at 3 d
 264 as well as 0.99 at 10 d for lettuce. At these 3 d and 10 d in lettuce, the total fractions of pesticide in leaf
 265 surface with foliar spray application were 0.44 and 0.067, respectively, due to possible dissipation. For
 266 tomato, the pesticide fraction in fruit increased (in leaf) along the time and the ratio at 30 d was 0.16.
 267 Hence, whereabouts of thiamethoxam demonstrated different temporal and spatial distribution and
 268 translocation process after application in the different crops.

269 **Figure 3.** Evolution of whereabouts of applied thiamethoxam ending up as residue in wheat, lettuce and
 270 tomato after soil and foliar spray application. (Line describing evolution of fraction in the edible crop
 271 parts related to total residues mass for thiamethoxam after foliar spray application) (Data from
 272 DynamiCROP)
 273

274

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3.4 Residue levels obtained from field trials and QuEChERS LC-MS

Presently, pesticide residue analysis is preferred using QuEChERS LC-MS due to its advantages of satisfactory recoveries, high efficiency, high throughput, and low costs. Hence, QuEChERS LC-MS methods have been established for thiamethoxam as well as its metabolite clothianidin in three matrices. Matrix matched calibration were with acceptable quantitation, satisfactory recoveries and limits of quantitation (LOQs) in wheat grain, lettuce and tomato (Table S4). Thiamethoxam and clothianidin had good linearity in wheat grain, lettuce and tomato in the range of 0.005 to 5 µg/mL. Recoveries in three fortified levels in three matrices were in the range of 70 to 110% (Table S4) with RSD% in the range of 3.4%-11.3% in all cases. The reason why the quantitation included its metabolite was due to the definition of residue for thiamethoxam by JMPR, namely, the sum of both two considering the molecular weight ratio of 1.168. Thus, the developed QuEChERS LC-MS and matrix matched calibration could provide reliable residue levels for thiamethoxam. The maximum residues were consistent with model results across studied crops (Table 3).

In field trials, real formulations were applied to different crops with doses as low as 0.11 to 1.98 mg/m² (Table 1) following good agricultural practice to imitate real world applications. Representative samples of wheat, lettuce and tomato were analyzed by the developed QuEChERS LC-MS method. Residue levels in different matrices and with different applications and pre-harvest intervals (PHIs) were obtained (Table S5). For wheat and lettuce, residues were lower than LOQ irrespectively of PHIs. For tomato, HRs were higher than LOQ in the range of 0.19 to 0.43 mg kg⁻¹ with different PHIs. Generally, HRs decreased with the increase of PHIs for all crops.

Residue levels in wheat and lettuce were so low that they could not be detected. Usually, HR was thus maximized to be LOQ for safety concerns. Thus, deviation and uncertainty occurred due to the reliance on the sensitivity of the utilized method. Here, except HR of tomato, HRs of wheat and lettuce were chosen as the LOQ sum of thiamethoxam and its metabolite after molecular weight transformation.

3.5 Acute dietary risk assessment

Acute dietary risk assessment involves the calculation of ARfD% with HR. Different countries or districts have different average body weight, food intake and dietary structure. Here, we took China as example country with a population of 1.4 billion and one of the biggest consumers of pesticides worldwide [40].

Field trials resulted in HRs of thiamethoxam in wheat grain, lettuce and tomato (Table 3 and Table S4), which were either around LOQs or low with considerable deviation. ARfD% were calculated based on equation 2 assuming no U_e for wheat and $U_e < LP$ for lettuce and tomato. The corresponding ARfD%s for different crops were 0.023% for wheat grain, 0.034% for lettuce, and 0.5% for tomato, indicating that at realistic harvest times, all residues fell well below 1% of the applied pesticide mass in any edible food crop component.

Modelling the pesticide residues in dynamiCROP gave maximum residues (Table 2). After the transformation into dosage, theoretical HRs of modelling with experimental application were calculated and shown in Table 3 and in the range of 0.015 to 0.033 mg kg⁻¹. Due to the intrinsic nature of modelling, deviation and uncertainty of residues were greatly lowered.

As shown in Table 3, the obtained ESTIs were in the range of 2.5×10^{-4} to 3.9×10^{-4} mg kg⁻¹ bw and the corresponding ARfD% were in the range of 0.025 to 0.039%. Modelling results were generally consistent with those based on field trials, indicating that thiamethoxam did not provide any unacceptable dietary risk for humans across these three food crops, which was in line with other studies showing that this pesticide showed little dietary pathway related effects on humans compared to other pesticides (Fantke et al., 2012; Karmakar and Kulshrestha, 2009). This simulation gave an example of acute dietary risk assessment in different plants with fast, cost-efficient, and effective processing. Although this study took thiamethoxam in wheat, lettuce, and tomato as an example, it could be applied to many other future applications of such a system for the analysis of other pesticides and their residues and food crops and other plants in support of regulatory and non-regulatory decision-making.

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Crops	LP ^a (g/person)	Ue ^b (g)	v ^c	Average body weight (kg)	ARfD ^d (mg/kg bw)	Modelling			Field		
						HR ^e	ESTI ^f	ARfD% ^g	HR ^e	ESTI ^f	ARfD% ^g
						(mg/kg)	(mg/kg bw)		(mg/kg)	(mg/kg bw)	
Wheat	732.96	--	--			0.033	3.9×10 ⁻⁴	0.039	0.02	2.3×10 ⁻⁴	0.023
Lettuce	451.93	305.4	3	63	1	0.015	2.5×10 ⁻⁴	0.025	0.02	3.4×10 ⁻⁴	0.034
Tomato	376.77	174.6	3			0.032	3.6×10 ⁻⁴	0.036	0.51	5.0×10 ⁻³	0.5

331

^aLP = large portion

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^bUe = unit weight

333

^cv = variability factor

334

^dARfD = acute reference dose

335

^eHR = the highest residue level

336

^fESTI = the estimated short-term intake

337

^gARfD% = ESTI/ARfD × 100

338

Table 3. Acute dietary risk assessment of thiamethoxam by field trials and computational simulation in China

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4 Conclusions

The present study explored the possibility of using a combination of field trials and dynamic modelling, allowing for both fast and reliable data processing as well as direct and transparent demonstration of the evolution, distribution and source apportionment of pesticides in the plant-environment system. The results provided highest residue levels of thiamethoxam for acute dietary risk assessment in wheat, lettuce and tomato, consistent with the outcome of confirmatory LC-MS. This simulation gave an example of acute dietary risk assessment in different plants with fast, cost-efficient, and effective processing. Although this study took thiamethoxam in wheat, lettuce, and tomato as an example, it can be applied to other applications of such a system for the analysis of other pesticides and their residues and food crops and other plants in support of regulatory and non-regulatory decision-making.

Abbreviation:

Acute reference dose (ARfD); Estimated short-term intake (ESTI); The highest residue levels (HR); Joint meeting on pesticide residue (JMPR); Large portion of food (LP); Liquid chromatography (LC); Mass spectrometry (MS); Supervised trials median residue levels (STMR); Unit weight (Ue); Variability factor (v)

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Supporting information description

There are 5 Tables, 1 Figure, 7 pages in total in the supporting material.

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Competing financial interest

The authors declare no competing financial interest.

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Figure captions

Figure 1. Evolution of masses of thiamethoxam with main driving compartment in wheat (a), soil for lettuce (b), and tomato (c). (Data from DynamiCROP)

Figure 2. Evolution of contribution of initial thiamethoxam masses in air, soil, leaf surface, and grain surface to masses in leaf and fruit. (Line describing evolution of the harvest fractions in the edible crop parts) (Data from DynamiCROP)

Figure 3. Evolution of whereabouts of applied thiamethoxam ending up as residue in wheat, lettuce and tomato after soil and foliar spray application. (Line describing evolution of fraction in the edible crop parts related to total residues mass for thiamethoxam after foliar spray application) (Data from DynamiCROP)

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Thiamethoxam

**Modelling &
Field trials**

Dietary risk assessment

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