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Research Article

Fate characteristics and risk quantification of cyflumetofen from tomato cultivation to processing based on large–scale applications

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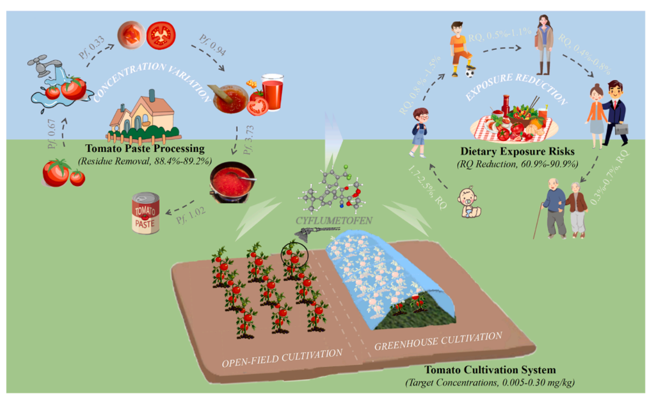
HIGHLIGHT

- Cyflumetofen was metabolized fast in greenhouse than in field with high residual magnitude.
- Peeling effectively removed cyflumetofen and washing was recommended for 2-TFMBA.
- Up to 59.3% cyflumetofen was metabolized to 2-TFMBA from cultivation to processing.
- Comparative risk assessment was conducted among population lifecycle by multi-models.
- High chronic exposure risks were observed for urban consumers than that for rural groups.

GRAPHICAL ABSTRACT



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ABSTRACT

Elucidating the fate characteristics of cyflumetofen and its main metabolite 2–TFMBA in tomato from cultivation to processing is crucial for safeguarding the environment and humans from hazardous effects. Cyflumetofen and 2-TFMBA could exist stably in tomato matrices for at least 343 days under frozen and dark conditions according to UHPLC–MS/MS, with a limit of quantitation of 0.001 mg/kg and retention time within 2.12 min. The occurrence, dissipation, and concentration variation of cyflumetofen were reflected by original depositions of 0.02–0.44 mg/kg, half–lives of 1.7–7.2 days, and terminal magnitudes of 0.005–0.30 mg/kg, respectively, with various influencing factors, e.g., climate conditions and tomato cultivars. Additionally, 13.5–59.3% of cyflumetofen was metabolized to 2-TFMBA, showing significant toxicological effects ranging from cultivation to processing. When the concentration decreased by 0.06 mg/kg, cyflumetofen was effectively removed by peeling, while washing was the recommended method for removing 2–TFMBA with a processing factor of 0.70. The comparative dietary risks of sum cyflumetofen were assessed for all life cycle populations using deterministic and probabilistic models. The risk quotients decreased to 1.3–4.8 times during the preparation of home canning

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tomato paste. Despite the low exposure risk, the potential health hazards of sum cyflumetofen should be considered, given its ubiquity and cumulative effects.

1. Introduction

Pesticides are widely used in commercial agriculture by controlling insects, maintaining crop yield, and minimizing losses [1]. However, heavy concentrations of pesticides are detected in the environment during manufacturing, use, and disposal, which are obvious threats to food security, human health and welfare, etc. [2]. The United Nations Sustainable Development Goals (UNSDGs) call for achieving sustainable agriculture and food safety [3]. It is essential to quantify the hazard effects of exposure to typical pesticides on environmental safety and human health. Cyflumetofen, a novel benzoyl acetonitrile acaricide, is suitable for use in integrated pest management systems and has been widely applied in 15 countries, including China, Japan, and the United States (US) [4]. It was assumed that this treatment would be effective at all developmental stages of *Tetranychus urticae* infection in tomato fields by inhibiting mitochondrial electron transport [5,6]. Tomato appear to be among the most widely grown and consumed vegetables worldwide, with a production of 184.79 million tons in 2021 [7]. As the best antioxidant, tomatoes can decrease cancer risk for consumers due to the presence of carotenoids, such as the lipid solubility lycopene [8], with more than 85% of lycopene has been reported to be derived from dietary tomato foods [9]. Tomato paste is a more important nutrient source for elderly individuals in “food deserts” than raw tomatoes [10,11], and approximately 200 million dollars of tomato paste were consumed worldwide in 2022 [12].

However, cyflumetofen poses health hazards to humans via Cramer class III viruses [13], which can cause toxicity and oxidative stress in liver hepatocellular and carcinoma (HepG2) cells [14]. And it considered a possible carcinogen with a high acute 48 h concentration for 50% of maximal effect (EC_{50})$>$ 0.063 mg/L toward Daphnia magna and an accumulated toxicity at 1000–3000 ppm to rats [15]. Moreover, cyflumetofen is principally hydrolysed to 2-((trifluoromethyl) benzoic acid (2–TFMBA) in plants, possibly leading to toxicity due to its high mobility [16]. Given that 2–TFMBA was the only metabolite mandatory for estimation of dietary intake by Joint Meeting on Pesticide Residues (JMPR) [17], the existing health risk assessment of cyflumetofen was incomplete and inaccurate only based on the residual levels of the parent. Furthermore, high residual levels of cyflumetofen were detected in apple and soil, resulting in potential hazards for consumers and earthworms [4,18,19]. These strains were not only affected by the hydrophobic character of cyflumetofen, which has a high octanol–water partition coefficient (log Kow=4.3, pH 7, 20 °C) and a low vapour pressure of 0.0059 mPa [20], but also by abiotic factors, such as cultivation conditions and climate characteristics. In addition, the concentrations of agrichemicals could change significantly during tomato home-canning processing [21,22]. Research on cyflumetofen has focused mainly on the dissipation of the parent in raw tomatoes [23], whereas that of its main metabolite 2-TFMBA has been less well understood from field to processing. Additionally, various methods for analysing cyflumetofen in plants and soil matrices have been reported, with a limit of quantitation (LOQs) of 0.01–0.5 mg/kg and retention times of 3.52–12.55 min [4,14,19,24], these methods included ultra-performance convergence chromatography coupled with triple quadrupole (UFC2-MS/MS) and ultra–high-performance liquid chromatography tandem mass spectrometry (UHPLC–MS/MS). It is necessary to develop a method for tracing the fate tendency of cyflumetofen and 2-TFMBA in home canned tomato paste, which is the key for efficient application in agroecosystems and protection of dietary safety for humans.

In view of the above concerns, this study aimed to clarify the fate characteristic of cyflumetofen and 2-TFMBA in tomatoes from cultivation to processing, highlighting precise risk values for consumers through the use of multidimensional assessment models. First, the storage stabilities of cyflumetofen and 2–TFMBA were confirmed by sensitive UHPLC–MS/MS in tomato matrices, confirming the stability of the samples from field trials to indoor conditions and providing accurate data on the compounds. Second, the occurrence, dissipation and metabolism of cyflumetofen during tomato cultivation were investigated for influencing factors, including climate conditions, tomato cultivar, and cultivation system. Third, the changes in the concentrations of cyflumetofen and its metabolites were elucidated with P*f*s from the raw products to commercial commodities, including washing, peeling, homogenization, simmering, and sterilization. Finally, the dietary exposure risks of cyflumetofen were estimated among agricultural tomato products using deterministic and probabilistic assessment models for populations of various ages, regions and sexes. This investigation revealed the fate characteristics and safety of agricultural products throughout the whole chain, providing a theoretical basis for the scientific and rational use of pesticides and health risk avoidance for humans.

2. Method and material

2.1. Plant care and pesticide application

The twelve cultivation origins of tomato plants were selected from the main producing provinces or municipalities of China spanning seven climate zones; these provinces have no history of cyflumetofen or 2–TFMBA or other analogues in the past three years. Based on the Organization for Economic Co–operation and Development Guidelines (OECD) for the Testing of Chemicals No. 509 Crop Field Trial [25], three trial plots were chosen to avoid random errors, and one plot was employed as a control. Each plot was 50 m^2 and separated from the next plot using a buffer area of one meter. 20% cyflumetofen SC was applied at a dosage of 180 g a.i./ha (gram of active ingredient per hectare) for tomatoes. The application frequency and interval of pesticides were 1 and 3 days, respectively, according to good agricultural practice (GAP) recommendations. The dosage was used to determine the pharmacokinetic dissipation and terminal concentration of cyflumetofen in different tomato cultivations. The typical geographic information, climatic factors, soil characteristics and tomato cultivars used are summarized in Table S1.

2.2. Sample preparation and processing

Representative tomato samples were obtained from each work plot, excluding the edges and ends of the plots, as far as preferably intact rind, disease–free and firm fruits. The samples were collected at increasing intervals on day 0 (2 h after treatment) and 1, 3, 5, and 7 days after treatment for dissipation investigation, and the samples collected at 3 and 5 days were used to determine the terminal concentrations. The collected samples of tomatoes were subjected to removal of exterior impurities, chopped, homogenized, divided into subsamples, and subsequently stored in the dark at –20 °C for further analysis. The storage stability of cyflumetofen and 2–TFMBA in tomato was further investigated to estimate the degradation rates of cyflumetofen from sample collection to the determination period according to the OECD Guidelines [25]. The tomato blank samples were exposed to 0.3 mg/kg working solutions of cyflumetofen and 2–TFMBA and then stored at − 20 °C in the dark. The concentrations of cyflumetofen and 2-TFMBA were determined at preset intervals of 0, 18, 28, 221 and 343 days in tomato.

Tomato samples prepared for home canning tomato paste were collected directly three days after the last treatment, yielding as much as 15 kg of whole tomatoes. These samples were placed in polyethylene bags and processed according to the designed procedure within 24 h. A streamlined household processing procedure involving washing, peeling, homogenization, simmering and sterilization was used for the canned tomato paste in the study. A total of 27 representative samples containing three duplications were collected from different processing steps to investigate the residue removal and P*f* evaluation of cyflumetofen and its metabolites during the whole processing procedure, e.g., from tomato skin, pulp, puree, seeds, juice, and paste (Fig. 1).

2.3. Quality assurance/quality control

A blank assay of the tomato matrix was conducted to verify the specificity of the described method, where there was no detectable interference at the retention times of cyflumetofen (2.12 min) and 2–TFMBA (1.35 min). Satisfactory linearity was observed for 0.01 and 1.0 mg/L cyflumetofen according to the calibration curves obtained from the solvent MeCN and matric extracts, with reference to correlation coefficients (R^2) of 0.9943–0.9990 for cyflumetofen and 0.9978–0.9992 for 2–TFMBA (Table S2). Interference or coeluting matric parts affected the ionization efficiency of the electrospray ionization interface for tandem mass spectrometry, resulting in ion suppression or enhancement. A significant matrix suppressive effect of cyflumetofen was observed in tomato with an ME% of –29%, and there was a significant matrix positive effect for 2–TFMBA with an ME% of 43%. The marked differences in matrix effects between cyflumetofen and 2–TFMBA were closely related to the organic compounds contained in tomatoes, such as lycopene and β–carotene [26,27]. Consequently, external matrix–matched standards were selected for accurate quantitation of cyflumetofen and 2–TFMBA to reduce the matrix effect and obtain true detection data in the sample. The limit of detection (LOD) of cyflumetofen was 2.25×10^{-4} mg/kg, and that of 2–TFMBA was 4.81×10^{-4} mg/kg, determined at a signal–to–noise ratio of 3 under the above conditions. The LOQ of the agrichemicals was estimated to be 0.001 mg/kg in the associated matrices, which was taken as the lowest concentration level with satisfactory recoveries (70–120%) and relative standard deviations (RSD) less than 20%. The LOQ of the developed method was less than the MRL (0.3 mg/kg) fixed by GB 2763–2021 [28]. Recovery experiments were performed by spiking a standard working solution of cyflumetofen and 2–TFMBA at low (10–fold LOQ), medium (300–fold LOQ) and high (1000–fold LOQ) concentrations with five replicates. The mean recoveries of cyflumetofen were estimated to be 96–102% with 1.1–7.6% RSD in tomato, and those of 2–TFMBA were 90–102% with 7.7–9.6%. The stability of cyflumetofen and 2–TFMBA was also evaluated weekly in working and matrix–matched solutions during the experiments, and no significant differences were found for the concentrations of cyflumetofen and 2–TFMBA in the study, with p values greater than 0.05 at a 95% probability. Satisfactory validation criteria for specificity, linearity, ME, LOD, LOQ, repeatability, reproducibility and stability were obtained based on SANTE/11312/2021 [29], providing a 10–500–fold increase in sensitivity and saving 3/7–4/5 of the time compared to previous studies [18,23,24,30].

2.4. Statistical analysis

The differences in datasets that were normally distributed were assessed by *t*test and one–way analysis of variance (ANOVA) with Duncan's post hoc test using SPSS 22.0 (IBM, IL, USA). The differences between nonnormally distributed datasets were assessed by Kruskal—Wallis one–way ANOVA. The p value < 0.05 was considered to indicate statistical significance within a confidence level of 95%. Monte Carlo simulations were applied to estimate the posterior distribution of pesticides in crops to reduce uncertainty in exposure assessments.

3. Results and discussion

3.1. Factors influencing the storage stability of cyflumetofen and 2–TFMBA in tomato

The concentrations of cyflumetofen and 2-TFMBA in tomatoes barely changed from 0.30 ± 0.02 to 0.31 ± 0.01 mg/kg and from 0.28 ± 0.01 to 0.33 ± 0.01 mg/kg, respectively, during frozen storage for 343 days in the dark (Table S3). The mean degradation rates of cyflumetofen ranged from –3% to 13%, with a quantity control (QC) ranging from 81% ± 14.85% to 102% ± 2.12%, and those of 2–TFMBA ranged from

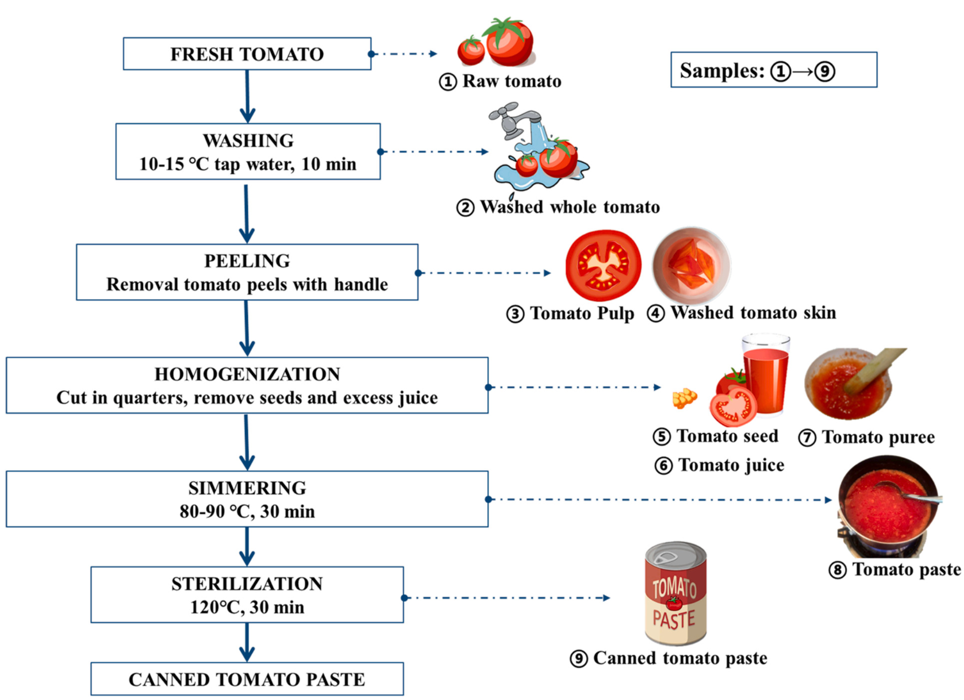

Fig. 1. Household processing scheme for tomato plants designed in the study at specific sampling points.

–16% to –7%, with a QC ranging from 79 ± 3.54% to 109 ± 0.71%. These results showed that cyflumetofen and its metabolite 2–TFMBA remained stable in tomato matrices, with degradation rates less than 30% [25]. A freezing storage temperature of –20 °C and dark storage conditions favored the storage of cyflumetofen and 2–TFMBA in tomatoes, resulting from the decreased respiratory intensity of tomato plants under these conditions [31]. Moreover, the relatively low water solubility of cyflumetofen (0.028 mg/L) was beneficial for its stable storage in high–water content tomato matrices (94.5%) [20]. Furthermore, the slight changes in the concentrations of cyflumetofen and 2–TFMBA should be related to the acidic environment of the tomato matrices (4.0–4.6). The molecular structure of cyflumetofen is prone to ionization under acidic conditions, and 2–TFMBA undergoes a condensation reaction. Additionally, the storage stability of cyflumetofen and 2–TFMBA might be affected by the enzyme system in the matrix. The carbon–nitrogen bond and ester group in cyflumetofen are easily decomposed by amidase [32], and the carboxyl group in 2–TFMBA likely reacts with alkaline substances. Notably, the mean degradation rates of cyflumetofen (−3–13%) were lower than those of 2–TFMBA (−16––7%), indicating the greater stability of the parent in tomatoes compared with its metabolite. The relatively smaller molecular weight of 2–TFMBA (188.99) resulted in more rapid potential migration in the matrices than in the parent (447.40), which was not conducive to storage in tomato [16]. Overall, the storage stabilities of cyflumetofen and its metabolite in tomato matrices were affected by multiple factors, and the specific underlying mechanisms need to be further investigated.

3.2. Environmental fate of cyflumetofen and its metabolites during tomato cultivation

3.2.1. Occurrence, degradation and metabolism of cyflumetofen in tomato

The initial depositions of cyflumetofen ranged from 0.02 to 0.44 mg/kg in tomato fruits in Trials #1, #3, #5, and #11. The greatest levels of cyflumetofen appeared at 2 h in Trials #5 and #11, with concentrations of 0.02 and 0.44 mg/kg, respectively, which were rapidly dissipated by more than 50% after 7 d. In contrast, the concentrations of cyflumetofen reached a maximum at 0.11 and 0.05 mg/kg on the first day after application in Trials #1 and #3, respectively, and then decreased to 1/3 after 7 d. The cases appeared in Trials #1 and #3 were attributed to the foliage application mode, with the majority of compounds deposited in the stems and leaves of tomato plants. The compounds were subsequently translocated to tomato fruits based on the strong transpiration of tomato plants, for which the coefficient reached 800 [33]. Furthermore, the initial concentration of cyflumetofen in the *Mao Fen 802 tomato plants* was 0.02 mg/kg, which was far lower than that in the *Yv Fan 1 tomato* (0.04 mg/kg), *Tian Zheng 1567 tomato* (0.04 mg/kg), and *Ai Mei Te tomato* (0.44 mg/kg). This observation was mainly due to the rapid growth of the *Mao Fen 802 tomato*, which had 9–10 inflorescences on the main stem, these characteristics are not conducive to the deposition of cyflumetofen. Interestingly, the deposition of cyflumetofen in tomatoes under open–field conditions was 10.7–21.0 times greater than that under greenhouse conditions in the present study, breaking the general phenomenon that severe deposition of pesticides occurs in greenhouses [9].

The half–lives ($T_{1/2}$) of cyflumetofen were 1.7–7.2 days, with a determination coefficient (R^2) of 0.6235–0.9622. Specifically, the $T_{1/2}$ of cyflumetofen was 7.2 d in Trial #11 under a subtropical monsoon climate, which was relatively higher than that in Trials #1, #3, and #5 (1.7–4.7 d) under a temperate monsoon climate. The higher temperature (16.0 °C) and precipitation (1054.5 mm) in Trial #5 tended to shorten the half–lives of the compounds by 2.3–2.8 times compared with those in Trials #1 and #3 under the same climate zone. Volatilization, hydrolysis, and washing away of cyflumetofen were accelerated under the these conditions in Trial #5, which was verified in the study of cyflumetofen in an aquatic environment [16]. Furthermore, the $T_{1/2}$ values of cyflumetofen for *Yv Fan 1*, *Tian Zheng 1567* and *Mao Fen 802* tomatoes were 4.7, 3.9 and 1.7 days, respectively. The fastest dissipation rate was observed for *Mao Fen 8* tomatoes because of the rapid growth of fruits with great dilution properties, and the half–lives of penthiopyrad in tomatoes presented similar results [34]. Additionally, the $T_{1/2}$ of cyflumetofen in open-field cultivation was 7.2 days, which was significantly longer than that in the greenhouse (1.7–4.7 days), with $p < 0.05$. This difference was mainly attributed to the high initial deposition of cyflumetofen (0.44 mg/kg) in open–field cultivated tomatoes. The more mutable weather conditions in the field might be the nonnegligible reason for the slow dissipation of these compounds [35]. In addition, the half–lives of cyfluentofen were possibly due to the corresponding functional enzyme systems in tomatoes, and the enrichment of pathogenic bacteria might result in a shortened half–life of these compounds in crops [36].

Approximately 0.1–2.9% of cyflumetofen was metabolized to 2–TFMBA after application, with a concentration ≤ LOQ–0.012 mg/kg. The initial concentrations of 2–TFMBA were ≤ LOQ–0.006 mg/kg and then reached maximum values of 0.002–0.012 mg/kg after 7 days in Trials #1, #5, and #11, this concentration was 0.004 mg/kg after 3 days in Trial #3. There was a decreasing trend in the 2–TFMBA concentration in Trial #3 after 3 d because the dissipated magnitudes of 2–TFMBA were greater than those metabolized from the parent. Moreover, up to 2.9% of the parent compound was metabolized to 2-TFMBA in tomato plants under a subtropical monsoon climate, whereas no more than 1.0% of the cyanumetofen was metabolized under a temperate monsoon climate. This result was consistent with the high deposition of the parent cyflumetofen under the subtropical monsoon climate above. The relatively high temperature in the subtropical monsoon climate of 15–24.5 °C contributed to the hydrolysis of cyflumetofen to 2–TFMBA. Note that the concentrations of 2-TFMBA in the *Ai Mei Te* tomatoes ranged from 0.006 to 0.012 mg/kg, which were far greater than those in the *Yv Fan 1*, *Tian Zheng 1567*, and *Mao Fen 802* tomatoes (≤ 0.003 mg/kg). Additionally, 2–TFMBA was detected in open-field-cultivated tomatoes (0.006–0.012 mg/kg) in comparison with greenhouse-cultivated tomatoes (≤ LOQ–0.004 mg/kg). This phenomenon was strongly associated with the no enclosed condition of the field and was conducive to the metabolite of the compound [35]. In addition, aerobic conditions have been confirmed to accelerate the generation of 2–TFMBA compared with anaerobic conditions [37], and crop type plays a role in the generation of metabolites [17]. Overall, the generation of 2–TFMBA in tomatoes was closely related to the concentrations of the parent cyflumetofen, climate conditions, and tomato cultivars.

3.2.2. Terminal levels and MRL comparisons of cyflumetofen in tomatoes

The sum magnitudes of cyflumetofen and 2–TFMBA were calculated as 0.005–0.30 mg/kg (expressed as sum cyflumetofen; similarly, hereinafter) across nationwide cultivation systems (Table 1), according to the definition of the residue for estimation of dietary intake in plant commodities [17]. The supervised trial median residue (STMR) and highest residue (HR) of sum cyflumetofen were recommended at 0.04 and 0.30 mg/kg, respectively. The greatest terminal levels of sum cyflumetofen in tomatoes ranged from 0.01 to 0.3 mg/kg in Trials #7–#11 under a subtropical monsoon climate, followed by 0.005–0.11 mg/kg in Trials #1–#6 under a temperate monsoon climate and 0.02 mg/kg in Trial #12 under a tropical monsoon climate. Notably, the minimum concentration of total cyflumetofen was 0.01 mg/kg in Trial #10, which was obviously lower than that at the other sites in the same climate zone. The highest temperature (22.5 °C) and highest amount of heavy rain (1540.0 mm) occurred in Trial #10, which were conducive to evaporation, codistillation, thermodegradation, and compound leaching. Furthermore, the greatest terminal level of sum cyflumetofen was observed in the *Ai Mei Te tomato* plants at 0.25–0.30 mg/kg, which was 12.5–60–fold greater than the minimum level in the *Xin Mao Fen 802 tomato plants*. The results indicated that the high water content, growth rate, and plant lipids of the *Xin Mao Fen 802 tomato* were not conducive to the residual fate of the compounds [38,

Table 1
Terminal levels of cyflumetofen and metabolites in tomatoes.

Cultivation condition	Trial sites	Tomato cultivars	Terminal concentrations (mg/kg)		
			Cyflumetofen	2–TFMBA	Sum cyflumetofen
Greenhouse	Trial #1 (125.98°E, 46.07°N)	*Yv Fan 1*	0.07	0.002	0.05–0.07
	Trial #3 (116.65°E, 39.92°N)	*Tian Zheng 1567*	0.03–0.04	0.002–0.004	0.03–0.04
	Trial #5 (117.00°E, 36.65°N)	*Mao Fen 802*	0.003	0.001–0.002	0.01–0.02
	Trial #7 (116.97°E, 33.63°N)	*Fan Qie Da Wang 1:168*	0.02–0.03	0.001–0.002	0.02–0.04
	Trial #8 (120.12°E, 30.16°N)	*Ying Guo 903*	0.06–0.08	0.003	0.07–0.09
	Trial #9 (114.23°E, 30.40°N)	*He Zuo 903*	0.10–0.13	0.010–0.011	0.13–0.16
Open–field	Trial #2 (113.98°E, 36.20°N)	*Xin Mao Fen 802*	0.004–0.02	0.001	0.005–0.02
	Trial #4 (117.30°E, 39.73°N)	*Tianjiao 7*	0.08–0.11	0.002	0.09–0.11
	Trial #6 (112.59°E, 35.09°N)	*Luo Yang 92–18*	0.007–0.01	≤ 0.001	0.009–0.01
	Trial #10 (108.33°E, 22.84°N)	*Yi Feng Yi Dai*	0.009–0.04	0.002–0.004	0.01–0.04
	Trial #11 (106.63°E, 26.65°N)	*Ai Mei Te*	0.24–0.28	0.007	0.25–0.30
	Trial #12 (110.32°E, 20.03°N)	*Xiu Li*	0.010–0.02	0.005	0.02

39]. Additionally, more residual levels of sum cyflumetofen were detected in open-field-cultivated tomatoes (0.005–0.30 mg/kg) than in greenhouse-cultivated tomatoes (0.01–0.16 mg/kg). The fruit setting of the open field tomato plants was controlled by a single weight greater than 250 g, which was much greater than that of the greenhouse tomato plants (200 g). The environmental conditions of open field cultivation effectively improved the setting and coverage rate of tomato fruits, as indicated by the appropriate annual average temperature of 12–22.5 °C and rainfall of 447.3–1540 mm. These results directly indicated that more sum cyflumetofen was attached to the open-field tomato fruits than to the greenhouse tomatoes. In addition, the concentration of cyflumetofen varied with crop type and preceding crop. A higher concentration of cyflumetofen was observed in citrus plants (1.60–1.65 mg/kg) than in tomatoes (0.005–0.30 mg/kg) [14].

The terminal concentrations of cyflumetofen in tomatoes ranged from 0.004 mg/kg to 0.28 mg/kg, which accounted for 0.3–28.0% of the applied concentration; as a result, 0.2–2.5% of cyflumetofen was metabolized to 2–TFMBA in tomatoes during cultivation periods. The highest concentration of cyflumetofen was observed at 0.28 mg/kg, meeting the established residual limit for plant commodities and preharvest intervals after pesticide application [17]. The maximum residual limit (MRL) of cyflumetofen was established at 0.3 mg/kg by the Ministry of Agriculture and Rural in China [28], which was lower than that in Japan and Korea (0.4 and 1.0 mg/kg, respectively) [40,41]. It was suggested that relevant departments in China improve the information reserve library of tomato import restrictions to strengthen the residual detection of cyflumetofen in tomatoes imported from Japan and Korea while avoiding trade risks caused by excessive pesticide residues, given the great import value of 8.941 million dollars in 2022 in China [12]. A precise and comprehensive risk assessment of cyflumetofen was also performed to protect humans from toxic effects, as dietary intake appears to be the major pathway for human exposure to pesticides.

3.3. Effect of canning on residue removal of cyflumetofen and its metabolites

Evaluating the residual removal of sum cyflumetofen was carried out among household canning tomato paste, with concentrations decreasing from 0.12 mg/kg to 0.09 mg/kg and a processing factor of 0.79 for the sum cyflumetofen (Pf_{sum}) (Fig. 2, Table S4). The washing method was assumed to reduce non systematic cyflumetofen in tomatoes effectively, with a Pf_{sum} value of 0.67. It was also confirmed that washing was efficient at reducing the concentration of thiophanate-methyl in tomatoes [21,42]. The greatest magnitude of sum cyflumetofen was obtained in tomato skin at 0.81 mg/kg, indicating that the cuticles of tomatoes play essential roles in protecting fruits from physical deposition. Peeling was proven to be the most effective procedure for removing 78.0% of the cyflumetofen in the present study, with a Pf_{sum} of 0.33. This result was closely related to the high octanol–water partition coefficient of 4.3 (pH 7, 20 °C) of non systemic and hydrophobic cyflumetofen, which contributed to the difficult transport of agrochemicals into the internal parts of tomato fruits [43,44]. Notably, the concentration of sum cyflumetofen was greater in 0.03 mg/kg tomato puree than in tomato juice (0.01 mg/kg) and seeds (0.01 mg/kg), demonstrating the crucial role of increasing concentrations of these compounds through homogenization [45]. The relatively low concentration of sum cyflumetofen in tomato juice (0.002 mg/kg) was closely related to the poor solubility of the compounds in water matrices (0.028 mg/L) [20]. Furthermore, 3.9–fold more compounds were detected in tomato paste than in tomato paste in the simmering link, with a Pf_{sum} value of 3.73. This result was consistent with the evaporation of excess water in tomato matrices at 80–90 °C for 30 min, which was consistent with the results obtained for acetamiprid in honeysuckle [46]. Finally, sterilization had little impact on the reduction in the concentration of sum cyflumetofen, which rarely changed by 0.09 mg/kg, this might be affected by microbial variation in the home canning of tomato paste. And this approach has been found to be the least effective method for limiting pesticide residues in apples [47,48].

Moreover, the concentration of cyflumetofen significantly decreased from 0.10 to 0.01 mg/kg among home–canned tomato links, with a processing factor of 0.15 (Fig. 2**B**). Among the whole processing steps, cooking effectively removed cyflumetofen, and 92.0% of the cyflumetofen was removed from the waxed tomato skin. The minimum magnitude of action of cyflumetofen was observed at 0.004 mg/kg in tomato puree. Homogenization was the second most effective procedure for reducing concentrations of cyflumetofen, with concentrations decreasing from 0.008 to 0.004 mg/kg. Interestingly, the concentration of cyflumetofen accounted for less than 30% of the sum cyflumetofen

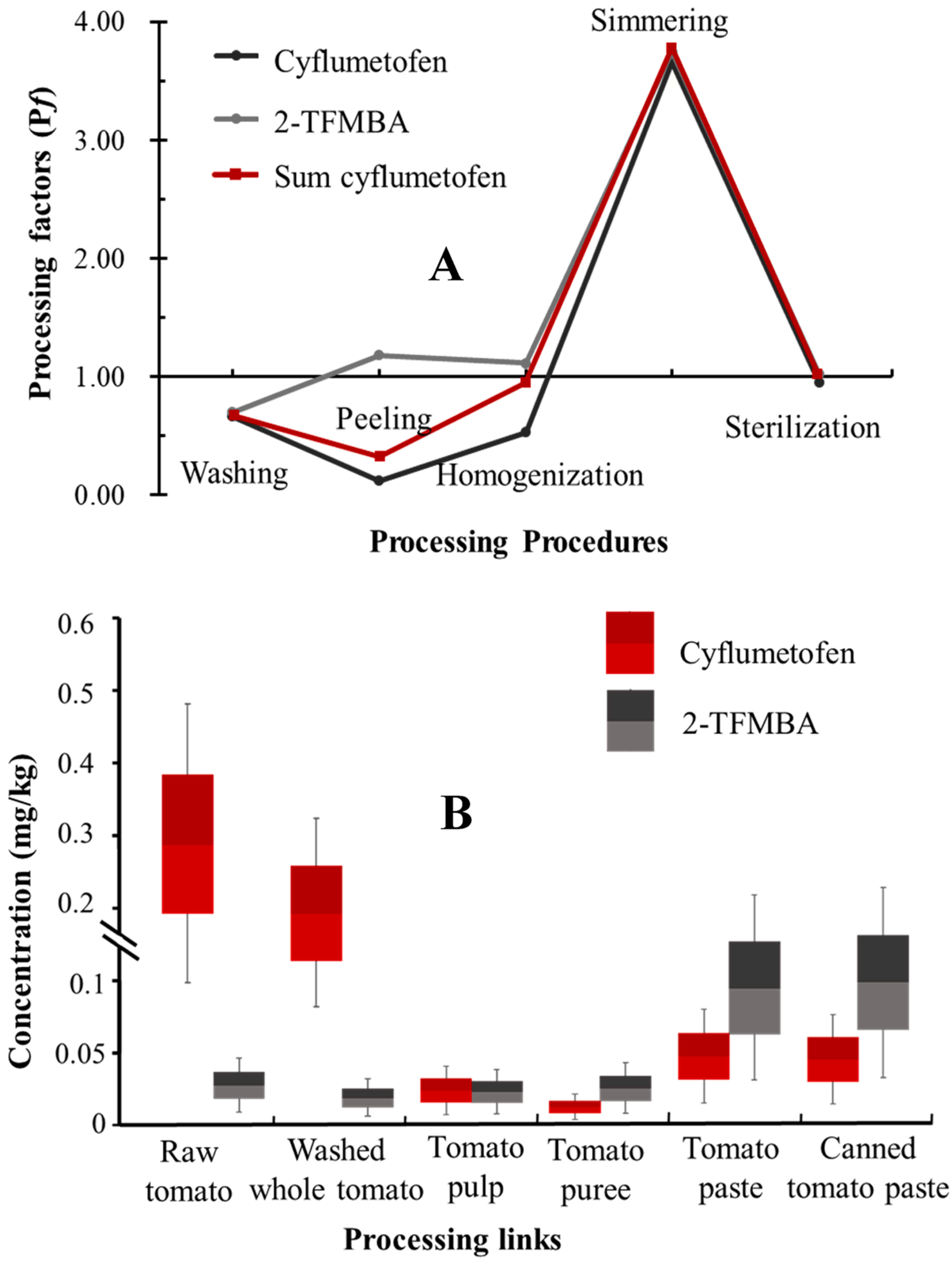

Fig. 2. Variations in processing factors (A) and residual concentrations (B) of cyflumetofen and 2–TFMBA among home canning tomato paste links.

among the home-canning tomato paste links, because up to 59.3% of the cyflumetofen were metabolized to 2–TFMBA. The processing factor of metabolite (Pf_m) values of 2–TFMBA were greater than the threshold line ($Pf = 1$) among most processing links. Washing was the only effective method for removing 2-TFMBA from tomatoes, in which the concentration decreased from 0.009 to 0.007 mg/kg and the Pf_m value was 0.70.

3.4. Dietary risk assessment of cyflumetofen from raw to tomato paste using deterministic and probabilistic models

Total long-term dietary risks were determined for sum cyflumetofen in registered crops, with chronic risk quotients (RQs) of 0.226–2.471%, revealing acceptable health hazards for consumers with a long-term diet (Fig. 3C). The dietary risk of sum cyflumetofen was analysed for different population groups, including different age (infants aged 2–6, children aged 7–13, adolescents aged 14–17, youth aged 18–44, middle-aged 45–69, elderly aged ≥ 70), region (urban and rural), and sex groups (male and female). First, the greatest RQ of sum cyflumetofen was observed in the infant group (1.666–2.471%), and the minimum was in the elderly group (0.226–0.651%). This difference was due to the high dietary intake per body weight of infants (0.016–0.025 mg/kg), which indicated that children's dietary intake of pesticides increases through their activities [49]. Second, the RQs of sum cyflumetofen for urban groups (0.477–2.471%) were significantly greater than those for rural groups (0.226–2.203%), with a p value of 1.04×10^{-5} at a 95% probability, mainly resulting from the consumption of crops for rural groups (117.7–244.8 g) being much lower than that for urban consumers (102.5–178.6 g) [50]. Interestingly, the risk values of sum cyflumetofen for urban and rural populations were both maximized in the 2–3–year–old group, at 2.471% and 2.203%, respectively. The minimums were 0.477% for the urban group aged 30–44 years and 0.266% for the rural group aged ≥ 70 years. Third, the RQs for males were 0.216–2.455%, which were similar to those for females

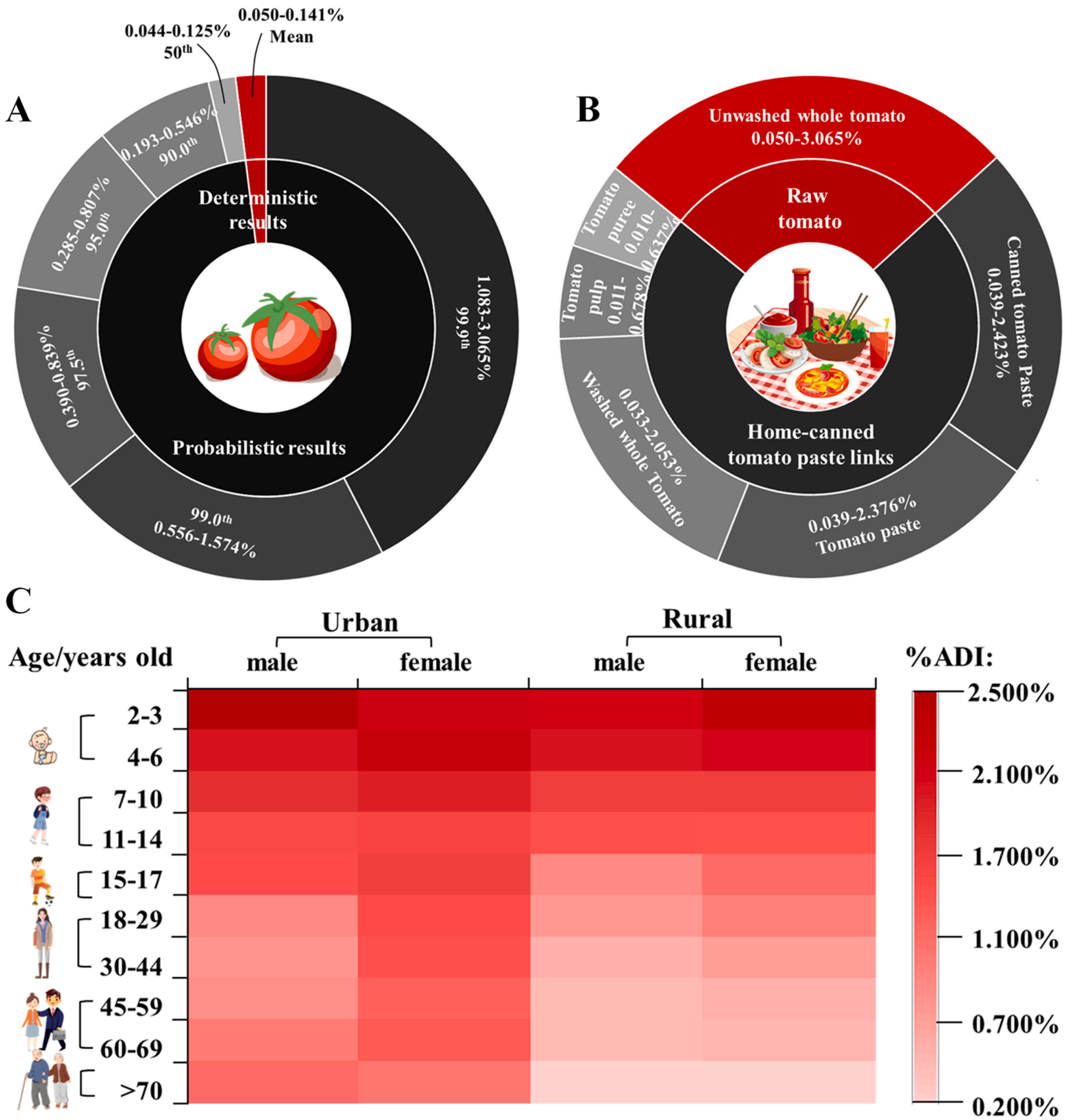

Fig. 3. Chronic dietary risks of sum cyflumetofen from raw tomatoes (A) to home-canned tomato paste (B) as well as in registered crops (C) for population groups.

(0.218–2.183%), with $p > 0.05$ at a 95% probability.

Furthermore, the health risks associated with multiple foods consumed were much greater than those associated with dietary single crops. The risk quotients of the sum cyflumetofen in tomatoes were 0.050–0.141%, accounting for 9.5% of the total dietary risk values; these values are far lower than those in strawberry and citrus fruits (0.037–0.552% and 0.123–1.812%, respectively). Moreover, a more precise dietary risk assessment of sum cyflumetofen in tomatoes was carried out using a probabilistic assessment model (Fig. 3**A,** Table 2). The probabilistic results were 0.044–0.125%, 0.193–0.546%, 0.285–0.807%, 0.390–1.105%, 0.556–1.574% and 1.083–3.065% at the 50.0th, 90.0th, 95.0th, 97.5th, 99.0th, and 99.9th percentiles, respectively. The deterministic result (0.050–0.141%) was similar to the P50 level of the probabilistic results (0.044–0.125%), which showed that conservative risk values were obtained from the deterministic model and that the probabilistic model could offer specific risk values and provide a better description of uncertainty by establishing distributions using Monte Carlo methods [51]. Therefore, the probabilistic model was recommended for estimating the dietary risk of exposure to home canning tomato paste in this study.

The dietary exposure risk of sum cyflumetofen decreased from 0.009–2.423% at 50–99.9th percentiles during home canning tomato links. Overall, there was a 1.3–4.8–fold reduction in dietary exposure risk during home canning tomato paste links (Fig. 3B). Specifically, the RQs of the sum cyflumetofen in washed whole tomatoes ranged from 0.030% to 2.053% at the 50.0–99.9th percentiles. The risk values of sum cyflumetofen in tomato pulp decreased to four-fifths of that in raw tomatoes, with RQs ranging from 0.010 to 0.678%. It was resulted from

Table 2
Chronic dietary risks of cyflumetofen in raw tomato and processed tomato products for consumers by deterministic and probabilistic models.

Procedures	Region	Deterministic Results	Probabilistic Results					
		Mean	P50.0	P90.0	P95.0	P97.5	P99.0	P99.9
Raw tomato	Urban	0.050–0.107%	0.044–0.095%	0.193–0.414%	0.285–0.613%	0.390–0.839%	0.556–1.196%	1.083–2.328%
	Rural	0.062–0.141%	0.056–0.125%	0.241–0.546%	0.373–0.807%	0.489–1.105%	0.697–1.574%	1.356–3.065%
Washed whole tomato	Urban	0.033–0.072%	0.030–0.064%	0.129–0.278%	0.191–0.411%	0.261–0.562%	0.373–0.801%	0.725–1.559%
	Rural	0.042–0.094%	0.037–0.084%	0.162–0.366%	0.239–0.541%	0.328–0.740%	0.467–1.055%	0.908–2.053%
Tomato pulp	Urban	0.011–0.024%	0.010–0.021%	0.043–0.092%	0.063–0.135%	0.086–0.186%	0.123–0.264%	0.239–0.515%
	Rural	0.014–0.031%	0.012–0.028%	0.053–0.121%	0.079–0.178%	0.108–0.244%	0.154–0.348%	0.300–0.678%
Tomato puree	Urban	0.010–0.022%	0.009–0.020%	0.040–0.086%	0.059–0.127%	0.081–0.174%	0.116–0.248%	0.225–0.484%
	Rural	0.013–0.029%	0.012–0.026%	0.050–0.113%	0.074–0.168%	0.102–0.230%	0.145–0.327%	0.282–0.637%
Tomato paste	Urban	0.039–0.083%	0.034–0.074%	0.149–0.321%	0.221–0.475%	0.303–0.651%	0.431–0.927%	0.839–1.804%
	Rural	0.048–0.109%	0.043–0.097%	0.187–0.423%	0.227–0.626%	0.379–0.857%	0.540–1.221%	1.051–2.376%
Canned tomato paste	Urban	0.039–0.085%	0.035–0.075%	0.152–0.328%	0.225–0.485%	0.309–0.664%	0.440–0.945%	0.856–1.840%
	Rural	0.049–0.111%	0.044–0.099%	0.328–0.432%	0.282–0.638%	0.387–0.874%	0.551–1.245%	1.072–2.423%

77.9% of the compounds being removed through peeling. The valley point was observed in tomato puree, with RQs ranging from 0.009 to 0.637%. There was an obvious increase in the dietary risk of sum cyflumetofen in tomato paste, with a p value of 0.03 at a 95% probability, which was closely related to the 3.7–fold increase in the concentration of sum cyflumetofen during simmering. The RQs were maximized at 0.035–2.423% in the canned tomato paste, which was far lower than that in the raw tomatoes (0.044–3.065%). The potential health hazards of sum cyflumetofen in tomato products should be considered continuously despite the acceptable exposure risk, given its ubiquity and cumulative effects.

3.5. Perspective

The fate characteristics and dietary risks of large-scale cyflumetofen applied during cultivation and processing were investigated in this study, and four aspects of concern should be addressed in future work. First, the fate characteristics and risk assessment of multiple pesticides are urgently needed from the perspective of different pesticide types and formulations, such as insecticides, fungicides, acaricides, water-based pesticides, and nano pesticides. And the risk quantification of compounds in multiple crops was also scarce and required equal attention because the dietary risk values of cyflumetofen in registered crops were far greater than those in tomatoes in the study. Second, it is necessary to evaluate the safety of tomato byproducts in follow–up work to protect human health from hazards based on the fact that tomato skin is an important source of lycopene with high residual levels of sum cyflumetofen. Third, the more comprehensive health exposure risks of cyflumetofen for consumers were assessed through various exposure pathways, including oral intake, inhalation and dermal contact, based on the dietary exposure risks of sum cyflumetofen through the intake of tomato products. In addition, the influence of specific cultivation methods on the fate characteristic of compounds needs to be verified in future work, given thatthe high residual concentration of total cyflumetofen on open field tomato plants was investigated from the aspects of influencing plant coverage and fruit setting.

4. Conclusion

The fate characteristics and dietary risks of cyflumetofen have been clarified from tomato cultivation to processing, contributing to the achievement of the UNSDG in regard to human health and agroecosystem safety. The metabolic rate of cyflumetofen was greater in greenhouse tomato cultivation with a low residual level than in open field cultivation, which was closely related to the tomato cultivar and climate factors. Peeling played a key role in removing cyflumetofen from tomatoes, whereas washing was recommended for its main metabolite 2–TFMBA. Up to 59.3% of the cyflumetofen was hydrolysed to 2–TFMBA during home canning tomato paste. The dietary exposure risks of sum cyflumetofen were evaluated for consumers throughout the whole life cycle using deterministic and probabilistic models. The probabilistic model was recommended with acceptable risk quotients of 0.044–3.065% at the 50.0–99.9th percentiles. These exposure risks of cyflumetofen should be considered continuously for vulnerable populations on the basis of the cumulative amplification effect for exposure risks of sum cyflumetofen in multiple crops.

CRediT authorship contribution statement

Li Xianbin: Writing – review & editing. **Chen Zenglong:** Writing – review & editing, Visualization, Methodology. **Chen Li:** Writing – review & editing. **Ren Xin:** Writing – review & editing. **Zhao Lilin**: Writing-review & editing. **Kang Shanshan:** Writing – review & editing. **Zhang Hongxia:** Writing – review & editing, Visualization. **Wang Xi:** Writing – original draft, Software, Investigation, Formal analysis.

Environmental Implication

Cyflumetofen is a novel acaricide posing potential health hazards to humans, major metabolite (2-TFMBA) of which is also showed high toxicity. This first experimental evaluation on the cyflumetofen and 2-TFMBA in tomatoes reveals the environmental fate with regard of influencing factors. Variation of concentration and dietary risks for described agrichemicals were investigated from raw tomato to home canning tomato paste links using processing factors and risk quotients. We present a comprehensive environmental study of cyflumetofen and metabolite in tomatoes from fields to table, providing scientifical references for protect human health and environmental safety from hazard.

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

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2024.133496.

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