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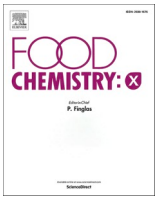

Risk assessment of multiple pesticide residues in *Agrocybe aegerita*: Based on a 3-year monitoring survey

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ABSTRACT

The presence of pesticide residues in *Agrocybe aegerita* has raised an extensive concern. In this paper, based on a 3-year monitoring survey, the dietary exposure risks through *A. aegerita* consumption for different population subgroups were assessed using both deterministic and semi-probabilistic approaches under the best-case and the worst-case scenarios. Among the 52 targeted pesticides, 28 different compounds were identified in the concentration range of 0.005–3.610 mg/kg, and 87.4 % of samples contained one or more pesticide residues. The most frequently detected pesticide was chlormequat, followed by chlorfenapyr and cyhalothrin. The overall risk assessment results indicated extremely low chronic, acute, and cumulative dietary exposure risks for consumers. Using the ranking matrix, intake risks of pesticides were ranked, revealing endsoluran, chlorpyrifos, and methamidophos to be in the high-risk group. Finally, considering various factors such as the toxicity and risk assessment outcomes of each positive pesticide, use suggestions were proposed for *A. aegerita* cultivation.

Introduction

Although pesticide use has negative effects on human health and environmental safety, it remains a pivotal and effective measure to control agricultural pests and diseases, thereby ensuring better yields and quality (Song et al., 2020). Therefore, pesticide residues on agricultural products and in the environment are always an inevitable risk to human health, especially for sensitive populations such as children and pregnant women (Tang et al., 2021).

The black poplar mushroom (*Agrocybe aegerita*) is an important edible mushroom with reported high nutritional value and anti-tumor properties due to the presence of palmitic acid, ergosterol, glucosans, mannitol, and trehalose (Song et al., 2020; Li, Liu, Cong, Deng, & Zheng, 2021; Diyabalanage, Mulabagal, Mills, DeWitt, & Nair, 2008). In recent years, *A. aegerita* has been widely cultivated and consumed in the United States and Asia (Lin, Ching, Lam, & Cheug, 2017). However, because of its unique aroma, long growth cycle, and mild cultivation environment, *A. aegerita* is susceptible to many pathogens and insect pests, such as *Mucor* spp., *Trichoderma* spp., *Aspergillus* spp., and *Mycetophila sciarid* (Choi et al., 2010; Jiao, Shi, & Wu, 2019). Therefore, the application of pesticides is common and essential during *A. aegerita* cultivation. Unfortunately, many mushroom farmers encounter significant challenges due to the scarcity of registered pesticides, leading to indiscriminate application of unregistered alternatives. As a result, pesticide residues exceeding the maximum residue limits (MRLs) have been found in a number of *A. aegerita* samples, which makes *A. aegerita* an important and prominent concern for China's relevant surveillance schemes. Whereas the surveillance focuses on the proper use of pesticides in terms of registration, the MRLs represent the highest pesticide residue that is legally permitted on a commodity. Although the surveillance output (the detection rate, and percentage of samples exceeding the MRL) provides a good indication, it lacks the information necessary for a proper interpretation and objectification in terms of food safety (Łozowicka, Kaczyński, Jankowska, Rutkowska, & Hrynko, 2012). Many previous publications have found that pesticide residues on agro-products can pose a potential hazard to human health (Tang et al., 2021; Kumari & John, 2019; Bommuraj et al., 2019). Consequently, a pivotal concern that perplexes regulators, farmers, and consumers revolves around determining the extent of pesticide consumption within *A. aegerita*. Does the dietary exposure resulting from these pesticide residues pose a

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significant health risk?

To ensure consumed product safety for the public, dietary exposure risk is often assessed before making appropriate risk management decisions. The deterministic (point estimate) and probabilistic (stochastic) approaches are well-known for quantitative exposure assessment (Quijano, Yusà, Font, & Pardo, 2016; Nougadère et al., 2012). Both approaches are used by combining values derived from chemical occurrence and food consumption data (Nougadère et al., 2012). Because the deterministic model does not consider information on variability in potential exposure, this simple, rapid, and inexpensive approach is often used as a low tier approach to determine whether there is an indication of concern for the given exposure (Hamilton et al., 2004; Efsa, 2012). The probabilistic approach requires mathematical modeling of the distribution of one or more parameters involved. The final risk estimate is most reflective of the realistic exposure, but the probabilistic models are complex and difficult to generate (FAO (Food and Agriculture Organization of the United Nations), 2006).

Therefore, in this paper, we aim to (i) uncover the presence of 52 pesticides that are potentially used during *A. aegerita* cultivation; (ii) calculate the individual and cumulative chronic exposure risk for various subpopulations using both deterministic and semi-probabilistic approaches; and (iii) perform a preliminary classification of positive pesticides and propose corresponding use suggestions. The information generated from this work can be used as a reference point for future pesticide registration and subsequent good agricultural practices (GAPs) established for *A. aegerita* cultivation.

Materials and methods

Sample collection and reagents

In 2021–2023, a total of 174 dry *A. aegerita* samples (500 g each) from plantations, markets, and wholesalers were collected according to the guidelines in China (SAC (Standardization Administration of China)., 2008). The producing areas were Fujian Province and Jiangxi Province of China. These are major producing regions of *A. aegerita*. 200 g of sample was chopped and powdered to prepare the laboratory samples, which were sealed in polyethylene bottles with labels for storage at 4℃. All processed samples were analyzed in 3 days.

Individual standard solutions of pesticides (Table 1) of purity 99.0–99.9 % were purchased from the Environmental Quality Supervision and Testing Center of the Ministry of Agriculture and Rural Affairs (Tianjin, China). High-performance liquid chromatography (HPLC) grade acetonitrile, ammonium formate, and formic acid were obtained from Merck (Darmstadt, Germany). Extraction salts including sodium chloride (NaCl), magnesium sulfate ($MgSO_4$), sodium citrate tribasic dihydrate (Na3C6H5O7), and sodium citrate dibasic sesquihydrate (Na2HC6H5O7) were from Shiyi Chemical Reagent Co., Ltd. (Shanghai, China). The PSA (primary and secondary amines, 40–60 μm) clean-up agent was from Sigma Aldrich (St. Louis, MO, U.S.A.). Polytetrafluoroethylene (PTFE) film was obtained from Jinteng Laboratory Instrument Co., Ltd. (Tianjin, China). Deionized water was prepared using a water purification system (Millipore Corporation, USA).

Table 1
The 52 pesticides monitored for *A. aegerita.*

Analytical method	Pesticide
GC–MS/MS (22) [a]	methamidophos, thimet, omethoate, acephate, chlorpyrifos, triazophos, fenvalerate, cypermethrin, bifenthrin, cyhalothrin, fenpropathrin, deltamethrin, cyfluthrin, permethrin, endosulfan, fipronil, chlorfenapyr, difenoconazole, buprofezin, pyridaben, tau-fluvalinate, flucythrinate,
LC-MS/MS(30) [a]	hymexazol, Chlormequat, cyromazine, thiabendazole, procymidone, chlorobenzuron, boscalid, prochloraz, pyraclostrobine, chlorantraniliprole, emamectin benzoate, aldicarb, dimethoate, malathion, isofenphos-methyl, diazinon, phosmet, phosalone, pyrimethanil, triadimefon, iprodione, phoxim, acetamiprid, imidacloprid, carbofuran, carbosulfan, isoprocorb, carbendazim, thiophanate-methyl, diflubenzuron,

[a] values in parentheses indicate the number of pesticide analyzed by the corresponding method.

Sample extraction, purification, and analytical method

The pesticide analysis and quality control were performed according to a QuEChERS method (MOA (Ministry of Agriculture of the People's Republic of China), 2021a) with minor modifications. One gram of powder sample was transferred to a 50 mL centrifuge tube, and 9 mL distilled water was added. After incubating for 30 min, 10 mL acetonitrile was added and vortexed for 1 min. Then, 1 g of NaCl, 4 g of anhydrous $MgSO_4$, 1 g of $Na_2HC_6H_5O_7$, and 0.5 g of $Na_3C_6H_5O_7$ were added. The tube was sealed and shaken for 5 min. The extracts were centrifuged for 5 min at the speed of 4200 rpm. 6 mL upper acetonitrile layer was transferred to a 25 mL centrifuge tube equipped with 900 mg anhydrous $MgSO_4$ and 150 mg PSA. The mixture was shaken for 1 min, and centrifuged for 5 min at 4000 rpm. 1 mL of the supernatant was filtered through a 0.22 μm PTFE film, and then it was subjected to HPLC-MS/MS analysis. 2 mL of the supernatant was transferred to a glass test tube and evaporated to near dryness with a flow of nitrogen at 40℃. The residue was re-dissolved in 1 mL of ethyl acetate and filtered through a 0.22 μm filter film into a 2 mL amber before injection into GC–MS/MS.

An ultra-fast liquid chromatography system coupled to an 8050 triple-quadrupole mass spectrometer (Shimadzu, Kyoto, Japan) was used to analyze 30 pesticides (Table 1). Chromatographic separation was performed on a Waters T3 column (100 mm × 2.1 mm, 1.8 μm) from Waters Corp. (Milford, MA, USA) with a gradient elution at a flow rate of 0.4 mL min^{-1}. The mobile phase consisted of eluent A (water containing 2 mmol/L ammonium acetate and 0.01 % formic acid) and eluent B (acetonitrile). The mobile phase was run with the following program: 0 min 10 % B, 1 min 10 % B, 4 min 50 % B, 10 min 75 % B, 12 min 95 % B, 16 min 95 % B, 17.1 min 10 % B, and 21 min 10 % B. The column temperature was maintained at 40℃. The injection volume was 2 μL. Detection was performed in the electrospray ionization (ESI) positive and negative ion mode using a multiple reaction monitoring (MRM) mode. The capillary voltage was set to 3.0 kV. The interface, desolvation, and heat block temperature were set to 300℃, 250℃, and 400℃, respectively. Nitrogen was used as the nebulizer gas, set to 3 L/min, and also used as the heating and drying gas with the flow rates of 10 L/min.

The 22 additional pesticides (Table 1) were analyzed by a 2010 plus gas chromatograph (Shimadzu, Kyoto, Japan) connected to an 8050 triple-quadrupole mass spectrometer (Shimadzu, Kyoto, Japan). Separation was performed on a Rxi-5Sil MS column (30 m × 0.25 μm, 0.25 μm) (Shimadzu, Kyoto, Japan). 1 μL of sample was injected in the splitless mode. The injector temperature was 250℃ and solvent delay time was set to 5 min. Helium (purity ≥ 99.999 %) at a flow rate of 1.7 mL min^{-1} was used as the carrier gas. The oven was maintained at 50℃ for 1 min, then ramped at 40℃ min^{-1} up to 200℃, finally at a rate of 15℃ min^{-1} up to 250℃, held for 3 min. The temperatures of the transfer line and ion source were set at 250℃ and 200℃, respectively. The triple-quadrupole mass spectrometer was operated in electron impact (EI) mode and multiple reaction monitoring (MRM) mode (conditions presented in Table S1 and Table S2).

To assess the reliability of the established method, the pesticide-free mushroom samples were spiked with various stand solutions and analyzed using the above procedure. Each experiment was conducted in sextuplicate. The parameters, including linearity, recovery, limits of detection (LOD), limits of quantification (LOQ), matrix effects (MEs), and precision were validated and listed in Table S3. The linearity was obtained with regression coefficients (r^2) over 0.995. The recoveries of the spiked standards ranged from 80 % to 118 %. Relative standard deviations (RSDs) for all pesticides were below 15 %. The limits of

detections (LODs) and limits of quantification (LOQs) were in the ranges of 1.5 ug/kg to 6 ug/kg and 5 ug/kg to 20 ug/kg, respectively, and were considered within the lowest concentration achieving a signal-to-noise ratio (S/N) of 3 and the lowest spiked level achieving a satisfactory recovery (70 %-120 %) with the relative standard deviation (RSD) less than 20 %.

Risk ranking

The Matrix Ranking is a method for prioritizing the risk of veterinary residues in the surveillance scheme (VRC (Veterinary Residues Committee), 2019). Various studies have shown that the Matrix Ranking with slight modification could also be used to prioritize the risk levels of pesticide residues in agro-products (Li et al., 2018). The prioritization score (PS) was obtained as a combination of the toxicity score of pesticides and the exposure score of consumers. It was calculated by Equation (1):

$$PS = (A+B) \times (C+D+E) \times F \quad (1)$$

The definition and score of indices are listed in Table 2. The toxicological data of pesticides (*A*) was obtained from the website of the Ministry of Agriculture, People's Republic of China (ICAMA, 2019). The score of potency (*B*) comes from the Acceptable Daily Intake (ADI) from the ICAMA and JMPR databases (ICAMA, 2019; WHO (World Health Organization), 2019). *C* is the score of the mushroom proportion in the total diet. The score of *D* is based on the frequency of dosing with a particular pesticide. *E* is the score of evidence of high exposure groups. *F* is the score of evidence of detectable residues.

Risk assessment

The acute and chronic exposure risk via *A. aegerita* consumption was calculated by dividing the estimated daily intake of pesticide residues with the corresponding acute reference dose (ARfD) and the acceptable daily intake (ADI), respectively. The cumulative exposure risk of the detected pesticides with the same kind of adverse effects was also assessed. To generate a more realistic comprehension of dietary exposure, the detected value of pesticide residue below the LOQ were treated as true zeros in the lower bound (LB) assessment (the best-case scenarios) and as LOQ in the upper-bound (UB) assessment (the worst-case scenarios) according to WHO recommendations (WHO (World Health Organization), 2005).

The relevant equations of risk assessment are as follows.

$$\%ADI = \frac{C \times F}{bw \times ADI} \times 100 \quad (2)$$

where %ADI is the chronic exposure risk, *C* is the monitored residue level of each pesticide (mg kg^{-1}), *F* is the average mushroom consumption per day (kg day^{-1}), and *bw* is the average body weight (kg). The consumption data were acquired from our previous questionnaire-based survey (Yao et al., 2024). The daily intake of mushrooms was 14.5 g, 12.3 g, 12.3 g, 13.1 g, 8.4 g, 13.1 g, and 13.5 g for male, female, consumers aged 14 to 17, consumers aged 18 to 60, consumers over the age of 61, respectively, and the corresponding average body weights were 67.1 kg, 54.9 kg, 51.9 kg, 61.3 kg, 61.8 kg, 60.4 kg, and 58.9 kg, respectively.

When *%ADI* < 100, the potential chronic risk is acceptable. While the value of *%ADI* is higher than 100, the potential risk is unacceptable. Thus, a higher %ADI values indicate a greater chronic exposure risk.

$$\%ARfD = \frac{U \times HR \times v + (LP - U) \times HR}{bw \times ARfD} \times 100 \quad (3)$$

where *%ARfD* is the acute exposure risk, *U* is the unit weight of the edible portion (for *A. aegerita*, U = 1.2 g), *HR* is the highest residue in collected samples (mg/kg), *v* is the variability factor (*v* = 3), *LP* is the large portion (97.5th percentile of eaters, for the general population *LP* = 46.3 g, for children *LP* = 12.7 g, referring to Australia), *bw* is body weight (kg). The value of *ARfD* was referenced to the EU pesticides database and the JMPR database (European Commission, 2019; WHO (World Health Organization), 2019).

When *%ARfD* < 100, the potential acute risk was considered to be acceptable. Conversely, the value of *%ARfD* higher than 100 indicated the potential risk is unacceptable. The higher *%ARfD* values indicate the greater acute exposure risk.

To assess the cumulative exposure risk, the relative potency factor (RPF) approach recommended by the United States EPA (2002) was applied. With this approach, the toxic potency of an individual compound is expressed as the equivalent residue of a so-called 'index compound' (IC), by applying one RPF per compound. In our study, acephate and fenpropathrin were chosen as the IC for organophosphorus (OPs) and pyrethrin and pyrethroids (PPs), respectively.

Results and discussion

Pesticide residues in A. aegerita samples

As depicted in Fig. 1, out of 174 *A. aegerita* samples analyzed for 52 pesticides, 158 samples (90.8 %) contained a positive level for at least one pesticide. A noteworthy 138 samples (87.4 %) displayed the presence of multiple pesticide residues, with 104 samples (59.8 %) harboring four or more pesticide residues. This indicated that farmers commonly used multiple pesticides or one formulation with several active ingredients due to the pests and fungal diseases frequently occurring during *A. aegerita* cultivation. Table 3 illustrates a more detailed overview of pesticide residues in *A. aegerita* samples. A total of 28 pesticides were identified, encompassing 23 insecticides (82.1 %), 4 fungicides (14.3 %), and 1 plant phytohormone (3.6 %). These pesticides were detected within a concentration range spanning from 0.005 to 3.610 mg/kg. Chlormequat with a detection rate of 79.3 % was the most frequently detected pesticide, followed by chlorfenapyr (65.5 %), cyhalothrin (54.0 %), and chlorpyrifos (51.7 %). The detection rates of the remaining positive pesticides ranged from 0.6 % to 25.3 %.

Because the MRLs of some positive pesticides are not available for mushrooms (MOA (Ministry of Agriculture of the People's Republic of China), 2021b; MOA (Ministry of Agriculture of the People's Republic of China), 2022) and mushrooms are classified into vegetables in the food world, the corresponding MRLs for vegetables established by Chinese Legislation were referenced. It was observed that 94 samples (54.0 %) exceeded MRLs. Of these, chlorpyrifos residue exceeding MRL was found in 86 samples (49.4 %), followed by endosulfan (6.9 %), emamectin

Table 2
Ranking criteria of pesticide residue risk of *A. aegerita*.

Indice	Index	Definition	Score	Definition	Score	Definition	Score	Definition	Score
A	Toxicity (mg kg^{-1})	Low	2	Mild	3	High	4	Extreme	5
B	Potency (mg kg^{-1})	> 10^{-2}	0	> 10^{-4} ~ 10^{-2}	1	> 10^{-6} ~ 10^{-4}	2	< 10^{-6}	3
C	Ratio of mushroom in diet (%)	<2.5	0	2.5 ~ 20	1	20 ~ 50	2	50 ~ 100	3
D	Frequency of dose (%)	<2.5	0	2.5 ~ 20	1	20 ~ 50	2	50 ~ 100	3
E	Evidence of high exposure group	No	0	Unlikely	1	Likely	2	No Data	3
F	Residual level (mg kg^{-1})	Nd	0	<1 MRL	1	≥1 MRL ~ 10 MRL	2	≥10 MRL	3

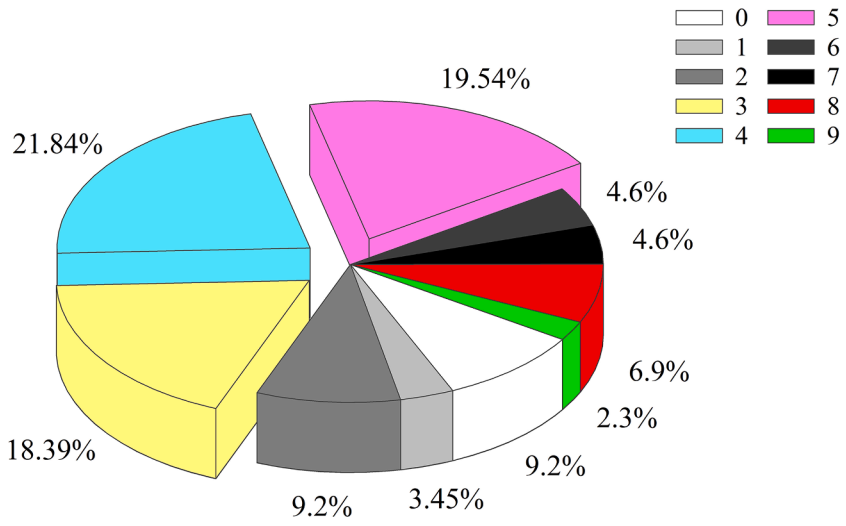

Fig. 1. The occurrence of pesticide residues on *A. aegerita* samples.

Table 3
Detection frequency and residual levels of detected pesticides on *A. aegerita* samples.

Pesticides	N > LOQ	Min (mg/kg)	Max (mg/kg)	Mean (mg/kg)		Median (mg/kg)		MRLs of China (mg/kg)	N > MRL
				LB	UB	LB	UB		
Chlormequat (U)	138(79.3 %)	0.021	0.485	0.129	0.131	0.066	0.066	1	0(0.0 %)
Methamidophos (B)	2(1.2 %)	0.013	0.023	0.000	0.010	0.000	0.010	0.05	0(0.0 %)
Cyromazine (U)	34(19.5 %)	0.015	0.199	0.015	0.023	0.000	0.010	7	0(0.0 %)
Carbendazim (U)	44(25.3 %)	0.005	0.137	0.010	0.014	0.000	0.005	2	0(0.0 %)
Isoprocarb (D)	1(0.6 %)	0.229	0.229	0.003	0.013	0.000	0.010	0.5	0(0.0 %)
Imidacloprid (U)	8 (4.6 %)	0.038	0.049	0.002	0.011	0.000	0.010	2	0(0.0 %)
Phoxim (U)	4(2.3 %)	0.030	0.073	0.001	0.011	0.000	0.010	0.05	2(1.2 %)
Buprofezin (U)	22(12.6 %)	0.013	0.183	0.010	0.019	0.000	0.010	2	0(0.0 %)
Chlorobenzuron (U)	10(5.8 %)	0.018	0.514	0.009	0.019	0.000	0.010	30	0(0.0 %)
Diflubenzuron (U)	10(5.8 %)	0.057	0.181	0.007	0.016	0.000	0.010	0.3	0(0.0 %)
Triazophos (B)	1(0.6 %)	0.029	0.029	0.000	0.005	0.000	0.005	0.05	0(0.0 %)
Boscalid (U)	2(1.2 %)	0.019	0.019	0.000	0.005	0.000	0.005	10	0(0.0 %)
Thiophanate-Methyl (U)	8 (4.6 %)	0.014	0.079	0.002	0.011	0.000	0.010	5	0(0.0 %)
Fenpropathrin (D)	8 (4.6 %)	0.011	0.051	0.002	0.011	0.000	0.010	1	0(0.0 %)
Chlorfenapyr (U)	114(65.5 %)	0.011	1.013	0.236	0.238	0.098	0.098	2	0(0.0 %)
Bifenthrin (B)	6(3.4 %)	0.011	0.019	0.001	0.010	0.000	0.010	0.5	0(0.0 %)
Emamectin Benzoate (B)	40(23.0 %)	0.006	0.107	0.008	0.011	0.000	0.005	0.05	4(4.6 %)
Malathion (U)	4(2.3 %)	0.034	0.050	0.001	0.010	0.000	0.010	0.5	0(0.0 %)
Chlorpyrifos (B)	90(51.7 %)	0.007	0.976	0.096	0.101	0.019	0.019	0.02	86(49.4 %)
Endosulfan (B)	12(6.9 %)	0.058	3.610	0.057	0.066	0.000	0.010	0.05	12(6.9 %)
Cyhalothrin (D)	94(54.0 %)	0.010	0.056	0.012	0.016	0.011	0.011	0.5	0 (0.0 %)
Cypermethrin (D)	18(10.3 %)	0.010	0.020	0.001	0.011	0.000	0.010	0.5	0(0.0 %)
Diazinon (B)	2(1.2 %)	0.079	0.099	0.001	0.010	0.000	0.010	0.2	0(0.0 %)
Phosmet (D)	4(2.3 %)	0.039	0.040	0.001	0.011	0.000	0.010	0.5	0(0.0 %)
Phosalone (D)	6(3.4 %)	0.046	0.052	0.002	0.011	0.000	0.010	1	0(0.0 %)
Cyfluthrin (U)	2(1.2 %)	0.045	0.045	0.001	0.010	0.000	0.010	0.3	0(0.0 %)
Tau-fluvalinate (B)	4(2.3 %)	0.036	0.054	0.001	0.010	0.000	0.010	0.5	0(0.0 %)
Iprodione (U)	1(0.6 %)	0.022	0.022	0.000	0.010	0.000	0.010	25	0(0.0 %)

LB: lower-bound scenario. UB: Upper-bound scenario. B: already banned from using in Chinese tea plantation. D: the use frequency of pesticide should be diminished. U: use with consideration of the pre-harvest interval.

benzoate (4.6 %), and phoxim (1.2 %). Another 24 pesticide residues in *A. aegerita* samples did not exceed the corresponding MRLs (Table 3). This implied that chlorpyrifos, a forbidden pesticide in vegetable cultivation, was frequently and extensively sprayed in *A. aegerita* cultivation by farmers who may lack food safety awareness. It is also worth emphasizing that the possible source of endosulfan and methamidophos in *A. aegerita* should be noticed because the use of these 2 pesticides has been banned in China.

Risk ranking for detected pesticides

As illustrated in Fig. 2, the 28 pesticides were categorized into three groups according to the overall scores calculated using the matrix ranking scheme. Three pesticides, including endosulfan, chlorpyrifos, and methamidophos, have high-risk with a score at or higher than 20 due to their high toxicology or high residual levels. Emamectin benzoate, triazophos, diazinon, bifenthrin, and tau-fluvalinate posed medium-risk, with a score ranging from 15 to 19. Hence, the use of these 8 pesticides should be banned for *A. aegerita* cultivation. Twenty other positive pesticides with a score below 15 were assigned to the low-risk group. Among these 20 pesticides, the use of isoprocarb, fenpropathrin, cyhalothrin, cypermethrin, phosmet, and phosalone should be reduced during *A. aegerita* cultivation due to their mild toxicity (oral medium lethal dose ranging from 50 mg kg^{-1} to 500 mg kg^{-1}). Other

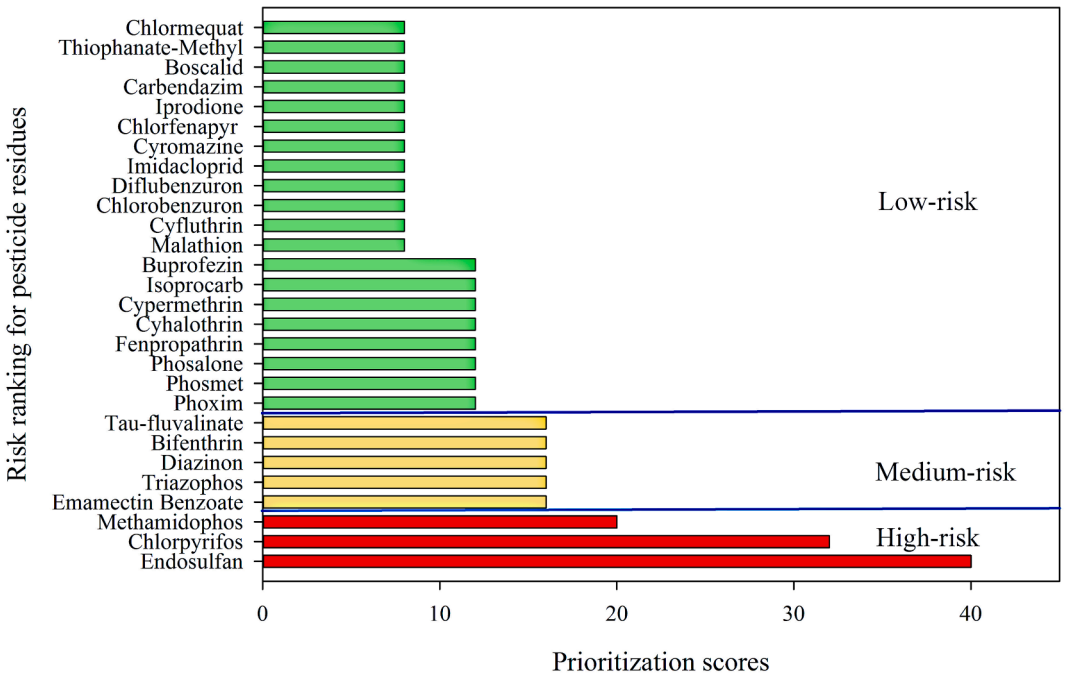

Fig. 2. Risk ranking for 28 detected pesticides in *A. aegerita* samples. Pesticides scored at or higher than 20, from 15 to 19, and lower than 15 were classified into the high-risk group, the medium-risk group, and the low-risk group, respectively.

pesticides in the low-risk group could be used with sampling intervals.

Assessment of the dietary exposure risk via A. aegerita consumption

Long-term intake and chronic exposure risk

The results of chronic dietary exposure risk assessment of 28 pesticide residues on *A. aegerita* for different subpopulations under the best-case and the worst-case scenarios are shown in Fig. 3 (a). As can be seen, the values of *%ADI* were much lower than 100 even when calculated with the P95 distribution model using the worst-case scenarios, therefore, the long-term dietary exposure risk of these pesticides was acceptable. It is worth mentioning that the chronic exposure risks from chlorpyrifos and emamectin benzoate were relatively higher than that of other pesticides. Among the 7 population sub-groups, females, adults aged 18 to 60, and rural residents exhibited elevated dietary exposure risks compared to their counterparts (males, adults in other age groups, or urban residents), attributed to their higher mushroom consumption levels. Values of *%ADI* ranged from 4.354 E to 05 to 5.411 E-01 when using the mean value distribution model, and from 0 to 2.118 under the P95 distribution model. Due to its extremely low value of ADI (0.0005 mg kg^{-1} bw day^{-1}), emamectin benzoate exhibited the highest %ADI value, followed by endosulfan, phoxim, and chlorpyrifos. Notably, despite the United States Environmental Protection Agency (US EPA) banning the use of chlorpyrifos due to its adverse effects on human health, particularly on child neural development (Tosi, Costa, Vesco, Quaglia, & Guido, 2018), this pesticide is still frequently found in various other agro-products, such as cucumber (Golge, Hepsag, & Kabak, 2018), peach (Li et al., 2018), and spinach (Omwenga et al., 2021). Furthermore, even though the production and use of endosulfan have already been prohibited in China, further research is crucial to identify the potential source of this compound. See (Fig. 4).

Short-term intake and acute exposure risk

Following JMPR recommendations, acute exposure risks should be assessed for foods that need to be recognized for potential hazards after a brief period of consumption (FAO (Food and Agriculture Organization of

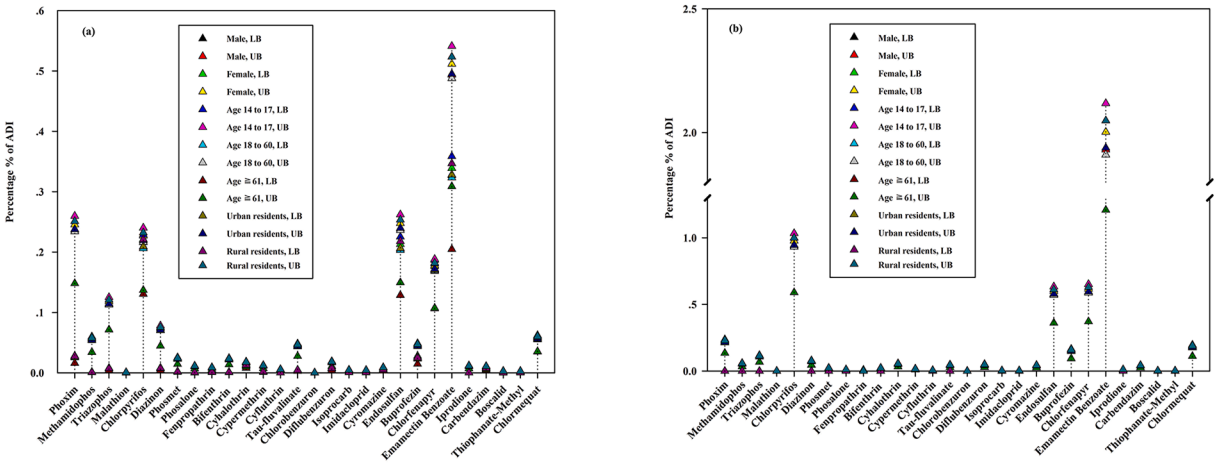

Fig. 3. Chronic exposure risk for different consumers at different levels when using mean value (a) or P95 distribution model (b) of pesticide residue.

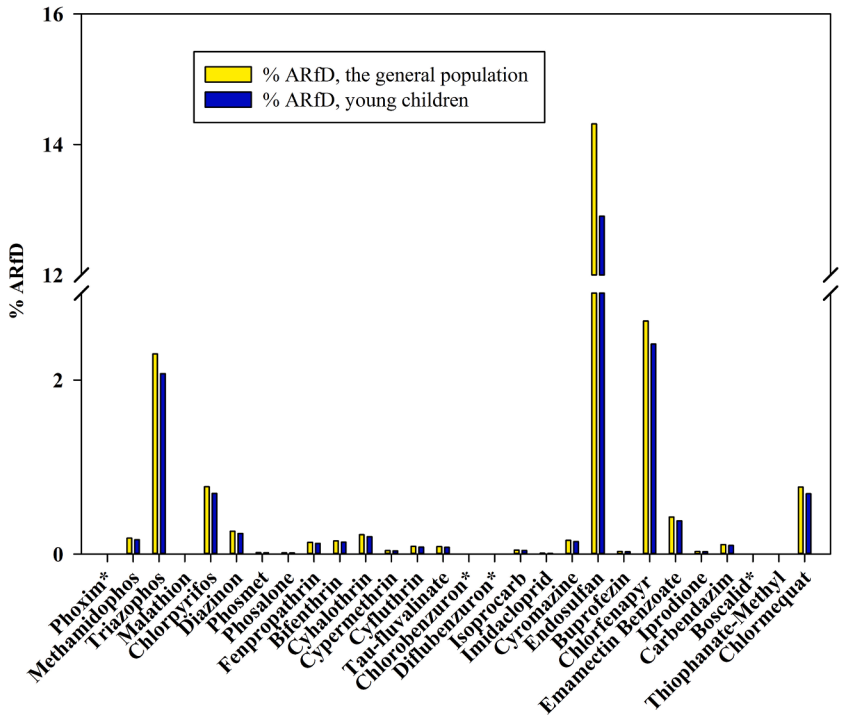

Fig. 4. Acute exposure risk of the positive pesticides for the general population and young children (* the value of *ARfD* was not available).

Table 4
Mode of action (MOA), chemical group, and acceptable daily intake (ADI) for pesticide residues on *A. aegerita* samples.

Compound	Chemical Group	Category	MOA	ADI (mg/bw/kg/day)	ARfD (mg/bw/kg)	Source
Phoxim	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.001	NA	JMPR
Methamidophos	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.004	0.01	JMPR
Triazophos	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.001	0.001	JMPR
Malathion	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.3	2	JMPR
Chlorpyrifos	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.01	0.1	JMPR
Diazinon	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.003	0.03	JMPR
Phosmet	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.01	0.2	JMPR
Phosalone	organophosphates	Insecticide	acetylcholinesterase inhibitor	0.02	0.3	JMPR
Fenpropathrin	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.03	0.03	JMPR
Bifenthrin	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.01	0.01	JMPR
Cyhalothrin	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.02	0.02	JMPR
Cypermethrin	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.02	0.04	JMPR
Cyfluthrin	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.04	0.04	JMPR
Tau-fluvalinate	pyrethrins, pyrethroids	Insecticide	sodium channel modulator	0.005	0.05	EC
Chlorobenzuron	benzoylureas	Insecticide	chitin synthetase inhibitor	1.25	NA	China
Diflubenzuron	benzoylureas	Insecticide	chitin synthetase inhibitor	0.02	NA	JMPR
Isoprocarb	carbamates	Insecticide	acetylcholinesterase inhibitor	0.06	0.4	JMPR
Imidacloprid	neonicotinoids	Insecticide	nicotinic acetylcholine receptor competitive modulator	0.06	0.4	JMPR
Cyromazine	triazines	Insecticide	insect growth regulator	0.06	0.1	JMPR
Endosulfan	organochlorine	Insecticide	GABA-induced chloride flux inhibitor	0.006	0.02	JMPR
Buprofezin	–	Insecticide	altered serum T3, T4 and PBI concentration	0.009	0.5	JMPR
Chlorfenapyr	–	Insecticide	oxidative removal of the *N*-ethoxymethyl group	0.03	0.03	JMPR
Emamectin Benzoate	macrocyclic lactone	Insecticide	disrupting neurotransmitters	0.0005	0.02	JMPR
Iprodione	dicarboximides	Fungicide	signal transduction	0.02	0.06	EC
Carbendazim	benzimidazoles	Fungicide	mitosis and cell division	0.03	0.1	JMPR
Boscalid	carboxylic acid amide	Fungicide	succinate-coenzyme Q reductase inhibitor	0.04	NA	JMPR
Thiophanate-Methyl	–	Fungicide	inducing the cellular damage	0.09	1	JMPR
Chlormequat	–	Plant growth regulators	–	0.05	0.05	JMPR

the United Nations), 2013). Herein, except for the unavailability of ARfD data for phoxim, chlorobenzuron, diflubenzuron, and boscalid, the acute dietary exposure risk of the remaining 24 positive pesticides for different population sub-groups was compared, as shown in Fig. 3(b). Values of *%ARfD* ranged from 0.002 to 14.317 for the general population and from 0.002 to 12.901 for young children. The acute exposure risk of the general population was higher than that of young children. Endosulfan had the highest *%ARfD* value, followed by chlorpyrifos and triazophos. The *%ARfD* values for other pesticides were lower than 1. In fact, most mushrooms were washed and thermally processed before consumption in China, which could lead to a significant reduction in pesticide residues (Kaushik, Satya, & Naik, 2009). A previous study reported that pesticide residues may lost through thermal degradation, evaporation, and co-distillation during thermal processing (Jaggi, Sood, Kumar, Ravindranath, & Shanker, 2001). Therefore, despite several pesticides having relatively high *%ARfD* values, the acute exposure risk they posed should be acceptable. See (Table 4).

Cumulative exposure risk

While chronic and acute dietary exposure risk assessment indicated the detected pesticides are not harmful to humans, special attention should be paid to the potential cumulative exposure risk of these chemicals due to frequent exposure to multiple pesticide residues simultaneously. Hence, values of the cumulative exposure risks were calculated for 9 OPs (acephate, methamidophos, phoxim, chlorpyrifos, triazophos, malathion, diazinon, phosmet, phosalone) and 6 PPs (fenpropathrin, cypermethrin, bifenthrin, cyhalothrin, cyfluthrin, tau-fluvalinate). Details on the type of inhibition, the RPFs, BMD10, chronic non-observed adverse effect levels (NOAELs), and cumulative exposure risks of the pesticides involved are listed in Table 5. The highest risks were found in the aged 14–17 group at the P95 distribution model under the worst-case scenarios, reaching 8.83 for OPs and 0.11 for PPs, respectively. It indicated that the levels of cumulative exposure risk posed by OP or PP residues on *A. aegerita* were acceptable. Chlorpyrifos was the main contributor in the OP cumulative exposure and accounted for 99.21 % of the total risk. For PPs, about 80 % of cumulative exposure risk was contributed by cypermethrin (33.36 %), tau-fluvalinate (25.50 %), and cyhalothrin (19.32 %). Concerning the socio-demographic variables, gender and place of residence did not have a significant influence, whereas consumers aged from 14 to 60 have higher exposure risk than that of consumers aged over 61. Furthermore, when comparing the two scenarios in which the pesticide residual levels below the LOD were extended with zero or LOQ, the fluctuation in the exposure results of PPs was greater than that of OPs. The plausible explanation is that the detection frequency and residual levels of PPs were significantly lower than that of OPs.

Uncertainties and limitations

According to WHO/IPCS, scientific uncertainty in risk assessment in the general sense is defined as “imperfect knowledge concerning the present or future state of an organism, system, or (sub-) population under consideration” (WHO/IPCS (World Health Organization/International Program on Chemical Safety), 2008). A clear uncertainty analysis is important for generating a more realistic comprehension of dietary exposure and improving the strength of risk assessment results, which is helpful to inform more scientific management decisions (Kettler et al., 2015). Hence, some uncertainties and limitations should be acknowledged for this study. Firstly, in daily life, people are not only exposed to mushrooms but also other sources, such as vegetables, fruits, and even drinking water and agricultural soils (Boobis et al., 2008; Montiel-León et al., 2019; Kafaei et al., 2020). To obtain a realistic population dietary exposure for these chemicals across the entire diet, a total diet study (TDS) should be further carried out. Secondly, the effect of common household processes (i.e. washing, blanching, and frying) on pesticide residue levels has not been investigated. As a consequence, the

Table 5
The cumulative exposure risk of OPs and PPs through *A. aegerita* consumption.

Category	Pesticide	NOAEL[a] (mg/kg)	BMD_{10}(mg/kg)	Effect	Source	RPF	*%ADI* for male/female				*%ADI* for consumer age 14–17/ 18–60/ age ≧61				*% ADI* for urban/rural residents			
							Mean		P95		Mean		P95		Mean		P95	
							LB	UB	LB	UB	LB	UB	LB	UB	LB	UB	LB	UB
OPs	Acephate (index compound)		1	brain/rat	USEPA	1	1.75/ 1.82	2.02/ 2.10	7.85/ 8.14	8.05/ 8.34	1.92/ 1.73/ 1.10	2.22/ 2.00/ 1.27	8.61/ 7.77/ 4.92	8.83/ 7.96/ 5.04	1.76/ 1.86	2.03/ 2.14	7.88/ 8.33	8.08/ 8.54
		2.5		brain/rat	JMPR	1												
	Chlorpyrifos	1		brain/rat	JMPR	2.5												
	Phoxim	0.375		brain/dog	EMEA	6.67												
	Triazophos	0.15		brain/rat	JMPR	16.67												
	Malathion	34		brain/rat	JMPR	0.074												
	Methamidodiphos	0.1		brain/rat	JMPR	25												
	Diazinon	0.3		brain/rat	JMPR	8.33												
	Phosmet		4	brain/rat	USEPA	0.62												
	Phosalone		8	brain/rat	USEPA	0.31												
PPs	Fenpropathrin (index compound)	8		brain/rat	JMPR	1	0.01/ 0.01	0.09/ 0.09	0.04/ 0.04	0.10/ 0.10	0.01/ 0.01/ 0.01	0.10/ 0.09/ 0.06	0.05/ 0.04/ 0.03	0.11/ 0.10/ 0.06	0.01/ 0.01	0.09/ 0.09	0.04/ 0.04	0.10/ 0.11
	Cypermethrin	4		brain/rat	JMPR	2												
	Bifenthrin	30		brain/rat	JMPR	0.27												
	Cyhalothrin	2.5		brain/dog	JMPR	3.2												
	Cyfluthrin	6.5		brain/dog	JMPR	1.23												
	Tau-fluvalinate	2		RBC/dog	NIH	4												

exposure risks calculated in the present study may be over-estimated. Nevertheless, such uncertainty would not pose a significant influence on the results since the risk values of pesticides studied are far below the corresponding *ADI* or *ARfD*. Thirdly, a limited number of recording days and sample size would increase the sampling uncertainty (Van Ooijen, Voet, & Bakker, 2009), particularly for foods with high variability in levels of pesticide residues. Hence, a sufficient sample size should be ensured for dietary exposure risk assessment, although it is an expensive approach to taking more samples. In this study, we collected 174 *A. aegerita* samples from plantations, markets, and wholesalers in 2021–2023 to reduce such uncertainty as much as possible. Fourthly, the handling of non-detects is an important issue in risk assessment. Although non-detects were substituted by true zeros or LOQ under the different scenarios, uncertainties of scenarios still arise due to gaps in scientific knowledge. The approach to reduce such uncertainties is to establish a more sensitive detection method to obtain the real residual levels of pesticides. Lastly, it should also be noted that this assessment does not apply to consumers of age younger than 16, as the average daily consumption amount of *A. aegerita* is extremely low.

Conclusion

Although the risk assessment based on a comprehensive 3-year monitoring survey shows that the pesticide residues from *A. aegerita* may not be considered a serious public health threat, a special precaution should be taken with the high occurrence rate (87.4 %) of pesticide residues, especially the multiple residues of highly toxic pesticides. To address this situation, various use suggestions for the 28 detected pesticides (i.e. 12 pesticides could be used in appropriate doses and restricting the spray frequency) were proposed, comprehensively considering the pesticide toxicity, the scores of risk ranking, and the dietary exposure risk levels. In summary, this study may provide a certain guiding significance to design future control programs and to establish the corresponding good agricultural practices (GAP) of *A. aegerita.*

CRediT authorship contribution statement

Qinghua Yao: Writing – original draft, Validation, Supervision, Software, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Desen Su:** Methodology, Formal analysis. **Yunyun Zheng:** Methodology, Investigation, Formal analysis. **Minmin Huang:** Software, Investigation, Formal analysis. **Meizhen Chen:** Investigation, Formal analysis. **Hui Xu:** Writing – review & editing. **Shaoxiao Zeng:** Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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Appendix A. Supplementary data

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