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Pollution characteristics and non-dietary human cumulative risk assessment of neonicotinoids in vegetable greenhouse soils: a case study in Shandong Province, China

Kai Cui[1] · Mingxiao Ning[1] · Jingyun Liang[1] · Shuai Guan[1] · Liping Fang[1] · Ruiyan Ding[1] · Jian Wang[1] · Teng Li[1] · Zhan Dong[1]

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Abstract

Purpose The benefits associated with the conventional use of neonicotinoids on greenhouse vegetables have lasted for several decades. Extensive use of neonicotinoids could result in their accumulation in the soils, thereby potentially threatening human health through ingestion, dermal contact and inhalation. This study aimed to clarify the pollution characteristics and non-dietary human cumulative risk of neonicotinoids in vegetable greenhouse soils.

Materials and methods A total of 283 soil samples were collected from celery, cucumber, pepper and tomato greenhouses across Shandong Province in China and analysed for nine widely used neonicotinoids. Furthermore, the potential health risks for both adults and children were assessed.

Results Among all the soil samples, imidacloprid, clothianidin and thiamethoxam were the top three detected neonicotinoids, with detection frequencies of 96.82–99.65%. The three neonicotinoids had higher average concentrations in the soils, with average concentrations of 27.55–157.64 μg/kg. All the soil samples contained at least two neonicotinoids, but most of the detected residues were at low levels with concentrations ranging from 0.02 to 1816.67 μg/kg. The levels of total neonicotinoids (calculated based on a relative potency factor method) in tomato and pepper soils were statistically higher than those in cucumber and celery soils. Although the exposure risk to children was far higher than that to adults, the health risk assessment for each neonicotinoid or total neonicotinoids was within the established safe limits (hazard index range, 1.07×10^{-10} to 1.95×10^{-3}, < 1). Despite the low health risk, potential hazards of exposure to neonicotinoid-contaminated soils should be continuously assessed due to the low-dose adverse effects and potential accumulation in human tissues.

Conclusions Our findings indicate that attention should be given to the neonicotinoids in vegetable greenhouse soils due to their ubiquity and toxicokinetic characteristics.

Keywords Neonicotinoids · Greenhouse soil · Residue · Relative potency factor · Human cumulative risk assessment

1 Introduction

Greenhouse cultivation has been globally developed to achieve a year-round supply of vegetables over several decades. In China, greenhouse vegetables account for nearly 20% of the total vegetable production area, and they generate 35% of output and 60% of economic value (Liang et al. 2019). However, greenhouse-grown vegetables are more vulnerable to various insect pests due to the closed, warm and humid greenhouse environments; hence, greenhouse cultivation requires more frequent application of pesticides in comparison with open-field cultivation (Dou et al. 2020).

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✉ Zhan Dong
zhandongsaas@163.com

[1] Shandong Provincial Key Laboratory of Test Technology On Food Quality and Safety, Institute of Quality Standard and Testing Technology for Agro-Products, Shandong Academy of Agricultural Sciences, Jinan, Shandong 250100, People's Republic of China

Neonicotinoids (NEOs), which act selectively on insect nicotinic acetylcholine receptors (nAChRs), are the most widely used insecticides for controlling populations of sucking, coleopteran, dipteran and lepidopteran pests on vegetables in China (Cui et al. 2021). As the largest sink of organic pollutants, soil ultimately carries a large amount of NEOs after their application (Yu et al. 2021). Additionally, it has been reported that NEOs are stable and persistent in the soils with a half-life in the range of 50–545 days (Wu et al. 2020). Overall, these results suggest that NEOs may persist and accumulate in the greenhouse soils after extensive use over successive years.

People may be exposed to NEOs through several principal routes, which include ingestion, inhalation and dermal contact of pesticide-contaminated soil (Bhandari et al. 2020). NEOs have been detected in agricultural soil, industrial soil, particulate matter (PM)2.5, dust and even soil particles of residential areas (Humann-Guilleminot et al. 2019; Wang et al. 2019; Zhang et al. 2020; Zhou et al. 2020, 2021). Moreover, they have been found in human urine, blood, breast milk, saliva, tooth and hair samples (Bonmatin et al. 2021; Chen et al. 2020a, b, 2021; Xu et al. 2021b; Zhang et al. 2021a, 2021b; Zhang and Lu 2022). In vitro and animal studies have demonstrated that NEOs may lead to neurotoxicity, immunotoxicity, genotoxicity, hepatotoxicity and reproductive toxicity (Annabi et al. 2019; Feki et al. 2019; Li et al. 2021a; Zhao et al. 2021, 2022). In addition, a review of Houchat et al. (2020) reported that NEOs could modulate neuronal distribution and induce oxidative stress, which can lead to several human neurodegenerative diseases, such as Alzheimer and Parkinson. Therefore, health risks associated with exposure to NEOs from contaminated soil must not be disregarded.

Several publications have described the ubiquitous existence of NEOs in soils of different land use types, soil depth, seasons or regions (Bonmatin et al. 2019; Humann-Guilleminot et al. 2019; Wu et al. 2020; Zhou et al. 2021; Zheng et al. 2022). In particular, Zhou et al. (2021) reported that the concentrations of NEOs in greenhouses were far higher than those found in the orchard, farm, park and residential areas, with the highest concentration being 459 ng/g in the spring and 252 ng/g in the fall. Moreover, another study determined the concentrations of nine NEOs in 18 soil samples that were collected from tomato and cucumber greenhouses and assessed the ecological risks of NEOs to non-target organisms, i.e. insects/spiders, worms, birds and invertebrates (Wu et al. 2020). However, previous works did not consider human cumulative health risks to NEO exposure through soil inhalation, ingestion and dermal contact. It has recently been suggested that human carcinogenic risks are strongly associated with farmland soil pollution, and exposure to pesticide-polluted soil poses serious health risks to humans (Yu et al. 2020; Zeng et al. 2019). A previous study has reported that approximately 25 million agricultural workers worldwide are affected by pesticide poisoning every year (Carvalho 2017). Therefore, considering the wide use of NEOs in vegetable greenhouses and their possible cumulative effects, it is particularly essential to ascertain the soil pollution status and further identify the potential health risks to the public health, especially for farmers and residents nearby greenhouses.

China is a prominent producer and user of NEOs worldwide, and these compounds occupy the largest insecticide market in the country. In recent years, a number of slow-release formulations of NEO products, such as granules, seed-treated agents and slow-release agents, have been produced, and these are largely used in the greenhouses. The wide use of these NEO products leads to the accumulation of the active ingredients in the soil, which persists for a long period of time. Statistically, Shandong Province ranks first in vegetable production among all provinces in China (88.01 million tons in 2021), and greenhouse cultivation accounts for nearly 50% of total cultivation areas. Therefore, we sampled 283 soil samples from four kinds of typical vegetable greenhouses (celery, cucumber, pepper and tomato) from three main cities that produce vegetables in Shandong Province. The primary objectives of this study are as follows: (1) to determine the residual levels of NEOs in greenhouse soils and check the differences in NEO levels among different vegetable greenhouses and (2) to evaluate the potential human health risk of NEO exposure through soil ingestion, inhalation and dermal contact for each NEO and their cumulative effects.

2 Materials and methods

2.1 Chemicals and reagents

Reference standards for imidacloprid (IMI), thiamethoxam (THM), dinotefuran (DIN), imidaclothiz (IMZ), clothianidin (CLO), nitenpyram (NIT), thiacloprid (THD), acetamiprid (ACE) and ACE-*N*-desmethyl (ACE-DE) were all purchased from Alta Scientific Co., Ltd. (Tianjin, China). Chromatographic-grade acetonitrile, methanol and formic acid were obtained from Macklin Biochemical Co., Ltd. (Shanghai, China). Chromatographic-grade ammonium acetate was obtained from Sigma-Aldrich Chemical Co., Ltd. (Darmstadt, Germany). Analytical-grade anhydrous magnesium sulfate ($MgSO_4$) and sodium chloride (NaCl) were purchased from Sinopharm Chemical Reagent (Shanghai, China). Pure water was obtained from Watson Group Hong Kong, Ltd., (Hong Kong, China), and primary secondary amine (PSA) was obtained from Agela Technologies (Beijing, China). Each of the standard stock solution (100 mg/L) was stored at − 18 °C in the dark.

2.2 Sample collection

From October 2021 to March 2022, a total of 283 soil samples were collected from celery, cucumber, pepper and tomato greenhouses in Shandong Province in China. These vegetable categories are associated with pesticide use and greenhouse cultivation. Sample locations are mainly distributed in three cities, which included Weifang City (WF), Liaocheng City (LC) and Linyi City (LY). These cities were assessed as the main producers of vegetables in Shandong Province and in the whole country. According to the greenhouse size, each soil sample was collected from five to ten cores (top 0 ~ 10 cm) using a stainless steel shovel at the vegetable harvest stage in each greenhouse, followed by proper mixing into one sample. After collection, all the soil samples were transported to the laboratory on ice and filtered for large stones, roots and leaves. Next, all the samples were freeze-dried and sieved using a 0.2-mm mesh. Finally, all the samples were frozen at − 18 °C until analysis.

2.3 Analysis of NEOs

Nine NEOs were extracted from each soil sample by an optimised QuEChERS (quick, easy, cheap, effective, rugged, safe) method (Anastassiades et al. 2003). Briefly, 5.0 g of freeze-dried soil was accurately weighed into a 50-mL Teflon centrifuge tube. Next, 5.0 mL of water and 10 mL of acetonitrile were successively added to each of these samples. The tubes were vigorously vortexed with a multi-tube vortex mixer at a speed of 2500 r/min for 5 min. Afterwards, 1.0 g of NaCl and 4.0 g of anhydrous $MgSO_4$ were simultaneously added to each sample and vortexed for additional 1 min. After centrifuging at 5000 r/min for 5 min, 1.5 mL of the supernatant for each sample was transferred into a 2-mL cleanup tube containing the sorbents of 50 mg PSA and 150 mg anhydrous $MgSO_4$. Each cleanup tube was then vortexed for 1 min and centrifuged at 5000 r/min for 5 min. Lastly, the extract was passed through a 0.22-μm nylon filter for subsequent high-performance liquid chromatography tandem mass spectrometry (HPLC–MS/MS) analysis.

Quantitative analysis of nine analytes was performed with a 1290 Infinity II HPLC coupled with a 6495 triple-quadrupole mass spectrometer system (Agilent, USA) in positive electrospray ionisation (ESI +) in multiple reaction monitoring (MRM) mode. Chemical separation was performed on a Poroshell 120 EC-C18 column (100 mm × 4.6 mm, i.d., 2.7 μm, Agilent). The column temperature was 40 °C, and sample injection volume was 5 μL. Acetonitrile (buffer A) and water containing 0.2% formic acid and 5 mmol/L ammonium acetate (buffer B) were used as the mobile phases (0.4 mL/min). Gradient elutions were as follows: 0–0.5 min, 5% A; 0.5–3.0 min, 5–95% A; 3.0–8.0 min, 95% A; 8.0–8.1 min, 95–5% A; and 8.1–10.0 min, 5% A. The gas temperature was 250 °C (14 L/min), the sheath gas temperature was 250 °C (11 L/min) and the nebuliser was 45 psi. All MS/MS parameters were automatically optimised using an Agilent MassHunter Optimiser software program, including precursor ions, product ions and collision energy. Detailed retention time and MS/MS parameters for all analytes are listed in Table S1.

The proposed method was checked with respect to specificity, linearity, limit of quantification (LOQ), matrix effect (ME), precision and accuracy according to the SANTE/11312/2021 guidelines (EC 2021). Specificity was assessed by analysing blank soil samples to ensure the absence of any interference or contamination near the retention time of the target NEOs. Linearity was assessed by the coefficient (R^2 values) for each analyte computed through the calibration curves. The LOQ of each NEO was defined as the lowest spiked concentration in the soil matrix that could be quantified with acceptable precision and accuracy. ME reflected the signal suppression/enhancement exerted by the soil co-extractives and was calculated as follows: %ME = (slope in matrix / slope in solvent − 1) × 100. Generally, |ME| ≤ 10% indicates no matrix effect, ME < − 10% indicates matrix suppression and ME > + 10% indicates matrix enhancement (Cui et al. 2021). Accuracy and precision were validated with a recovery and repeatability test by spiking each NEO standard into blank soil matrix at five different concentrations (LOQ, 1 μg/kg, 10 μg/kg, 100 μg/kg and 1000 μg/kg) with five replicates.

2.4 Relative potency factor

The relative potency factor (RPF)-integrated method was used to measure total NEO content in each soil sample, and the principle involves the integration of mixed chemicals sharing similar molecular structures and modes of action to an index compound. For NEO groups, IMI was always selected as the index compound due to its wide use in agriculture and inclusion in numerous toxicity studies (Zhou et al. 2020). The RPF values for all NEOs were derived from their chronic reference doses (cRfDs), which were obtained from the USEPA website (https://ordspub.epa.gov/ords/pesticides/f?p=122:3). All RPFs were calculated using Eq. (1), as shown in Table S2. ACE-DE is the main metabolite of ACE, and therefore, they have the same cRfD value (Chen et al. 2020a, b). However, NIT and IMZ were not considered in the RPF calculation because their cRfD values were not obtained in the current databases.

$$RPF_i = cRfD_{IMI}/cRfD_i \tag{1}$$

In Eq. (1), i represents each NEO considered.

2.5 Human health risk assessment

In the evaluation process, non-cancer human health risks for each NEO and for total NEOs were taken into consideration based on the USEPA models (USEPA 2021), which have been widely used for human health risk assessment of commonly used pesticides in the soils, including insecticides, fungicides and herbicides (Bhandari et al. 2020; Degrendele et al. 2022; Yadav et al. 2016). The models were used to determine the chronic daily intake (CDI, μg/kg body weight (BW)/day) of NEOs, covering incidental ingestion, dermal contact and inhalation of NEO-contaminated soils in children and adults. CDI values were determined using Eqs. (2)–(4), and they are expressed as CDI_{ing}, CDI_{der} and CDI_{inh}, respectively.

$$CDI_{ing} = C_{soil} \times IRS \times EF \times ED \times CF/BW/AT \quad (2)$$

$$CDI_{ing} = C_{soil} \times SA \times AF \times ABS \times EF \times ED \times CF/BW/AT \quad (3)$$

$$CDI_{inh} = C_{soil} \times InhR \times EF \times ED/PEF/BW/AT \quad (4)$$

In the above equations, C_{soil} represents the concentration of each NEO or IMI_{RPF} (total NEOs) in the soils (μg/kg). Detailed parameters/exposure factors, i.e. ingestion rate of soil (IRS), exposure frequency (EF), exposure duration (ED), conversion factor (CF), BW, average exposure time (AT), skin surface area (SA), soil adherence factor (AF), dermal absorption factor (ABS), inhalation rate (InhR) and particulate emission factor (PEF), can be found in Table S3.

Afterwards, non-cancer health risks of exposure to each NEO or total NEOs from soils were estimated in terms of hazard quotient (HQ), calculated using Eq. (5). The total health risks of NEOs through multiple exposure routes were denoted as hazard index (HI), calculated using Eq. (6).

$$HQ = CDI_j/RfD_j \quad (5)$$

$$HI = \Sigma\, HQ_j \quad (6)$$

In Eq. (5), j represents the different exposure routes. The reference dose (RfD) values differed for different exposure routes, as shown in Table S2. To calculate the HQs of total NEOs, RfD values for IMI were used. When an HQ or HI value was larger than 1, the risk was deemed unacceptable. The larger the HQ or HI value, the higher the exposure risk.

2.6 Data analysis

For all statistical tests, non-detected (ND) concentrations of NEOs were assigned half of the LOQ (Chen et al. 2020a, b). All pictures were drawn using Origin software (version 2017, OriginLab Corporation, USA). One-way analysis of variance (ANOVA) with Duncan's test was used to reveal statistically significant differences between groups in SPSS software (version 22.0, IBM Corporation, USA). A p value < 0.05 (two-tailed) was considered statistically significant.

3 Results

3.1 Method validation

Nine NEOs were identified in the soil samples and quantified using HPLC–MS/MS with external standards based on their retention time and peak areas in comparison with the standard calibration curves. The calibration curves were constructed using a concentration range of 0.01–1000 μg/L for ACE, IMZ, THD and ACE-DE and of 0.05–1000 μg/L for CLO, DIN, IMI, NIT and THM, with satisfactory regression coefficients (R^2) > 0.99 (Table S4). LOQ for ACE, IMZ, THD and ACE-DE was 0.02 μg/kg, whereas LOQ for each of the other five NEOs was 0.10 μg/kg. To estimate the accuracy and precision of the method, blank samples for the WF, LC and LY soils were spiked with all the target analytes at LOQ, 1 μg/kg, 10 μg/kg, 100 μg/kg and 1000 μg/kg each in quintuplicate. The results suggested that the average recoveries of the spiked standards ranged from 72.74 to 112.21%, with relative standard deviation (RSD) values of 0.28–19.13% in different soil samples (Fig. 1). This indicated that our method achieved acceptable precision and accuracy for the analysis of nine NEOs in the soils. For different NEOs, ME values ranged from −0.11 to −39.53% for the different soil samples. Certain co-extractives in the soils may potentially suppress the response of some NEOs (ME < −10%). Therefore, matrix-matched calibration curves were used to quantify all NEOs in the soils to avoid any potential ME-related bias.

3.2 Residual NEOs in the soils

All the NEOs were detected in the 283 soil samples collected from four kinds of typical vegetable greenhouses across Shandong Province in China. Descriptive statistics for each of residual NEOs is presented in Table 1. Among all the soil samples, IMI, CLO and THM were the top three detected NEOs, with their respective detection frequencies of 99.65%, 99.65% and 96.82%, followed by ACE (90.46%), DIN (67.14%), ACE-DE (61.48%), NIT (56.89%), IMZ (18.02%) and THD (1.77%). For the different greenhouse soils, NEOs that were found in all the samples included the following: ACE in pepper soils; CLO in celery, pepper and tomato soils; DIN in tomato soils; IMI in celery, cucumber and tomato soils; and THM in cucumber soils. Moreover, the highest level of NIT was detected in cucumber soils (81.08%), whereas ACE-DE and IMZ were detected in

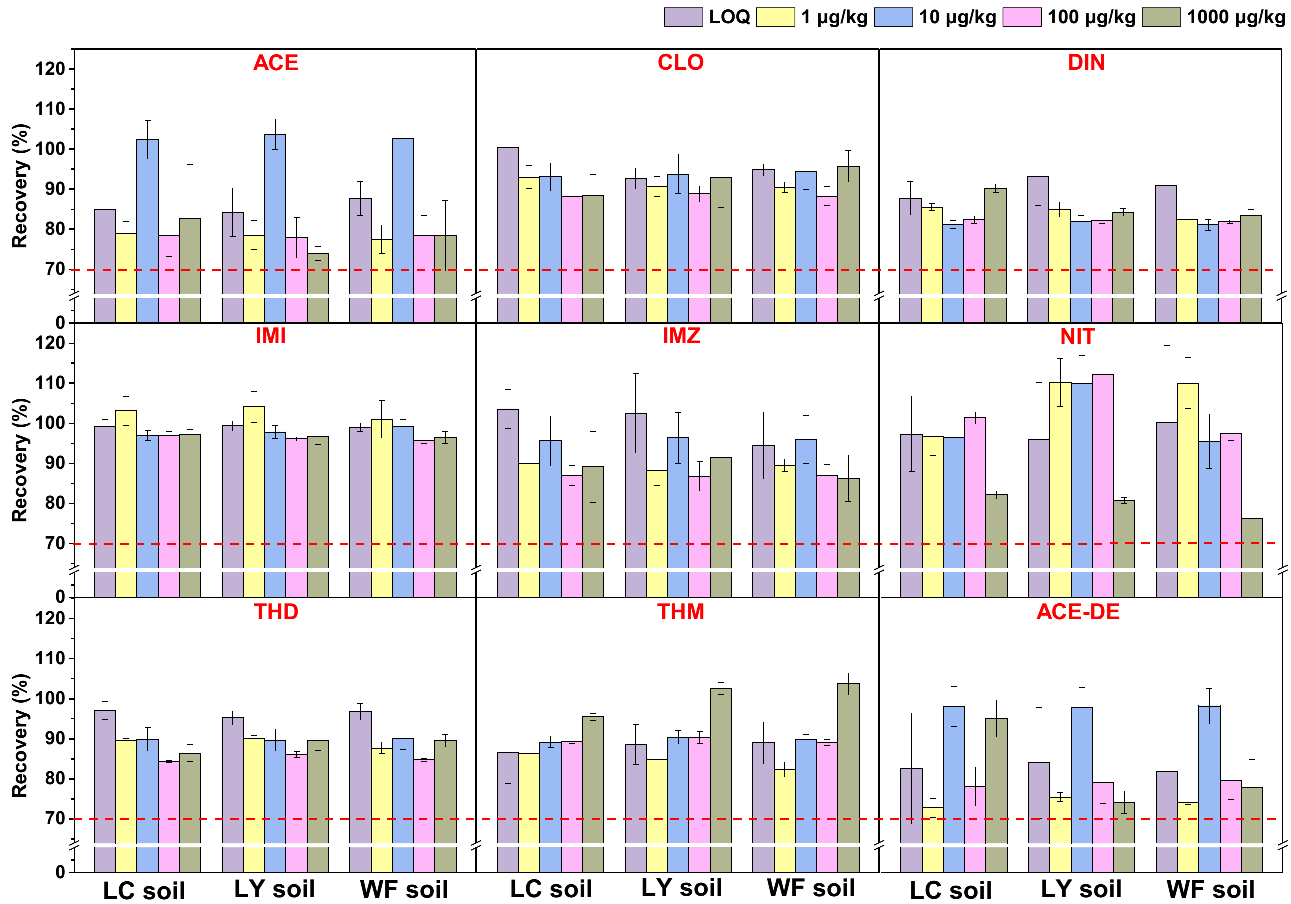

Fig. 1 The recovery of nine NEOs at five concentrations ($n=5$) for the different soils

pepper soils (94.44% and 40.28%, respectively). However, THD was detected in < 3% of the samples, ranging from 0.00 to 2.82% for the different greenhouse soils.

Multiple NEOs were diffusely found in the samples. All the 283 samples were contaminated with 2–8 detectable NEOs. As shown in Fig. 2, 0.35% of these samples contained two NEOs, 6.36% contained three NEOs, 19.43% contained four NEOs, 24.38% contained five NEOs, 36.04% contained six NEOs and 12.72% contained seven NEOs. For the different vegetable soils, 5.63–33.33% contained four NEOs, 16.67–32.39% contained five NEOs, 13.64–55.41% contained six NEOs and 0.00–30.56% contained seven NEOs (Fig. 3). Moreover, only celery soil samples contained 2–3 NEOs, with detection frequencies of 1.52% and 27.27%, respectively. Significantly, ≥ 4 NEOs were detected in all of the cucumber, pepper and tomato soil samples, and 94.37% of tomato soil samples and 93.24% of the cucumber soil samples contained ≥ 5 NEOs. Additionally, one cucumber soil sample and one pepper soil sample contained 8 NEOs.

The abundance of residual NEOs differed substantially with the different soil samples, with concentrations ranging from ND to 1816.67 μg/kg, and most of the detectable residues were at low levels (Table 1). For all the samples, average THM concentration was the highest (157.64 μg/kg), followed by CLO (50.21 μg/kg), IMI (27.55 μg/kg), DIN (7.86 μg/kg), ACE (4.99 μg/kg), NIT (3.22 μg/kg), ACE-DE (0.18 μg/kg), IMZ (0.09 μg/kg) and THD (0.01 μg/kg) (Table 1). Notably, outlier values for average NEO concentrations were observed in specific vegetable soils, including THM in tomato (269.83 μg/kg), pepper (189.34 μg/kg), cucumber (112.54 μg/kg) and celery (52.94 μg/kg) soils; CLO in pepper soils (152.01 μg/kg); and IMI in cucumber (36.78 μg/kg) and tomato (33.77 μg/kg) soils. In contrast, the average concentrations of IMZ, THD and ACE-DE were < 1.00 μg/kg in different vegetable soils. In order to facilitate the assessment of total NEO concentrations for different vegetable soils, we introduced the RPF method. The IMI_{RPF} ranged from 4.80 to 12,129.48 μg/kg for all the samples. Moreover, the tomato and pepper soils were characterised with statistically higher concentrations of NEOs than those found in cucumber and celery soils (ANOVA, $p < 0.05$) (Fig. 3).

Table 1 Descriptive statistics for NEO residues (μg/kg) in the different soils

Statistics	ACE	CLO	DIN	IMI	IMZ	NIT	THM	THD	ACE-DE	IMI_{RPF}
Total samples (283)										
Frequency (%)	90.46	99.65	67.14	99.65	18.02	56.89	96.82	1.77	61.48	–
Mean	4.99	50.21	7.86	27.55	0.09	3.22	157.64	0.01	0.18	1126.68
SD	15.64	113.35	24.18	66.37	0.35	12.90	282.68	0.01	0.41	1895.69
Min	ND	ND	ND	ND	ND	ND	ND	ND	ND	4.80
25% percentile	0.06	2.01	ND	2.42	ND	ND	7.21	ND	ND	83.39
Median	0.31	9.58	0.35	5.42	ND	0.16	49.35	ND	0.04	440.59
75% percentile	1.91	29.52	2.61	15.85	ND	0.69	149.76	ND	0.22	1199.91
Max	114.99	1070.33	176.35	531.88	3.28	127.92	1816.67	0.07	5.15	12129.48
Celery soil (66)										
Frequency (%)	72.73	100.00	30.30	100.00	1.52	25.76	90.91	0.00	42.42	–
Mean	0.23	12.37	1.40	23.15	0.01	0.79	52.94	0.01	0.15	386.96
SD	0.43	30.69	5.98	45.49	0.00	1.98	186.48	0.00	0.35	1260.04
Min	ND	0.24	ND	0.49	ND	ND	ND	ND	ND	4.80
25% percentile	ND	1.92	ND	1.51	ND	ND	0.86	ND	ND	15.06
Median	0.05	3.89	ND	5.19	ND	ND	1.46	ND	ND	37.09
75% percentile	0.20	10.82	0.21	20.85	ND	0.16	8.71	ND	0.06	96.73
Max	2.03	236.27	35.14	238.38	0.03	9.81	1210.61	ND	1.85	8086.35
Cucumber soil (74)										
Frequency (%)	91.89	98.65	82.43	100.00	21.62	81.08	100.00	1.35	60.81	–
Mean	1.75	19.61	9.89	36.78	0.07	5.77	112.54	0.01	0.10	806.49
SD	3.24	52.05	23.11	99.97	0.24	21.02	196.40	0.01	0.12	1322.82
Min	ND	ND	ND	0.52	ND	ND	1.03	ND	ND	9.05
25% percentile	0.08	1.09	0.15	2.87	ND	0.15	9.69	ND	ND	128.39
Median	0.28	2.69	0.57	6.83	ND	0.48	30.05	ND	0.04	278.87
75% percentile	2.23	12.44	4.59	20.65	ND	2.26	97.87	ND	0.15	784.32
Max	15.58	339.44	108.79	531.88	1.33	127.92	855.55	0.07	0.45	5807.84
Pepper soil (72)										
Frequency (%)	100.00	100.00	52.78	98.61	40.28	56.94	98.61	2.78	94.44	–
Mean	11.34	152.01	8.93	15.97	0.25	5.22	189.34	0.01	0.25	1417.29
SD	21.39	181.39	35.63	41.95	0.62	13.29	265.39	0.01	0.21	1763.56
Min	0.13	3.48	ND	ND	ND	ND	ND	ND	ND	67.66
25% percentile	0.87	16.33	ND	3.14	ND	ND	62.38	ND	0.11	551.23
Median	1.62	118.17	0.15	4.80	ND	0.20	118.57	ND	0.22	939.81
75% percentile	7.87	222.80	0.63	8.49	0.16	0.65	180.26	ND	0.33	1356.15
Max	81.69	1070.33	176.35	279.69	3.28	54.26	1776.05	0.07	1.21	11861.07
Tomato soil (71)										
Frequency (%)	95.77	100.00	100.00	100.00	7.04	60.56	97.18	2.82	46.48	–
Mean	6.37	14.04	10.67	33.77	0.01	0.78	269.83	0.01	0.22	1853.33
SD	20.82	19.15	20.59	57.72	0.00	2.20	389.44	0.00	0.69	2603.21
Min	ND	0.36	0.12	0.52	ND	ND	ND	ND	ND	10.10
25% percentile	0.05	1.53	0.93	2.41	ND	ND	32.98	ND	ND	293.14
Median	0.18	7.14	2.58	7.10	ND	0.13	97.30	ND	ND	653.47
75% percentile	0.83	19.11	13.23	42.01	ND	0.44	316.19	ND	0.13	2176.64
Max	114.99	129.16	119.37	261.57	0.03	12.79	1816.67	0.04	5.15	12129.48

NEOs below LOQ were defined as non-detected (ND)

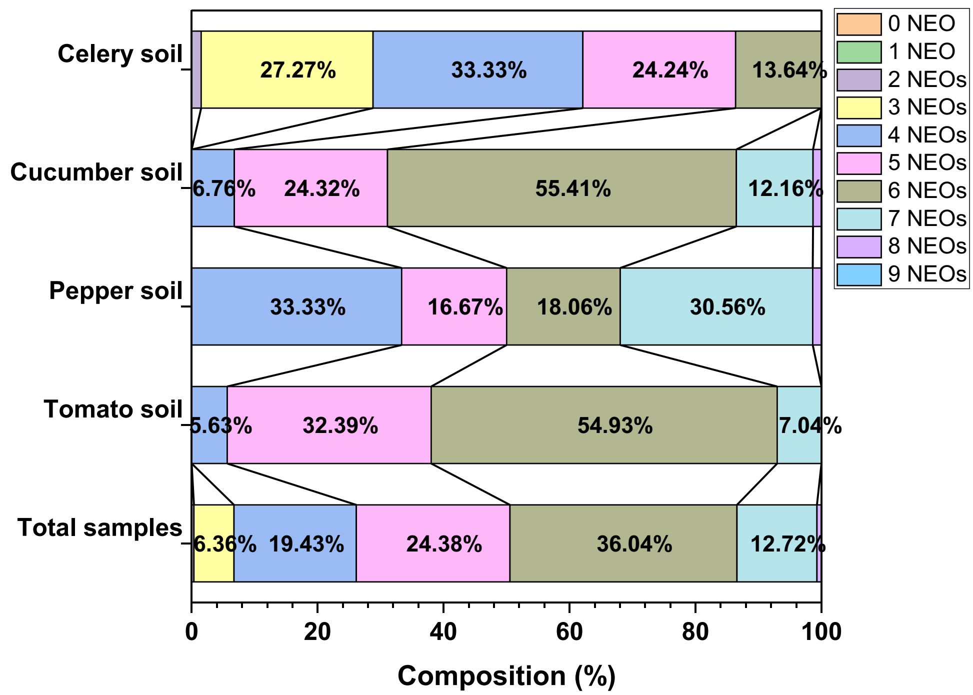

Fig. 2 Number of NEOs detected for the different soils

3.3 Health risk assessment

The chronic daily intake of each NEO and total NEOs from the three routes, which included ingestion, dermal contact and inhalation, is summarised in Table S5. The CDI values for each NEO (μg/kg BW/day) ranged from 1.55×10^{-8} to 2.82×10^{-3} for adults and from 9.99×10^{-8} to 1.81×10^{-2} for children through ingestion, from 5.84×10^{-9} to 1.06×10^{-3} for adults and from 2.84×10^{-8} to 5.17×10^{-3} for children through dermal contact and from 1.65×10^{-12} to 3.01×10^{-7} for adults and from 2.75×10^{-12} to 5.00×10^{-7} for children through inhalation. From the CDI values, the daily exposure doses through ingestion were higher than those through dermal contact and inhalation (Table S5; Fig. 4), indicating ingestion as a primary exposure pathway. Among all NEOs, THM, CLO and IMI mostly had the top three average CDI values for different vegetable soils for both adults and children, whereas IMZ, ACE-DE and THD had smaller CDI values (Fig. 4). Furthermore,

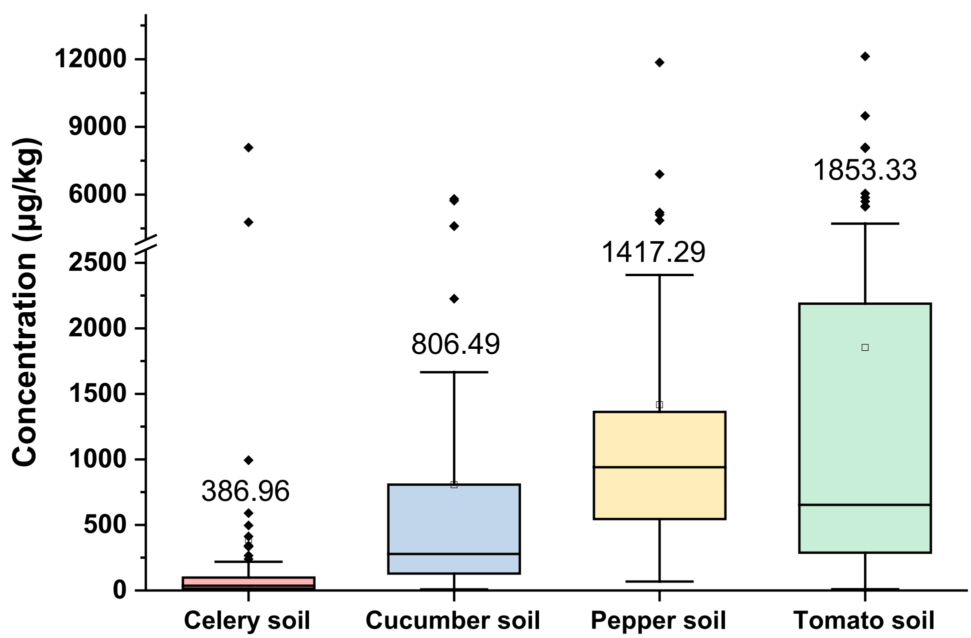

Fig. 3 Total NEO concentrations (expressed as IMI_{RPF}) for the different soils. The digits represent the average concentrations

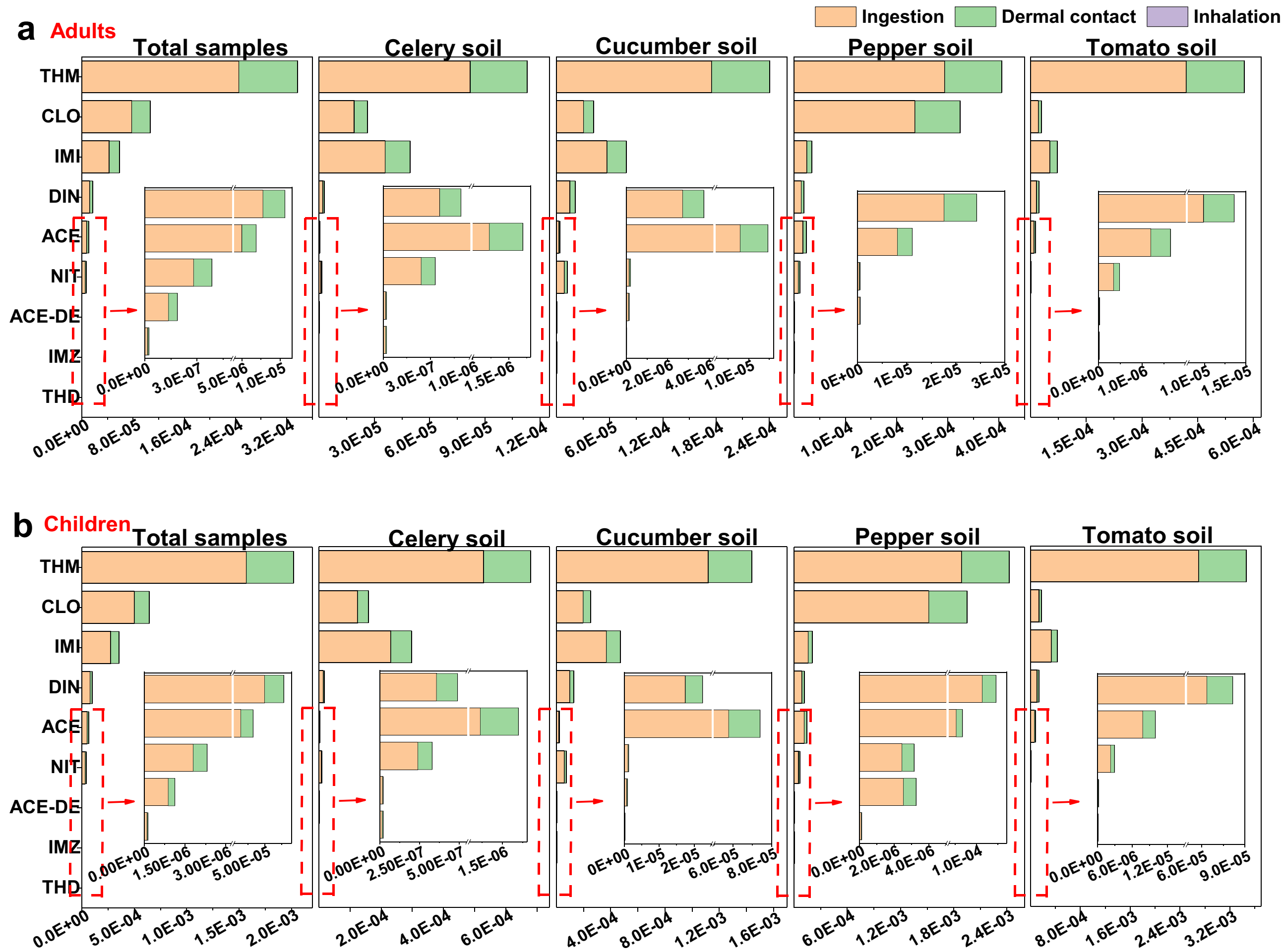

Fig. 4 The CDI values for each NEO via ingestion, dermal contact and inhalation exposure for adults (**a**) and children (**b**) for the different soils

the CDIs for total NEOs were calculated based on IMI_{RPF} as the total NEO content for each soil sample. The CDIs for total NEOs (μg/kg BW/day) ranged from 7.44×10^{-6} to 1.88×10^{-2} for adults and from 4.79×10^{-5} to 0.12 for children through ingestion, from 2.80×10^{-6} to 7.08×10^{-3} for adults and from 1.36×10^{-5} to 3.45×10^{-2} for children through dermal contact and from 7.93×10^{-10} to 2.01×10^{-6} for adults and from 1.32×10^{-9} to 3.34×10^{-6} for children through inhalation. As shown in Fig. 5, tomato soils had the highest average CDI values for both adults and children, followed by pepper, cucumber and celery soils.

Based on CDI values, HQs were calculated and expressed as a percentage of their respective RfD values for different exposure pathways and are shown in Table S6. However, the HQs from inhalation were not taken into consideration for the absence of reference dose of inhalation (RfC_i) for all NEOs. The HI values for each NEO or total NEOs were summed together based on the HQs from soil ingestion and dermal contact. For each NEO, the HI values ranged from 1.07×10^{-10} to 3.23×10^{-4} for adults and from 6.42×10^{-10} to 1.94×10^{-3} for children, which were all < 1 (Table S6). THM had the highest average HI values in tomato soils (4.80×10^{-5} for adults and 2.89×10^{-4} for children), followed by THM in pepper (3.37×10^{-5} for adults and 2.02×10^{-4} for children), cucumber (2.00×10^{-5} for adults and 1.20×10^{-4} for children), and celery (9.42×10^{-6} for adults and 5.66×10^{-5} for children) soils and by CLO in pepper soils (3.31×10^{-6} for adults and 1.99×10^{-5} for children) (Fig. 6a, b). For total NEOs, the HI values ranged from 1.28×10^{-7} to 3.24×10^{-4} for adults and from 7.69×10^{-7} to 1.95×10^{-3} for children, which were also < 1 (Table S6). In different vegetable soils, average HI values for total NEOs were in the order of tomato, pepper, cucumber and celery soils for both adults and children (Fig. 6c, d). Overall, human health risks associated with exposure to NEOs from the soils in the surveyed greenhouses were minimal.

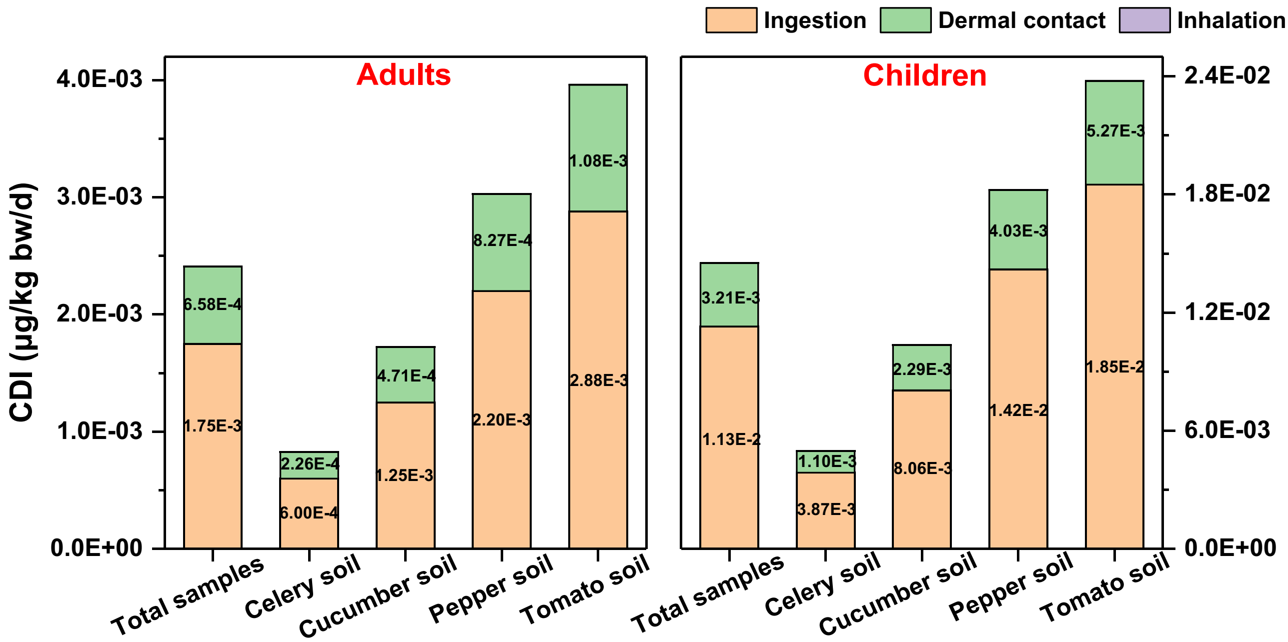

Fig. 5 The CDI values for total NEOs through ingestion, dermal contact and inhalation exposure for adults and children for the different soils

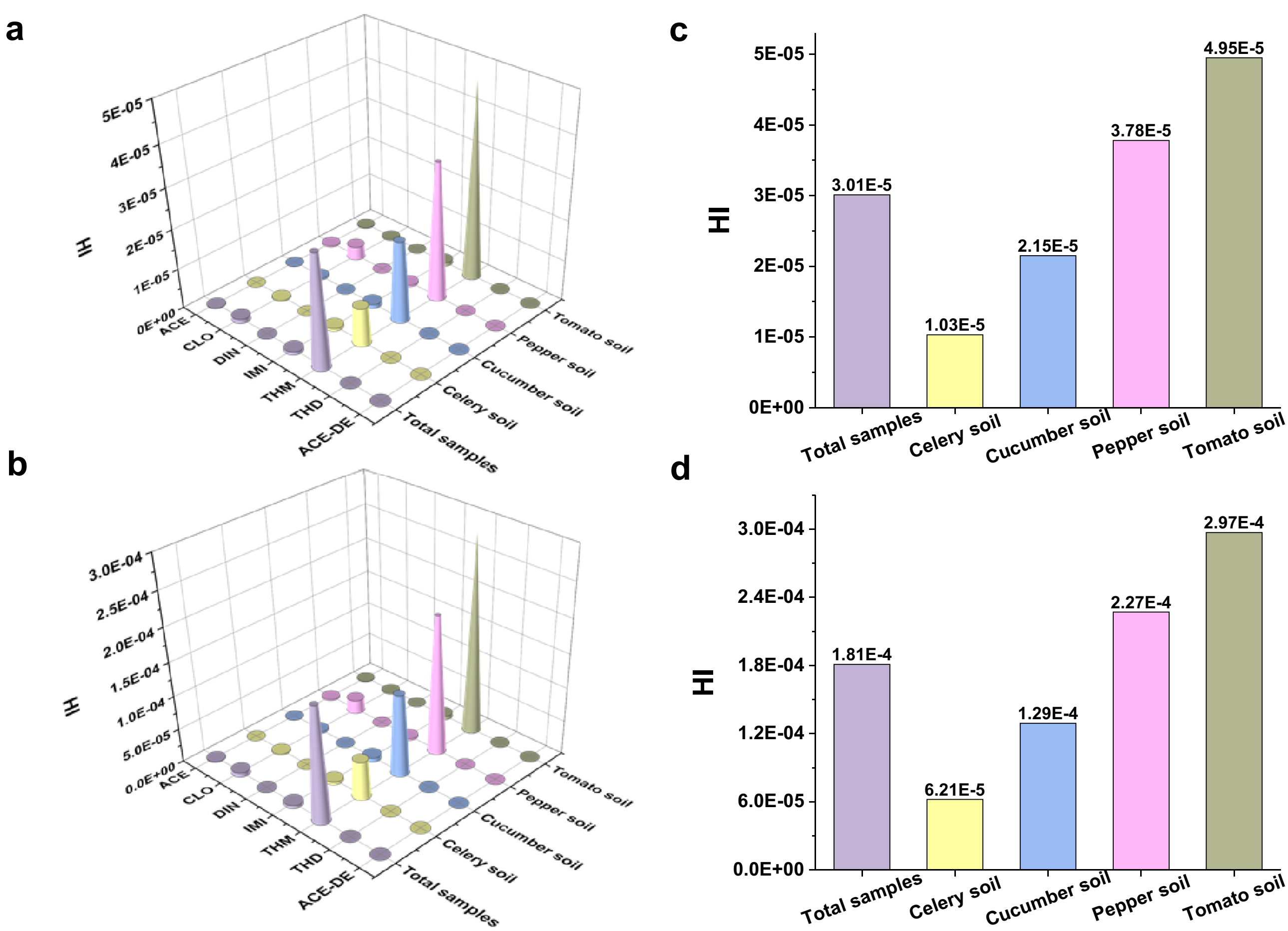

Fig. 6 The HI values for each NEO (**a** adults, **b** children) and total NEOs (**c** adults, **d** children) for the different soils

4 Discussion

NEOs, which are characterised by a long persistence and strong transferability, are the most widely used insecticides for the control of various field pests in China. Recently, many studies have confirmed an increase in the level of pesticide residues in greenhouse soils (Li et al. 2021b; Sun et al. 2018; Wu et al. 2020). In this study, IMI, CLO and THM were the most commonly detected NEOs, with detection rates of > 96.00%. In addition, the average concentrations of these three NEOs were higher than those of the other NEOs analysed, with average concentrations of 27.55–157.64 μg/kg. IMI and THM are the typical representatives of the first-generation and second-generation NEOs, which are the commercial products that account for more than 50% of total NEO-containing products in China (http://www.chinapesticide.org.cn). CLO is not only used as another NEO insecticide, but it is also the main metabolite of THM in soils (You et al. 2020), which may finally result in higher detection frequency and residue amounts. Although most of the detected NEO residues were at low levels, all the soil samples we analysed contained multiple NEOs (≥ 2 NEOs), of which 93.29% contained ≥ 4 NEOs. Similarly, several publications also concluded that multiple NEOs occurred ubiquitously in different soils (Humann-Guilleminot et al. 2019; Wu et al. 2020; Yu et al. 2021; Zhou et al. 2021). For instance, Zhou et al. (2021) found that all the 61 soil samples in the spring and 84.30% of the 158 samples in the fall contained ≥ 2 NEOs. Moreover, IMI, ACE, THM and CLO were the top four detected NEOs (detection rates of 52.50–100.00% in the spring and 32.30–93.00% in the fall) with average concentrations of 3.32–101.00 μg/kg in the spring and 1.81–45.10 μg/kg in the fall. Various factors influence pesticide residues in soils, including pesticide type, soil property, soil microbiome, local climate, cultivation patterns and pest-specific differences (Khan 2016).

Due to the co-presence of NEO residues in a given soil sample, the potential additive effects of all NEOs must be considered in order to achieve a comprehensive evaluation of their health risks to the residents. The HI values for each NEO (1.07×10^{-10} to 1.94×10^{-3}) or total NEOs (1.28×10^{-7} to 1.95×10^{-3}) were much less than 1 (risk threshold value), indicating that the health risks of exposure to NEOs from the soils in the surveyed greenhouses were low for both adults and children. Similar to our results, Yu et al. (2021) also concluded that the risks of exposure to each of the six NEOs (IMI, CLO, ACE, IMZ, DIN and flonicamid) from 351 soil samples in vegetable farms, rice paddies and fruit farms posed a negligible non-cancer risk; however, this study failed to check the possible cumulative effects of total NEOs. We also noticed that the health risks of exposure to NEOs from the soil samples for adults were lower than those for children, possibly due to the lower amounts of soil exposure per unit body weight, compared with that for children (Zhou et al. 2020). Although these results indicated no obvious health risks for the residents, the long-term effects of low-dose exposure to NEOs should not be neglected. Katić et al. (2021) reported that oral exposure of male Wistar rats to IMI at doses of 0.06 mg/kg BW/day, 0.80 mg/kg BW/day and 2.25 mg/kg BW/day for 28 consecutive days induced obvious DNA damage in the brain tissues and influenced the plasma oxidative stress parameters, which negatively affected the rat nervous system. Xu et al. (2021a) reported that all the seven NEOs were found in different rat tissues after 60 days of oral co-exposure at environmental doses (100 μg/L for each NEO), and ACE and THD accumulated in the liver and spleen tissues, indicating potential accumulation capacity of NEOs in human tissues. Besides, increasing evidence suggests that NEOs could be easily absorbed by plants from NEO-contaminated soils and accumulate in different plant tissues (Li et al. 2018, 2019; Wang et al. 2021, 2022). In addition to the accumulation in the roots, NEOs have a greater tendency to accumulate into edible leaves or fruits through the xylem during the general transpiration. For instance, when komatsuna (*Brassica rapa* var. *perviridis*) was grown in NEO-contaminated soils, the concentrations of NEOs in edible shoots were up to several dozen folds higher than those in the roots and soils (Li et al. 2018). Generally, most of NEOs enter into the plants through roots; however, the remaining amounts may be absorbed directly from the air. NEOs are commonly found in air particulate matter (Forero et al. 2017; Zhou et al. 2020). The above-ground biomass of plants can absorb NEOs from soils through the precipitation of volatile contaminants or through aerial deposition of contaminants from ambient air. With the accumulation of NEOs in plants, there is an increase in the risks of dietary exposure to NEOs through the food chain. Considering the potential health risks of NEOs to humans, proper measures should be taken to control NEO residues in the soils. On the one hand, non-chemical alternative methods could replace NEOs to decrease the use of the pesticides at source, including predators, parasitoids, entomopathogenic microorganisms, semiochemicals and genetically improved plant defense (Jactel et al. 2019). On the other hand, effective remediation methods could be used to remove NEO residues from contaminated soils, including microbial degradation, solar heating, ozonation and solarisation. (Martínez-Escudero et al. 2022; Pang et al. 2020; Sarkar et al. 2019; Vela et al. 2017).

We acknowledge that there are still some limitations associated with this study. First, to assume a worst-case scenario, all the soil samples were collected at the harvest stage for all vegetables. At this stage, vegetables are vulnerable to pest attack, and therefore, NEOs are more frequently used to control various pests, resulting in higher concentrations of NEO residues in the soils. Therefore, human health risks of exposure to NEOs from the surveyed soils may have been overestimated. Second, we analysed only 283 soil samples from four kinds of typical vegetable greenhouses; however, more soil samples in different vegetable greenhouses from different regions need to be assessed. Third, this work only considered the routes of soil exposure, whereas other possible dietary sources, especially water, fruits, vegetables and other food products, should be taken into consideration to achieve a complete understanding of the health risks of total NEOs to humans.

5 Conclusion

To the best of our knowledge, this is the first study to systematically describe the pollution characteristics of NEOs in typical vegetable greenhouses and apply the RPF method to evaluate the potential cumulative risks of human exposure to total NEOs from contaminated soils. The results of the present study indicated that IMI, CLO and THM were the most commonly detected NEOs, with detection rates of > 96.00%, and these three NEOs had higher average concentrations among different soils at concentrations of 27.55–157.64 μg/kg. Residual NEOs differ greatly among different individual samples, but most of the detected NEO residues were at low levels. All the samples contained ≥ 2 NEOs, and > 90.00% contained ≥ 4 NEOs. We noted that the health risks of exposure to each NEO or total NEOs for the children were higher than those for the adults, but all pose a negligible risk to human health. Given the ubiquity of NEOs in the soils and their potential risks, effective non-chemical alternative or remediation methods should be adopted to control the NEO residues in the soils. Overall, our results provide a preliminary insight into NEO residues in greenhouse soils and exposure risks for Chinese residents as well as a reference for the determination of the maximum residue limits of NEOs in soils and establishment of the future risk assessment programs.

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Declarations

Competing interests The authors declare no competing interests.

References

Anastassiades M, Lehotay SJ, Štajnbaher D, Schenck FJ (2003) Fast and easy multiresidue method employing acetonitrile extraction/partitioning and "dispersive solid-phase extraction" for the determination of pesticide residues in produce. J AOAC Int 86:412–431

Annabi E, Ben Salem I, Abid-Essefi S (2019) Acetamiprid, a neonicotinoid insecticide, induced cytotoxicity and genotoxicity in PC12 cells. Toxicol Mech Methods 29:580–586

Bhandari G, Atreya K, Scheepers PT, Geissen V (2020) Concentration and distribution of pesticide residues in soil: non-dietary human health risk assessment. Chemosphere 253:126594

Bonmatin JM, Noome DA, Moreno H, Mitchell EA, Glauser G, Soumana OS, van Lexmond MB, Sánchez-Bayo F (2019) A survey and risk assessment of neonicotinoids in water, soil and sediments of Belize. Environ Pollut 249:949–958

Bonmatin JM, Mitchell EA, Glauser G, Lumawig-Heitzman E, Claveria F, van Lexmond MB, Taira K, Sánchez-Bayo F (2021) Residues of neonicotinoids in soil, water and people's hair: a case study from three agricultural regions of the Philippines. Sci Total Environ 757:143822

Carvalho FP (2017) Pesticides, environment, and food safety. Food Energy Secur 6:48–60

Chen D, Liu Z, Barrett H, Han J, Lv B, Li Y, Li J, Zhao Y, Wu Y (2020a) Nationwide biomonitoring of neonicotinoid insecticides in breast milk and health risk assessment to nursing infants in the Chinese population. J Agric Food Chem 68:13906–13915

Chen D, Zhang Y, Lv B, Liu Z, Han J, Li J, Zhao Y, Wu Y (2020b) Dietary exposure to neonicotinoid insecticides and health risks in the Chinese general population through two consecutive total diet studies. Environ Int 135:105399

Chen Q, Zhang Y, Li J, Su G, Chen Q, Ding Z, Sun H (2021) Serum concentrations of neonicotinoids, and their associations with lipid molecules of the general residents in Wuxi City. Eastern China J Hazard Mater 413:125235

Cui K, Wu X, Wei D, Zhang Y, Cao J, Xu J, Dong F, Liu X, Zheng Y (2021) Health risks to dietary neonicotinoids are low for Chinese residents based on an analysis of 13 daily-consumed foods. Environ Int 149:106385

Degrendele C, Klánová J, Prokeš R, Příbylová P, Šenk P, Šudoma M, Röösli M, Dalvie MA, Fuhrimann S (2022) Current use pesticides in soil and air from two agricultural sites in South Africa: implications for environmental fate and human exposure. Sci Total Environ 807:150455

Dou R, Sun J, Deng F, Wang P, Zhou H, Wei Z, Chen M, He Z, Lai M, Ye T (2020) Contamination of pyrethroids and atrazine in greenhouse and open-field agricultural soils in China. Sci Total Environ 701:134916

European Commission (EC) (2021) Analytical quality control and method validation procedures for pesticide residues analysis in food and feed. SANTE/11312/2021. Available online: https://www.eurl-pesticides.eu/userfiles/file/EurlALL/SANTE_11312_2021.pdf

Feki A, Ben Saad H, Bkhairia I, Ktari N, Naifar M, Boudawara O, Droguet M, Magné C, Nasri M, Ben Amara I (2019) Cardiotoxicity and myocardial infarction-associated DNA damage induced by thiamethoxam in vitro and in vivo: protective role of Trigonella foenum-graecum seed-derived polysaccharide. Environ Toxicol 34:271–282

Forero LG, Limay-Rios V, Xue Y, Schaafsma A (2017) Concentration and movement of neonicotinoids as particulate matter downwind during agricultural practices using air samplers in Southwestern Ontario, Canada. Chemosphere 188:130–138

Houchat JN, Cartereau A, Le Mauff A, Taillebois E, Thany SH (2020) An overview on the effect of neonicotinoid insecticides on

mammalian cholinergic functions through the activation of neuronal nicotinic acetylcholine receptors. Int J Environ Res Public Health 17:3222
Humann-Guilleminot S, Binkowski ŁJ, Jenni L, Hilke G, Glauser G, Helfenstein F (2019) A nation-wide survey of neonicotinoid insecticides in agricultural land with implications for agri-environment schemes. J Appl Ecol 56:1502–1514
Jactel H, Verheggen F, Thiéry D, Escobar-Gutiérrez AJ, Gachet E, Desneux N, Group NW (2019) Alternatives to neonicotinoids. Environ Int 129:423-429
Katić A, Kašuba V, Kopjar N, Lovaković B, Marjanović Čermak A, Mendaš G, Micek V, Milić M, Pavičić I, Pizent A, Žunec S, Želježić D (2021) Effects of low-level imidacloprid oral exposure on cholinesterase activity, oxidative stress responses, and primary DNA damage in the blood and brain of male Wistar rats. Chem Biol Interact 338:109287
Khan SU (2016) Pesticides in the soil environment. Elsevier
Li S, Cao Y, Pan Q, Xiao Y, Wang Y, Wang X, Li X, Li Q, Tang X, Ran B (2021a) Neonicotinoid insecticides triggers mitochondrial bioenergetic dysfunction via manipulating ROS-calcium influx pathway in the liver. Ecotoxicol Environ Saf 224:112690
Li Y, Long L, Yan H, Ge J, Cheng J, Ren L, Yu X (2018) Comparison of uptake, translocation and accumulation of several neonicotinoids in komatsuna (Brassica rapa var. perviridis) from contaminated soils. Chemosphere 200:603–611
Li Y, Long L, Ge J, Li H, Zhang M, Wan Q, Yu X (2019) Effect of imidacloprid uptake from contaminated soils on vegetable growth. J Agric Food Chem 67:7232–7242
Li Z, Sun J, Zhu L (2021b) Organophosphorus pesticides in greenhouse and open-field soils across China: distribution characteristic, polluted pathway and health risk. Sci Total Environ 765:142757
Liang L, Ridoutt BG, Lal R, Wang D, Wu W, Peng P, Hang S, Wang L, Zhao G (2019) Nitrogen footprint and nitrogen use efficiency of greenhouse tomato production in North China. J Clean Prod 208:285–296
Martínez-Escudero C, Garrido I, Flores P, Hellín P, Contreras-López F, Fenoll J (2022) Remediation of triazole, anilinopyrimidine, strobilurin and neonicotinoid pesticides in polluted soil using ozonation and solarization. J Environ Manage 310:114781
Pang S, Lin Z, Zhang W, Mishra S, Bhatt P, Chen S (2020) Insights into the microbial degradation and biochemical mechanisms of neonicotinoids. Front Microbiol 11:868
Sarkar B, Tsang DC, Song H, Ding S, Vithanage M (2019) Technological innovation for soil/sediment remediation. J Soils Sediments 12:3881–3882
Sun J, Pan L, Li Z, Zeng Q, Wang L, Zhu L (2018) Comparison of greenhouse and open field cultivations across China: soil characteristics, contamination and microbial diversity. Environ Pollut 243:1509–1516
United States Environmental Protection Agency (USEPA) (2021) Regional screening levels (RSLs) - user's guide. Washington DC. Available online: https://www.epa.gov/risk/human-health-risk-assessment
Vela N, Fenoll J, Navarro G, Garrido I, Navarro S (2017) Trial of solar heating methods (solarization and biosolarization) to reduce persistence of neonicotinoid and diamide insecticides in a semiarid Mediterranean soil. Sci Total Environ 590:325–332
Wang A, Mahai G, Wan Y, Jiang Y, Meng Q, Xia W, He Z, Xu S (2019) Neonicotinoids and carbendazim in indoor dust from three cities in China: spatial and temporal variations. Sci Total Environ 695:133790
Wang F, Li X, Yu S, He S, Cao D, Yao S, Fang H, Yu Y (2021) Chemical factors affecting uptake and translocation of six pesticides in soil by maize (Zea mays L.). J Hazard Mater 405:124269.
Wang Y, Li X, Shen J, Lang H, Dong S, Zhang L, Fang H, Yu Y (2022) Uptake, translocation, and metabolism of thiamethoxam in soil by leek plants. Environ Res 211:113084
Wu RL, He W, Li YL, Li YY, Qin YF, Meng FQ, Wang LG, Xu FL (2020) Residual concentrations and ecological risks of neonicotinoid insecticides in the soils of tomato and cucumber greenhouses in Shouguang, Shandong Province. East China Sci Total Environ 738:140248
Xu L, Xu X, Guo L, Wang Z, Wu X, Kuang H, Xu C (2021a) Potential environmental health risk analysis of neonicotinoids and a synergist. Environ Sci Technol 55:7541–7550
Xu M, Zhang Z, Li Z, Kan S, Liu Z, Wang D, Liu Q, Zhang H (2021b) Profiles of neonicotinoid insecticides and characteristic metabolites in paired urine and blood samples: partitioning between urine and blood and implications for human exposure. Sci Total Environ 773:145582
Yadav IC, Devi NL, Li J, Zhang G, Shakya PR (2016) Occurrence, profile and spatial distribution of organochlorines pesticides in soil of Nepal: implication for source apportionment and health risk assessment. Sci Total Environ 573:1598–1606
You X, Jiang H, Zhao M, Suo F, Zhang C, Zheng H, Sun K, Zhang G, Li F, Li Y (2020) Biochar reduced Chinese chive (Allium tuberosum) uptake and dissipation of thiamethoxam in an agricultural soil. J Hazard Mater 390:121749
Yu H, Liu Y, Shu X, Ma L, Pan Y (2020) Assessment of the spatial distribution of organochlorine pesticides (OCPs) and polychlorinated biphenyls (PCBs) in urban soil of China. Chemosphere 243:125392
Yu Z, Li XF, Wang S, Liu LY, Zeng EY (2021) The human and ecological risks of neonicotinoid insecticides in soils of an agricultural zone within the Pearl River Delta. South China Environ Pollut 284:117358
Zeng S, Ma J, Yang Y, Zhang S, Liu GJ, Chen F (2019) Spatial assessment of farmland soil pollution and its potential human health risks in China. Sci Total Environ 687:642–653
Zhang C, Yi X, Chen C, Tian D, Liu H, Xie L, Zhu X, Huang M, Ying GG (2020) Contamination of neonicotinoid insecticides in soil-water-sediment systems of the urban and rural areas in a rapidly developing region: Guangzhou. South China Environ Int 139:105719
Zhang D, Lu S (2022) Human exposure to neonicotinoids and the associated health risks: a review. Environ Int 163:107201
Zhang H, Zhang N, Zhou W, Zeng X, Wang X, Zhan M, Xu W, Huang Y, Lu L, Li Z (2021a) Profiles of neonicotinoid insecticides and their metabolites in paired saliva and periodontal blood samples in human from South China: association with oxidative stress markers. Ecotoxicol Environ Saf 212:112001
Zhang N, Wang B, Zhang Z, Chen X, Huang Y, Liu Q, Zhang H (2021b) Occurrence of neonicotinoid insecticides and their metabolites in tooth samples collected from south China: associations with periodontitis. Chemosphere 264:128498
Zhao GP, Li JW, Yang FW, Yin XF, Ren FZ, Fang B, Pang GF (2021) Spermiogenesis toxicity of imidacloprid in rats, possible role of CYP3A4. Chemosphere 282:131120
Zhao Y, Ren Z, Yang H, Li Y (2022) A novel multi-criteria framework for optimizing ecotoxicological effects and human health risks of neonicotinoid insecticides: characterization, assessment and regulation strategies. J Hazard Mater 432:128712
Zheng T, Zhang J, Tang C, Zhang Y, Duan J (2022) Persistence and vertical distribution of neonicotinoids in soils under different citrus orchards chrono sequences from southern China. Chemosphere 286:131584
Zhou Y, Guo J, Wang Z, Zhang B, Sun Z, Yun X, Zhang J (2020) Levels and inhalation health risk of neonicotinoid insecticides in

fine particulate matter (PM2.5) in urban and rural areas of China. Environ Int 142:105822

Zhou Y, Lu X, Yu B, Wang D, Zhao C, Yang Q, Zhang Q, Tan Y, Wang X, Guo J (2021) Comparison of neonicotinoid residues in soils of different land use types. Sci Total Environ 782:146803