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RESEARCH ARTICLE

# Assessing dietary exposure risk to neonicotinoid residues among preschool children in regions of Taiwan

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## Abstract
Neonicotinoids (NEOs) are a class of pesticides widely used worldwide. This study analyzed post-cooking residues of NEO pesticides and assessed their potential health risks for preschool children (0–6 years old) by conducting a total diet study (TDS). It involved food sampling, preparation, analysis of pesticide residues, estimation of food consumption data, and assessment of food safety risks. Food sampling was conducted between March and June 2015. A total of 128 food samples were obtained from 4 parts of Taiwan. After the food had been prepared, the 128 samples were aggregated into 32 composite food items and the NEO residues analyzed. Acetamiprid had the highest detection rate of the NEO residues (59.4%), and the concentrations ranged from not detected to 80.5 μg/kg. The estimated daily intake (EDI) of NEO residues among preschool children was found to be lower than the adjusted acceptable daily intake (ADI) even for highly exposed groups. The results showed that NEO pesticides were primarily detected in preserved fruits, cherry tomato, rape, bell fruit, and baby bok choy. The main health risk posed by detected NEO residues at high consumption rates for preschool children was attributed to acetamiprid (34.20 %ADI) and imidacloprid (23.69 %ADI), respectively. Therefore, this research implicates that the present level of NEO residues in the diets for preschool children in Taiwan does not exceed 100 %ADI.

**Keywords** Food safety · Health risk assessment · Neonicotinoid · Total diet study · Preschool children · Pesticides

## Introduction

Monitoring of pesticide residues in Taiwan, as well as elsewhere, is mostly carried out through the sampling and testing of raw agricultural products. Tests for contaminants in food include inedible parts of food, while the impacts of processing methods such as cooking on the pesticide residues in food have not been considered. The human body is directly affected by residual concentrations of pesticide residues found only in cooked food. During the process that occurs from the harvesting of crops to the consumption of cooked food, residual pesticides may dissipate or degrade as a result of storage or preparation procedures such as washing (Dankyi et al. 2015; Holland et al. 1994; Soliman 2001). Although the high-temperature cooking process causes pesticide degradation and reduces the level of residue, it may also generate toxic metabolites (Randhawa et al. 2007).

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Neonicotinoid (NEO) pesticides are a class of neuro-active insecticides chemically similar to nicotine and affect neuronal proliferation, apoptosis, migration, differentiation, synapse formation, and neural-circuit formation when activating nAChRs (Chen et al. 2014). NEOs are systemic in design, transfusing into all parts of treated plants, including pollen, nectar, and guttation fluids, and foods grown by those plants. They are highly effective against difficult-to-control sucking, boring, and root-feeding insects (Cimino et al. 2016).

It was also found that NEOs could act on the nicotinic N-acetylcholine receptors, selectively displacing acetylcholine. Moreover, imidacloprid and acetamiprid have shown the excitatory effects on cultured cerebellar neurons from neonatal rats, suggesting possible neurotoxicity in developing mammalian brains (Chen et al. 2014). Imidacloprid is also evidenced to have high efficiency of absorption in intestinal cells (Roberts and Karr 2012).

The long half-life and repeated use of NEO contribute to their persistence in the environment for several years, revealing the potential risks of NEO applications for human health. Roberts and Karr (2012) also implicated that unintentional ingestion of NEO by children has considerably higher doses than that by adults for the greater intake of food per pound of body weight. Although most NEO residues reported in literatures were below the maximum residue levels established by the United States Environmental Protection Agency (USEPA), the protection of human health from long-term low-dose exposure should be taken into account (Chen et al. 2014).

Tests to assess exposure to pesticides that fail to take into account processing factors may not yield accurate results, because they overestimate the risk of pesticide residues to human health and fail to accurately reflect the actual food safety situation (Barlow et al. 2002). At the same time, inaccurate test results have adverse impacts on food safety standards, the setting of pesticide limits, and foreign trade. Due to significant differences in food processing methods, dietary exposure, and the distribution of pollutants between Taiwan and Western countries, it is necessary to consider different processing methods in relation to their actual use in Taiwan to produce a more accurate estimate of dietary exposure to residual pesticide concentrations across the population as a whole.

Total diet study (TDS) is a research method that can be applied to investigate the food consumption of an entire population. Because preschool children are sensitive, this study uses TDS to discuss the risks of preschool children. TDS samples are obtained for food that has been cooked and is ready to eat, thereby ensuring that the effect of cooking on chemical contaminants and nutrients is fully accounted for, and that the dietary conditions of consumers within a given period of time are captured (WHO/FAO 1985). The difference between the TDS method and other chemical monitoring methods lies in the former's focus on the presence of chemicals in the overall diet rather than in a single food. In addition, TDS is used to examine food prepared using home cooking methods.

Therefore, the possibility that home cooking may help to break down certain unstable chemicals and produce new compounds is taken into account. In order to determine the content of NEO residues following cooking, we obtained a representative sample of foods based on the eating habits of the Taiwanese population. After preparing the food according to standard recipes, we analyzed the contaminant residues in the food and calculated risk exposure to contaminants according to the dietary intake to estimate their health risks to preschool children (Egan 2002).

The objectives of this study are as follows: (1) to analyze NEO residues of food ingredients that have been prepared and are in a ready-to-eat state; (2) to assess the potential health risks associated with exposure to foods among preschool children; and (3) to provide recommendations for further follow-up and monitoring work for residual pesticides that contribute the greatest risk to each of the major food categories.

## Materials and methods

### Core food list among preschool children

The core food list is based on both the food consumption rate and the population of consumers, thus reflecting the population's dietary preferences and patterns (Pennington and Hernandez 2002). The consumption rate of 0–6-year-old children (preschool children) was obtained from the 2005–2008 Nutrition and Health Survey in Taiwan (NAHSIT) (Pan 2008; Tu et al. 2011). Using food classification principles and items from the 2005–2008 NAHSIT as reference, the consumption rates of each other's food items were assumed to contain pesticide residues. We calculated the overall consumption ratio, as well as the consumption ratio for each of the food items. Thirty-two food items with high consumption rates were listed first. We further reorganized the 32 foods items into 4 major categories: vegetable, fruit, cereal, and seafood (Table 1). The total consumption rate of the 32 food items accounted for a percentage of the preschool children's total consumption rate.

### Sampling and preparation of foods

The administration of Taiwan is divided into 4 regions: northern, central, southern, and eastern. We then selected the most urbanized cities or counties in each of the 4 cities: Taipei City, Kaohsiung City, Hualien County, and Taichung City. Moreover, the selected food items were obtained from an appropriate purchasing location of traditional wet markets, supermarkets, discount stores, night markets, or restaurants. Food sampling was conducted between May and June 2015.

**Table 1** Neonicotinoid concentrations in food samples

Analyte concentration (μg/kg)

| Food group | Food item | Acetamiprid[a] | Clothianidin[b] | Dinotefuran[c] | Flonicamid[d] | Imidacloprid[e] | Thiacloprid[f] | Thiamethoxam[g] |
|---|---|---|---|---|---|---|---|---|
| Vegetable | Kimchi | 12.3 | ND | ND | ND | 2.49 | ND | ND |
| | Pickled vegetables | 61.5 | ND | ND | ND | 6.14 | ND | 1.76 |
| | Dried pickled radish | ND | ND | ND | ND | ND | ND | ND |
| | Mustard greens | 35.5 | ND | ND | ND | ND | ND | ND |
| | Amaranth | ND | ND | ND | ND | ND | ND | ND |
| | Lettuce | 21.5 | ND | ND | ND | ND | ND | ND |
| | Baby bukchoy | 6.17 | ND | ND | ND | ND | ND | 47.8 |
| | Celery | ND | ND | ND | ND | ND | ND | ND |
| | Chinese cabbage | 8.49 | ND | ND | ND | ND | ND | ND |
| | Sweet potato leaves | 2.35 | ND | ND | ND | ND | ND | ND |
| | Spinach | ND | ND | ND | ND | ND | ND | 3.63 |
| | Rape | 80.2 | ND | 63.4 | ND | 78.5 | ND | ND |
| | Edible gynura | 21.2 | 2.55 | ND | ND | ND | ND | ND |
| | Chinese kale | 80.5 | ND | ND | ND | ND | ND | ND |
| | Garlic chives | 14.6 | ND | ND | ND | ND | ND | ND |
| | Scallion | ND | ND | ND | ND | ND | ND | ND |
| Fruit | Preserved fruits | 40.9 | ND | ND | ND | ND | ND | ND |
| | Guava | 5.89 | ND | ND | ND | ND | ND | ND |
| | Bell fruit | 3.4 | ND | ND | ND | 18.1 | ND | ND |
| | Starfruit | 15.4 | ND | ND | ND | 26.2 | ND | ND |
| | Tangerine | ND | ND | ND | ND | ND | ND | ND |
| | Juice | ND | ND | ND | ND | 3.18 | ND | ND |
| | Cherry tomato | ND | 2.09 | ND | ND | 5.69 | ND | ND |
| | Plum | ND | ND | ND | ND | ND | ND | ND |
| Cereal | Noodles | ND | ND | ND | ND | ND | ND | ND |
| | Baby malt extract | ND | ND | ND | ND | ND | ND | ND |
| | Sticky rice | ND | ND | ND | ND | ND | ND | ND |
| | Rice bran | ND | ND | ND | ND | ND | ND | ND |
| | Rice | ND | ND | ND | ND | ND | ND | ND |
| | Thin noodles | 3.28 | ND | ND | ND | ND | ND | ND |
| Seafood | Seaweed | ND | ND | ND | ND | ND | ND | ND |
| | Shellfish | ND | ND | ND | ND | ND | ND | ND |

[a] Limit of detection (LOD) for acetamiprid in different food matrix, 0.00158–0.00209 mg/kg (min-max)

[b] LOD for clothianidin in different food matrix, 0.00089–0.0012 mg/kg (min-max)

[c] LOD for dinotefuran in different food matrix, 0.00231–0.003 mg/kg (min-max)

[d] LOD for flonicamid in different food matrix, 0.00151–0.00291 mg/kg (min-max)

[e] LOD for imidacloprid in different food matrix, 0.00123–0.0022 mg/kg (min-max)

[f] LOD for thiacloprid in different food matrix, 0.00081–0.0022 mg/kg (min-max)

[g] LOD for thiamethoxam in different food matrix, 0.00127–0.00168 mg/kg (min-max)

A total of 32 food items were obtained from 4 cities, obtaining a total of 128 food samples. If the item could not be purchased, we would go to an additional purchasing location until the specified food was obtained. For each of the purchasing locations, we selected a business that was well patronized or well known locally. If there was no such business, we used random sampling to select an alternative.

Uncooked samples were steam cooked around 15 min in the laboratory. Furthermore, fruit was peeled and the seeds were removed according to the common food preparation processes before homogenization. After undergoing homogenization, the treated samples were stored in a freezer at − 20 °C. Following the preparation of homogenized samples, we carried out the homogeneous mixing which was proportional to each of the 4 sampling regions to obtain 32 national pooled samples for pesticide residue analysis.

## Analysis of neonicotinoid pesticide residues

NEO residue concentrations of the 32 national pooled samples were measured according to the Standard Method of Test for Pesticide Residues in Food of Taiwan—Multi-residue Analysis (TFDA (Taiwan Food and Drug Administration) 2011). The analyzed NEO residues contain acetamiprid, clothianidin, dinotefuran, flonicamid, imidacloprid, thiacloprid, and thiamethoxam. The matrix-revised pre-treatment process (Table 2) can be divided into three categories: vegetables and fruits (high moisture content) are class I, cereal (high carbohydrate content, low fat < 5%) is class II, and seafood (high protein, high fat > 5%) is class III. For class III, different food groups have different LODs; we increased the amount of C18 added from 400 to 600 mg to remove fat interference and increased the amount of graphitized carbon black (GCB) added from 45 to 64 mg to remove pigment interference. However, the addition of C18 and GCB is possible to increase the removal of aromatic compounds. Fifteen grams of the treated sample was collected in a centrifuge tube to which was added 1% acetic acid in 15 mL of acetonitrile solution, followed by the extracting powder.

Briefly, the tube was vigorously shaken several times to prevent caking, before being shaken vigorously again using a high-speed mixer at 1000 rpm for 1 min, and centrifuged for 1 min at 3000×*g* at 15 °C. Eight milliliters of supernatant was then collected by using a high-speed mixer at 1000 rpm for 1 min, and centrifuged for 2 min at 3000×*g* at 15 °C. Five hundred microliters of supernatant was obtained and mixed with 300 μL of methanol, and 200 μL of deionized water. After undergoing membrane filtration, the liquid, treated as test liquid I, was subjected to liquid chromatography/tandem mass spectrometry (LC/MS/MS) (API 5000, AB Sciex, Canada).

A quality control sample analysis was carried out for each batch, if there were less than 10 samples, or for every 10 samples. Each quality control sample analysis included analysis of blanks, duplicates, and matrix spikes. The method for determining the limit of detection should be implemented according to the steps for testing in the quality control sample analysis, producing three samples for analysis. As per the procedure followed, an *S*/*N* ratio greater than 10 indicates that the laboratory analysis is capable of reaching the limit of detection set out in the testing method. The recovery evaluation should include an appropriate amount of analyte standard in the sample before calculating the recovery rate (*R*%) (TFDA (Taiwan Food and Drug Administration) 2011).

## Risk estimation of neonicotinoid exposure

Figure 1 summarizes the overall study framework. Our study focuses on NEO residues in food, using the estimated daily intake (EDI) and adjusted acceptable daily intake of pesticide residues $p$ in foods ($ADI_p$) to assess the health risk of preschool children exposed to pesticide residues.

The hazard index (HI) in %ADI of NEO residues in 32 food items was determined by the following equation:

$$\sum_{i=1}^{n} \%ADI_{ij} = \sum_{i=1}^{n} \frac{EDI_{ij}}{ADI_P} \times 100\% = \sum_{i=1}^{n} \frac{C_i \times CR_{ij}}{BW_j \times ADI_P} \times 10^{-6} \times 100\% \quad (1)$$

where $EDI_{ij}$ (μg/kg bw/day) is the EDI of pesticide residues $p$ in foods $i$ consumed by exposure group $j$, $ADI_p$ (μg/kg bw/day) is the adjusted ADI of NEO residues $p$ in food, $C_i$ (μg/kg) is the concentration of NEO residues $p$ in food $i$, $CR_{ij}$ (g/day) is the consumption rate of food $i$ for each of the exposure groups $j$ in NAHSIT, and $BW_j$ (kg) is the body weight of each of the exposure groups $j$.

In view of Fig. 1, the mean indicates the whole group consumption rate, and the 95 percentile (P95) indicates high exposure group consumption rates, measuring the potential food safety risks of chronic exposure to pesticide residues in foods. The calculation results of the EDI and HI (%ADI) were further categorized into the lower bound (LB) and upper bound (UB) which were represented respectively not detected (ND) as 0 and the limit of detection (LOD) in the calculations.

**Table 2** The matrix-revised pre-treatment process

| Sample classification | | Vegetables and fruits (high moisture) | Cereal (high carbohydrate, low fat) | Seafood (high protein, high fat) |
|---|---|---|---|---|
| Solid extraction | | 6 g $MgSO_2$, 1.5 g $C_2H_3NaO_2$ | | |
| Centrifuge tube | | I | II | III |
| Purification | Anhydrous magnesium sulfate | 1200 mg | | |
| | PSA | 400 mg | | |
| | C18 | No added | 400 mg | 400 → 600 mg |
| | GCB | No added | No added | 45 → 64 mg |

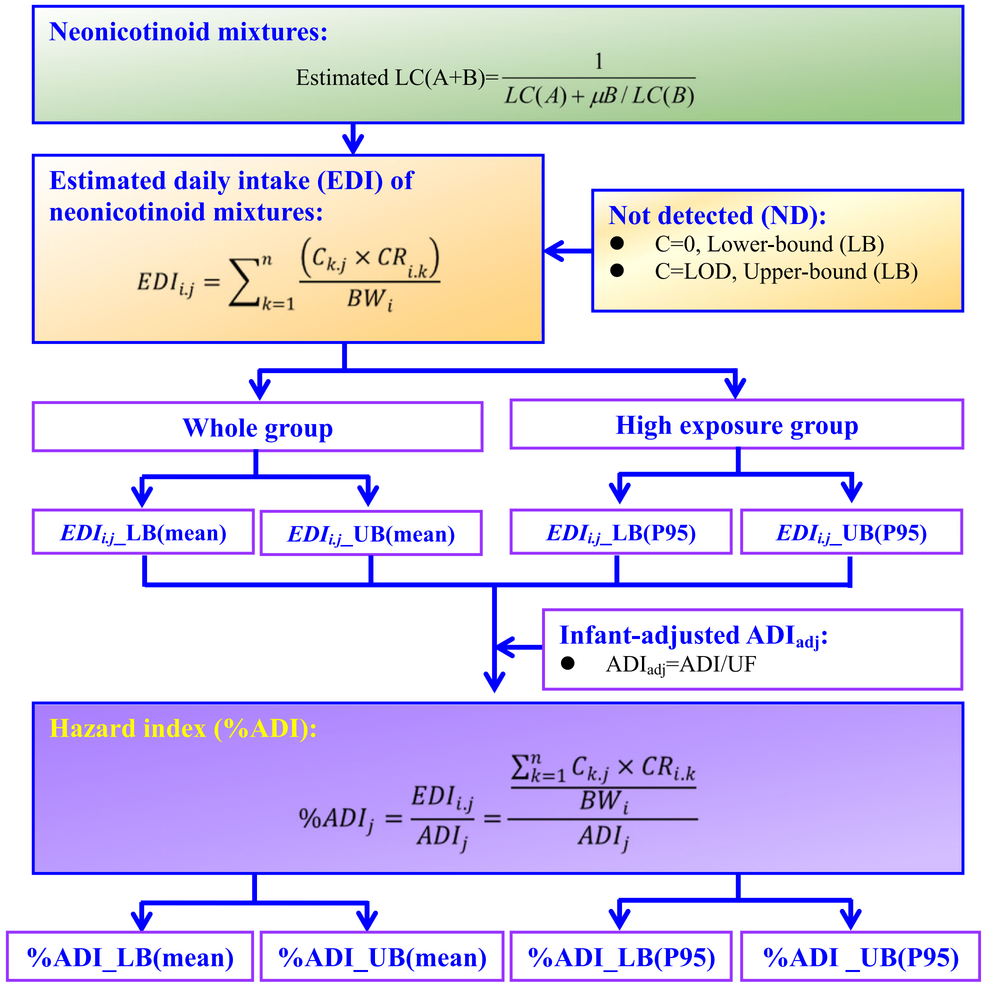


**Fig. 1** Flowchart of dietary exposure estimates for the neonicotinoid mixtures

From the NEO residue concentration results for the 32 food items, the average concentration for representative samples of each of the major categories was recorded, with ND recorded as zero. The method for calculating the average concentration of pesticide residue is based on a number of assumptions. According to the assumptions applied by GEMS/Food ERUO (WHO 1995) and USEPA (HUMAN PRI (HUMAN Principles for Responsible Investment) 2000) regarding the concentration of pesticide residue, in general, when the data contains a large number of samples (more than 10–15%) that are lower than the LOD, or the limit of quantification (LOQ), sensitivity analysis is recommended.

Sensitivity analysis assumes all ND results to be zero and LOD or LOQ, to assess changes in the exposure value and confirm whether different assumptions influence the final pesticide residue risk. The World Health Organization (WHO) assumes that unless pesticides are intentionally used, these chemicals are unlikely to be present (WHO 2009). Therefore, LB for the average concentration is used (ND = 0 is entered as lower bound) in the calculation of the food safety risk of pesticide residues (FSANZ (Food Standards Australia New Zealand) 2011; HUMAN PRI (HUMAN Principles for Responsible Investment) 2000; Vannoort and Thomson 2009).

## Results and discussion

### Concentrations of neonicotinoid pesticide residues

Table 1 shows the detected concentrations of 7 kinds of NEO pesticides in 16 types of vegetables, 8 types of fruits, 6 types of cereal, and 2 types of seafood. Acetamiprid was detected in many vegetable and fruit samples, as well as in cereal in a small quantity. The concentration of acetamiprid in cereal was higher than those of other kinds of NEO pesticides: the range was between 3.28 and 80.50 μg/kg. It was detected in 11 types of vegetables, with the highest concentrations in Chinese kale and rape (80.50 and 80.2 μg/kg, respectively); 4 types of fruits, with the highest concentration in preserved fruits (40.9 μg/kg); and 1 type of cereal, specifically thin noodles (3.28 μg/kg), and undetected in seafood. Imidacloprid was detected multiple times in the vegetable and fruit samples, among which bell fruit, starfruit, and cherry tomato had the highest concentrations.

Imidacloprid was detected in 3 types of vegetables, with the highest concentration in rape (78.50 μg/kg), and 4 types of fruits, with the highest concentration in starfruit (26.2 μg/kg), and undetected in cereal or seafood. Thiamethoxam was detected in only three types of vegetables, among which baby bok choy and spinach had the highest concentrations. Clothianidin was detected in only 1 type of vegetable and 1 type of fruit: edible gynura and cherry tomato (2.55 and 2.09 μg/kg, respectively). Dinotefuran was detected in only 1 type of vegetable: rape (63.4 μg/kg). Flonicamid and thiacloprid were not detected in the 32 samples.

The detection rate of acetamiprid was the highest among the rates of NEO pesticides (55%); imidacloprid had the second highest detection rate (24%); after that are thiamethoxam (10%), clothianidin (7%), and dinotefuran (4%). Overall, in the samples, NEO pesticides, particularly acetamiprid, imidacloprid, and thiamethoxam, were often detected in vegetables and fruits, were undetected in seafood, and were detected only in thin noodles among cereal.

Quality control in relative percent difference (RPD), recovery rate (*R*%) of sample, and recovery rate (*R*%) of standard for vegetable of matrix class I were 0.8–14.4%, 77.5–104.0%, and 87.0–121.7% and for fruit were 0.3–13.6%, 73.4–121.0%, and 84.4–114.0%, respectively. For matrix class II, they were 0.4–21.6%, 75.0–129.0%, and 77.9–121.7%, respectively. For matrix class III, they were 1.1–19.3%, 77.9–89.5%, and 68.0–74.0%, respectively.

Concentrations of NEO pesticide residues in fruits and vegetables of Taiwan were lower than those of Turkey and India. The acetamiprid residues in lettuce were 0.0215 and 0.01–0.86 mg/kg, respectively, in Taiwan and Turkey (Bakırcı et al. 2014). We also found that NEO pesticides were undetectable in plum and tangerine. However, it was observed that acetamiprid concentrations in plum and tangerine were 0.038 and 0.017 mg/kg, respectively, in Turkey (Bakırcı et al. 2014).

Furthermore, the imidacloprid residues in tomato were 0.0056, 0.012–0.088, and 0.08 mg/kg in Taiwan, Turkey, and India, respectively (Bakırcı et al. 2014; Kapoor et al. 2013). Imidacloprid concentrations of cabbage and rice were 0.0085 and undetectable in Taiwan, and 0.15 and 0.009 mg/kg in India (Kapoor et al. 2013).

Although most of the results show that the concentration of NEO residues in raw vegetables and fruits in these countries is greater than the concentration in food that has been cooked in this study, there is currently no evidence that the concentration of NEO residues will decrease after cooking. It is suggested that further research can be conducted on the concentration of neonicotinoids in food before and after cooking. We also found relatively high levels of NEO in tomato of Boston and guava of India, which were undetected NEO residues (Chen et al. 2014; Kapoor et al. 2013).

Consistent with results of this study, Chen et al. (2014) reported that most fruit and vegetable samples are detected with more than two different NEO pesticides in one sample. We also demonstrated that imidacloprid and acetamiprid are the most detected NEO pesticides in bell and preserved fruits. Moreover, the most detected NEO pesticide is varied among different countries. We found that acetamiprid is the most detected NEO pesticide among various fruits and vegetables. However, previous studies indicated that imidacloprid is the most commonly used NEO in the USA (Chen et al. 2014; Roberts and Karr 2012). Lozowicka et al. (2016) also observed that thiacloprid was the most detected NEO pesticide in fruits of Poland.

The NEO with the higher detection rate in fruits and vegetables of the USA was imidacloprid (88% for fruits, 58% for vegetables) based on 0.1 ng/g of the LOQ for NEO pesticides except flonicamid (0.2 ng/g) in fruit and vegetable samples (Chen et al. 2014). The American Bird Conservancy (ABC) investigated the NEO in cafeteria food and revealed that thiamethoxam (66%) was the most detected NEO pesticide (ABC (American Bird Conservancy) 2015). However, this study found that acetamiprid had the highest detection rate of NEOs in food in Taiwan (55%), and imidacloprid had the second highest detection rate (24%). Otherwise, Chinese kale and rape (0.08 mg/kg) had the maximum acetamiprid residues of fruits/vegetables in Taiwan, whereas USA had 0.1 mg/kg of apple (Chen et al. 2014). Rape and green pepper had the maximum imidacloprid residues of the fruits/vegetables of Taiwan and the USA, respectively. The highest number of multiple NEO residues was detected in green pepper (5 NEOs) in cafeteria food of the USA (ABC (American Bird Conservancy) 2015), whereas rape and salted vegetable in Taiwan had three NEOs. We revealed that rape had the highest number and higher residues of multiple NEO pesticides in Taiwan.

The LOD range of liquid chromatography coupled with tandem mass spectrometry (LC–MS/MS) for detection of NEO insecticide residues was 2–5 μg/kg (Dankyi et al. 2015), higher than those found in our study (0.0008–0.003 mg/kg). On the other hand, a lower detection range of 0.7–1.8 μg/kg was observed by using ultrahigh-performance liquid chromatography coupled with tandem mass spectrometry (UPLC–MS/MS) (Bakırcı et al. 2014). An enzyme-linked immunosorbent assay (ELISA) for the determination of dinotefuran residue, which was extracted with methanol in rice samples of 0.6 ng/mL (Watanabe et al. 2011), could be another analytical method with lower LOD in rice.

## Estimated daily intake of neonicotinoid

Table 3 shows the adjusted ADI for seven kinds of NEO pesticides. The calculation results were obtained from the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in that estimated ADI was divided by an uncertainty factor 10

**Table 3** EDI and %ADI of the selected food groups among the whole group and high-exposure group

| Analyte | Adjusted $ADI_{adj}$(μg/kg bw/day)[a] | Whole group | | | | High-exposure group | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | EDI (μg/kg bw/day) | | %ADI | | EDI (μg/kg bw/day) | | %ADI | |
| | | LB (mean) | UB (mean) | LB (mean) | UB (mean) | LB (P95) | UB (P95) | LB (P95) | UB (P95) |
| Acetamiprid | 7[b] | 0.08 | 0.11 | 1.16 | 1.60 | 2.39 | 3.14 | 34.20 | 44.81 |
| Clothianidin | 10[c] | 0.00 | 0.02 | 0.00 | 0.23 | 0.04 | 0.60 | 0.41 | 6.02 |
| Dinotefuran | 20[d] | 0.00 | 0.06 | 0.01 | 0.29 | 0.64 | 2.02 | 3.18 | 10.09 |
| Flonicamid | 2.5[e] | – | 0.036 | – | 1.45 | – | 1.02 | – | 40.97 |
| Imidacloprid | 6[f] | 0.01 | 0.05 | 0.25 | 0.85 | 1.42 | 2.25 | 23.69 | 37.42 |
| Thiacloprid | 1[g] | – | 0.04 | – | 3.91 | – | 0.94 | – | 93.78 |
| Thiamethoxam | 8[c] | 0.01 | 0.04 | 0.16 | 0.54 | 0.48 | 1.26 | 6.05 | 15.71 |

[a] $ADI_{adj}$ = ADI/UF (Schilter et al. 1996)

[b] JMPR (2011)

[c] JMPR (2010)

[d] JMPR (2012)

[e] EFSA (European Food Safety Authority) (2016)

[f] JMPR (2001)

[g] JMPR (2006)

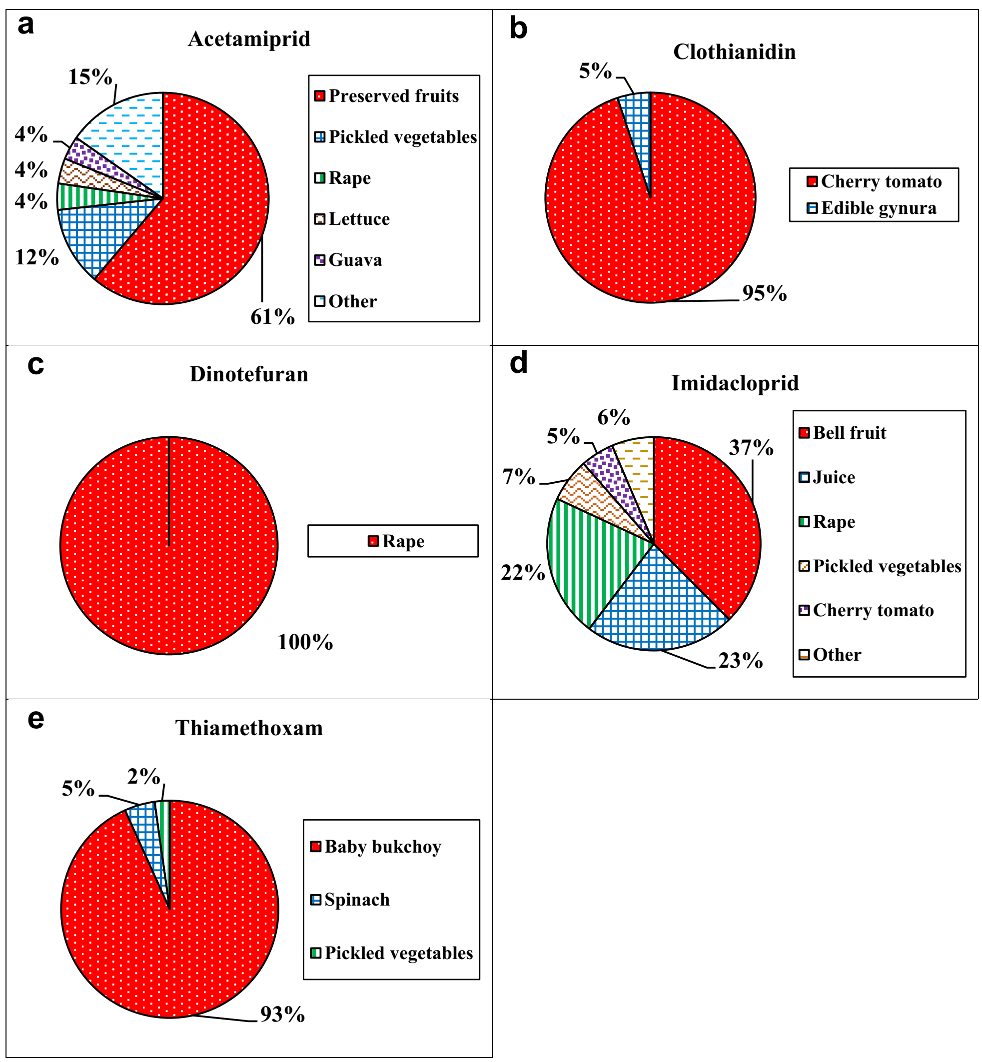


**Fig. 2** Percentage contribution of the major contributing foods to mean neonicotinoid dietary exposure for children. **a** Acetamiprid, **b** Clothianidin, **c** Dinotefuran, **d** Imidacloprid, and **e** Thiamethoxam

(Schilter et al. 1996). In this study, the undetected ratio was larger than 80%. The EDI of LB for the whole group was between ND and 0.08 μg/kg bw/day. Among the detected data, acetamiprid was the highest among all NEO pesticides, and clothianidin was the lowest. Both flonicamid and thiacloprid were undetected, which means that there was no EDI for these items. The EDI of UB was between 0.02 and 0.11 μg/kg bw/day, with acetamiprid being the highest among all NEO pesticides and flonicamid being the lowest. The EDI of LB for the high exposure group was between ND and 2.39 μg/kg bw/day. Among the detected data, acetamiprid was the highest among all NEO pesticides, and clothianidin was the lowest. Flonicamid and thiacloprid were undetected, which means that there was no EDI for these items. The EDI of UB was between 0.60 and 3.14 μg/kg bw/day, with acetamiprid being the highest among all NEO pesticides and clothianidin being the lowest.

## Hazard index of neonicotinoid

The LB for the whole group was between 0.00 and 1.16 %ADI. Acetamiprid had the highest and clothianidin had the lowest. Flonicamid and thiacloprid had no EDI, so no %ADI. The UB ranged between 0.23 and 3.91 %ADI, with thiacloprid having the highest %ADI and clothianidin having the lowest %ADI among all NEO pesticides. The LB for the high-exposure group was between 0.41 and 34.2 %ADI, among which the highest %ADI belonged to acetamiprid and the lowest %ADI belonged to clothianidin. Flonicamid and thiacloprid had no EDI, so no %ADI. The UB ranged between 6.02 and 93.78 %ADI, with thiacloprid having the highest %ADI and clothianidin having the lowest %ADI among all NEO pesticides. Overall, NEO pesticides in the whole group had the lower risk value, which was below 1.6 %ADI. As for the UB of the high-exposure group, thiacloprid had the highest risk among all the NEO pesticides, but none was above 100 %ADI.

## Food contributors to the exposure of neonicotinoid pesticide residues

Figure 2 shows the food contributors to the exposure of acetamiprid, clothianidin, dinotefuran, imidacloprid, and thiamethoxam among the detected NEO pesticides. The main food contributors to the exposure of acetamiprid were preserved fruits (61%), pickled vegetables (12%), rape (4%), lettuce (4%), guava (4%), and other (15%) (Fig. 2a). The main food contributors to the exposure of clothianidin were cherry tomato (95%) and edible gynura (5%) (Fig. 2b). The main food contributor to the exposure of dinotefuran was rape (for 100%) (Fig. 2c). The main food contributors to the exposure of imidacloprid were bell fruit (37%), juice (23%), rape (22%), pickled vegetables (7%), cherry tomato (5%), and other (6%) (Fig. 2d). The main food contributors to the exposure of thiamethoxam were baby bok choy (93%), spinach (5%), and pickled vegetables (2%) (Fig. 2e).

## Prioritization decision

The values of EDI and $ADI_{adj}$ listed in Table 3 were used as the estimates of exposure and toxicity, respectively. The evaluation of the RISK21 matrix showed that the mixture of seven NEO residues would be of low concern (green zone) for the whole group (Fig. 3a). However, for the high-exposure group (Fig. 3b, c), imidacloprid, acetamiprid, and thiacloprid would

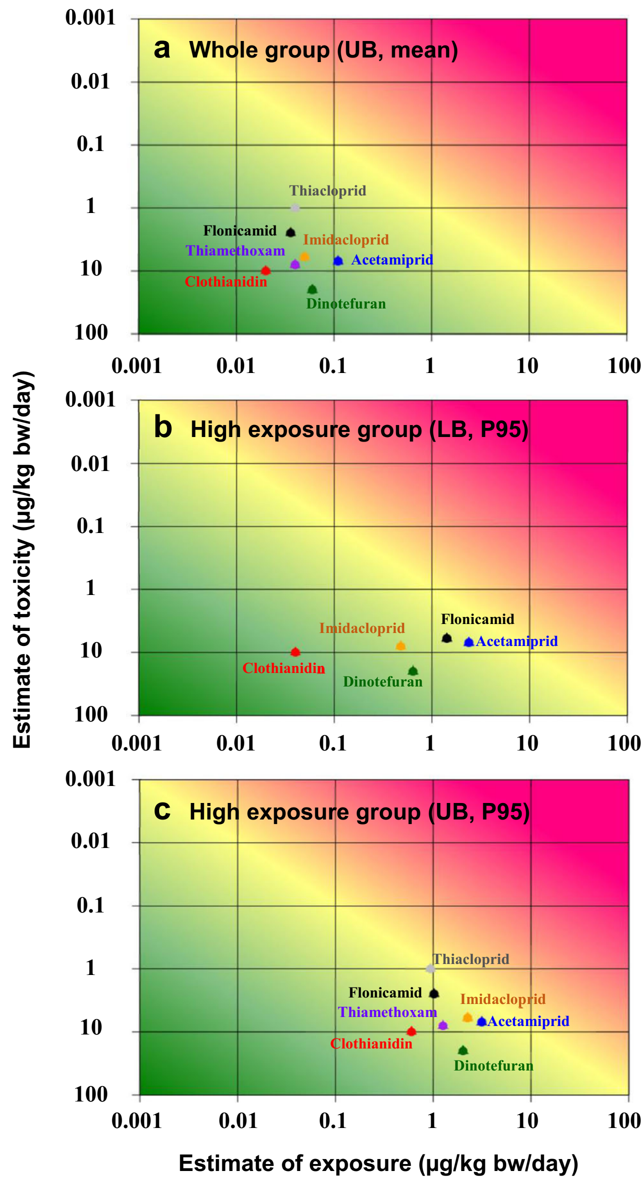


**Fig. 3** RISK21 matrix for neonicotinoid exposure and toxicity. **a** Whole group (UB, mean, **b** high-exposure group (LB, P95), and **c** high exposure group (UB, P95)

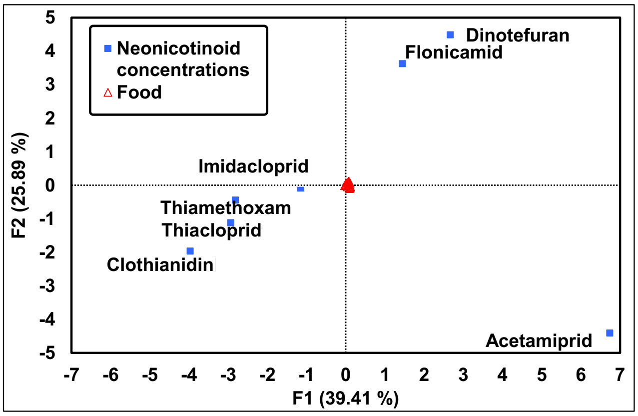


**Fig. 4** Principal component analysis

be of moderate concern due to their proximity to the yellow zone, implicating a high priority for risk management actions.

## Principal component analysis

Figure 4 shows the corresponding analysis of NEO pesticides and food categories. From the corresponding analysis, two dimensions can explain 65.3% of all the data. The assemblages appeared less distinct under all food categories.

## Conclusions

In this study, the %ADI of UB in the high-exposure group ranged from 15.71 to 93.78. Thiacloprid has the highest %ADI values (93.78) among the NEOs, indicating a possible fetal neurotoxic risk in the high-exposure group. Due to their potential adverse effects on neuro systems, fetal exposure to thiacloprid and thiamethoxam should be minimized. The much higher contribution (> 93%) for rape, baby bok choy, and cherry tomato resulted from the low detection rate for the 32 food items. Only one food item, rape, was detected with dinotefuran residues; only two food items (edible gynura and cherry tomato) were detected with clothianidin residues.

On the other hand, the Taiwan FDA had revised the pesticide residue standard in 2017 (https://consumer.fda.gov.tw/Law/PesticideList.aspx?nodeID=520). The standards of dinotefuran, thiamethodam, and imidacloprid residues in rape, baby bok choy, and bell fruit were set to be 2.0, 2.0, and 1.0 ppm, respectively. However, there are no standards for both acetamiprid in preserved fruit and for clothianidin in cherry tomato. In advance, we compared the detected concentration in our study with the residue standard, implicating that the detected concentrations in three food items were lower than the residue standard in Taiwan.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no competing interests.

**Research involving human participants and animal rights** The article does not contain any studies with human participants or animals performed by any of the authors.

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