Residue Dissipation, Degradation Dynamics, and Dietary Risk Assessment of Mandipropamid in Ginseng Under Field Application

Zhiguang Hou  
Jilin Agricultural University

Xingang Hou  
Jilin Agricultural University  
https://orcid.org/0000-0002-3854-4770

Li-Ping Wei  
Jilin Agricultural University

Zhanwen Cao  
Jilin Agricultural University

Zhou Lu  
Jilin Agricultural University

Hanju Liu  
Jilin Agricultural University

Zhongbin Lu (✉ luzong1979@aliyun.com)  
Jilin Agricultural University

Research Article

Keywords: mandipropamid, ginseng, HPLC-MS/MS, dissipation, dietary risk assessment

Posted Date: January 24th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1202328/v1

License: ©  This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Mandipropamid, a new fungicide for oomycete disease, has a strong effect on the blight of many crops and has been registered for the treatment of ginseng blight in China. However, no maximum residue limit (MRL) of mandipropamid has been identified for ginseng, and there have been few related studies. We established and verified the analysis method of mandipropamid in ginseng using high-performance liquid chromatography-tandem mass spectrometry. The method has good linearity and accuracy in the range of 0.002–0.5 mg/kg. The average recovery of mandipropamid was 87.4–101.6%, and the standard deviation was 1.1–10.1. The degradation dynamics showed that the half-life of mandipropamid in ginseng plant and soil was 13.8–28.0 and 9.8–27.4 d, respectively. After the recommended dose of mandipropamid was applied once, the residual content of mandipropamid in fresh ginseng, dried ginseng, red ginseng, ginseng plant, and ginseng soil was <0.01–0.185, <0.01–0.265, 0.085–1.544, 0.075–4.800, and <0.01–0.014 mg/kg, respectively. The dietary risk assessment of mandipropamid on ginseng showed that the risk quotient value was far less than 100%, indicating that the recommended dose of mandipropamid does not cause unacceptable risks to humans. Mandipropamid in ginseng plants and soil rapidly degraded following first-order kinetics models. After the recommended dose of mandipropamid was applied once, it did not cause unacceptable risks to humans. This study not only provides a reasonable spray dosage of mandipropamid to ginseng, but also offers a reference for the establishment of MRLs in China.

1 Introduction

Ginseng is the dried root and rhizome of Panax ginseng C.A.Mey (Zhang et al., 2021). As the largest ginseng planting and production country in the world, China has a long history of medicinal use of ginseng. Ginseng plays an important role in regulating human health and treating different diseases (Fan et al., 2020) through its antitumor, antioxidation, and antidiabetic properties (Park et al., 2017). The growth cycle of ginseng is relatively long, usually 4–6 years for garden ginseng and 15 years for forest ginseng. During the long growth cycle, the occurrence of diseases affects the quality of ginseng, which causes significant economic losses to ginseng farmers and affects the import and export of ginseng. Therefore, fungicides must be used to prevent diseases during the planting process. However, due to the irregular use of pesticides, excessive pesticide residues can be found in ginseng.

Mandipropamid is a new fungicide for oomycete diseases (Tang et al., 2011), which is the first commercial amygdalinamide compound with the chemical name of 2-(4-chlorophenyl)-n-[2-(3-methoxy-4-prop-2-ynynloxy-phenyl)-ethyl]-2-prop-2-ynloxy-acetamide. It has high activity in inhibiting conidial germination, mycelial growth and spore formation; it also has a good preventive and therapeutic effect on lychee downy mildew (Tang et al., 2011), pepper blight (Siegenthaler and Hansen, 2021), tomato late blight (Chen et al., 2021), and cucumber downy mildew (Liu et al., 2016, Zhang et al., 2015). In China, mandipropamid has been registered in tomato, pepper, potato, lychee, grape, watermelon, and ginseng and has been widely used to control blight and downy mildew in various crop sites. Mandipropamid is mainly used to treat ginseng blight. The application of mandipropamid to ginseng will inevitably cause pesticide residue problems in ginseng and the surrounding environment, thereby causing harm to human health. In recent years, the problem of pesticide residue has gained increasing attention; therefore, the rational use and risk assessment of mandipropamid is of great significance.

At present, the methods for detecting residues of mandipropamid in sesame leaves (Farha et al., 2016), grapes (Kwon et al., 2008; Malhat and Abdallah, 2012; Xu et al., 2020; Zhang et al., 2014), tomato (Kwon et al., 2008), pepper (Kwon et al., 2008; Zhang et al., 2014), cabbage (Kwon et al., 2008), potato (Kwon et al., 2008; Zhang et al., 2014), watermelon (Zhang et al., 2014), lettuce (Yang et al., 2020), and Cnidium (Dong et al., 2020) are mainly high-performance liquid chromatography (HPLC) and HPLC-tandem mass spectrometry (MS/MS). Moreover, residual behaviour analysis and research on mandipropamid in grapes (Malhat and Abdallah, 2012), lettuce (Yang et al., 2020), and Cnidium (Dong et al., 2020) have been undertaken. However, there have been no systematic studies on the residual behaviour, degradation dynamics, and dietary risk assessment of mandipropamid in ginseng. Therefore, in this study, we established a method for the detection of mandipropamid in ginseng using HPLC-MS/MS. Through field trials at five locations for 1 year, the residual behaviour and degradation dynamics of mandipropamid in ginseng were analysed. Additionally, the safety of mandipropamid use on ginseng was evaluated in combination with the Chinese dietary structure. Finally, reasonable suggestions were provided for the rational use of mandipropamid on ginseng, and the basis for the formulation of residue limits in ginseng was provided.

2 Materials And Methods
2.1 Instruments and reagents

The following materials were used: 1260-6470 HPLC-MS/MS (Agilent Technologies, USA), SHMADIU Model AUY220 Balance (Shmadiu Corporation, Japan), HUAPUDA Model YXJ-A Centrifugal Machines (Changzhou Huapuda Educational Instrument Corporation, China), Kunshan KQ-500 Ultrasonicator (Kunshan Ultrasonics Corporation, China), and a digital high-speed dispersive homogeniser (IKA T25, IKA Company, Germany).

Analytical standards of mandipropamid (Dr. Ehrenstorfer GmbH, Germany) were used. Acetonitrile and methanol were of HPLC grade (MREDA Technology Inc., USA), formic acid was of 96% HPLC grade (TEDIA Company, USA), ammonium acetate was of 98% analysis grade (SIGMA, Germany), both sodium chloride and magnesium sulphate were of analytical grade (Beijing Chemical Plant, China), and Cleanert PSA was of PR grade (Agela Technology, China).

2.2 Field trial

From August to September 2020, field trials were conducted at five locations over one year. The trial locations were Fusong County in Jilin Province, Huanren Manchu Autonomous County in Liaoning Province, Baishan City in Jilin Province, Ji’an City in Jilin Province, and Yanbian City in Jilin Province. The final residue experiment was carried out in all five locations, and the degradation experiment of the ginseng plant and soil was carried out simultaneously in Fusong, Huanren, and Baishan, and the experiments were designed according to NY/788-2018 (Pesticide Residue Test Guidelines) (Ministry of Agriculture and Rural Affairs of the People’s Republic of China, 2018).

The area of the experimental plots was 50 m². At the initial stage of the onset of ginseng disease, the spraying dose was 210.6 g a.i./ha of stem and leaf spray, dynamic soil application was soil spray mixed with water at 600 kg/ha, and the number of sprays was one. After one application, the ginseng plant and soil samples were collected at intervals of 0, 1, 3, 5, 7, 14, 21, 28, 35, 45, and 60 d. Residual samples of fresh ginseng, ginseng plant, and soil were collected at 14, 21, and 28 d.

2.2.1 Preparation of samples

Fresh ginseng samples were gently washed using cool water, and the surfaces of the samples were dried indoors. Fresh ginseng samples were baked at 55°C for 24 h to prepare dried ginseng, and fresh ginseng samples were placed in a cage on a pot filled with water at 80°C and heated to boiling for 2.5–3 h. Then, the heated ginseng was cooled and dried at 70°C for 6 h with a dryer. Next, the ginseng was infiltrated with water, and the ginseng was dried again at 55°C for 24 h. Ginseng plant samples were placed in a tissue masher, and mashed for 5 min, and then passed through a 40-mesh sieve.

2.3 Extraction and purification

Next, 5.0 (±0.05) g of the homogenised fresh ginseng, dried ginseng, red ginseng, ginseng plant, and ginseng soil samples were added to 50-mL centrifuge tube, and then, 5 mL of distilled water and 10 mL of acetonitrile were added to the tube. After standing immersion for 5 min, vortex extraction was performed for 2 min, and the samples were centrifuged at 5,000 g for 5 min.

An aliquot of 1 mL of the upper layer of fresh ginseng, dried ginseng, red ginseng, and ginseng soil was transferred to a centrifuge tube containing 50 mg PSA and 100 mg anhydrous magnesium sulphate. An aliquot of 1 mL of the upper layer of the ginseng plant was transferred to a centrifuge tube containing 50 mg PSA, 25 mg GCB, and 100 mg anhydrous magnesium sulphate. The mixture was shaken vigorously 100 times and centrifuged for 5 min at 5,000 rpm. The upper layer was filtered through a 0.22-μm nylon syringe filter disc and analysed by HPLC-MS/MS.

2.4 Instrumental parameters

2.4.1 Chromatographic conditions

The chromatographic column used was an Agilent Zorbax RRHD Eclipse Plus C18 (3.0 ×100 mm, 1.8 μm at 30°C) column. The mobile phase was composed of acetonitrile (A) and water containing 0.1% formic acid and 5 mmol ammonium acetate (B) with a linear gradient. The linear mobile phase gradient was 0–2 min, 90–80% A; 2–3 min, 80–70% A; 3–5.5 min, 70–10% A; 5.5–7 min,
10% A; 7–9 min, 10%–30% A; 9–9.5 min, 30–60% A; 9.5–10 min, 60–90% A; and 10–15 min, 90% A. The flow rate was 0.3 mL/min, and the injection volume was 5 µL.

2.4.2 Mass spectrometry conditions

The ionisation source mode was electrospray ionisation, ionisation source polarity was positive ion mode (ESI+), scanning mode was multiple reaction monitoring, atomising gas was nitrogen, nebuliser gas pressure was 45 psi, ion spray voltage was 4,000 V, sheath gas temperature was 350°C, sheath gas was 12 L/min, quantitative ion of mandipropamid was 412/328.1, qualitative ion of mandipropamid was 412/328.1 and 412/124.8, fragmentor was 60 V, and collision energy was 412/328.1 (13 V) and 412/124.8 (35 V).

2.5 Statistical analysis

In this study, the standard curve and matrix standard curve of the same concentration were detected under the same chromatographic conditions, and the matrix effect was calculated according to the slope of the two standard solutions. When the matrix effect was within 100% (± 20), it was ignored; when it was greater than 120%, it showed enhancement, and when this was less than 80%, it showed inhibition. The calculation formula is as follows (Fang et al., 2019):

\[ ME(\%) = \frac{K_S}{K_m} \times 100 \]

where \( K_S \) is the slope of the standard curve and \( K_m \) is the slope of the matrix standard curve.

The dissipation dynamics of mandipropamid in ginseng plants and soil were evaluated using first-order kinetics as follows (Fang et al., 2019; Vargas-Pérez et al., 2020):

\[ C_t = C_0 \times e^{-kt} \]

\[ T_{1/2} = \frac{\ln 2}{k} \]

where \( C_t \) (mg/kg) is the residual concentration of mandipropamid in the ginseng plant or soil, \( C_0 \) (mg/kg) is the initial concentration of mandipropamid in the ginseng plant or soil, \( k \) (day\(^{-1}\)) is the dissipation rate constant, and \( T_{1/2} \) is the pesticide half-life of pesticide degradation.

2.6 Dietary intake risk assessment

Dietary exposure and risk assessments were performed to ensure the rational use of mandipropamid. RQ>100% indicated that there was an unacceptable risk to human health; the larger the value, the greater the risk. RQ<100% indicated that the risk to human health was acceptable; the smaller the value, the smaller the risk.

The chronic dietary risk assessment was undertaken by calculating RQ as follows (Fang et al., 2019):

\[ NEDI = \frac{\sum STMRI \times Fi}{bw} \]

\[ RQ = \frac{NEDI}{ADI} \times 100 \]

where NEDI (mg/kg, bw) is the national estimated daily intake, STMRI (mg/kg) is the supervised trial median residue level, Fi (kg/d) is the average daily food intake, bw (kg) is the average Chinese body weight (63 kg), and ADI (mg/kg, bw) is the acceptable daily intake.

3 Results And Discussion

3.1 Method validation
The mandipropamid standard substance (0.0101 g) was accurately weighed, diluted to 10 mL with acetonitrile, sonicated for 10 min, and stored in a refrigerator at −4°C. This was then diluted with acetonitrile and blank matrix solution to 0.002, 0.005, 0.01, 0.02, 0.05, 0.1, 0.2, and 0.5 mg/L series solutions. Machine detection was performed according to the 2.3 method. With the concentration as the abscissa and the peak area as the vertical coordinates, a standard curve was drawn, resulting in the linear regression equation of mandipropamid. The results are presented in Table 1.

Table 1 The linear regression equation of mandipropamid in different matrices

| Matrix          | Linear regression equation   | Coefficient (R) | ME (%) |
|-----------------|------------------------------|-----------------|--------|
| Fresh ginseng   | \( y = 57171927.30 \times + 199740.39 \) | 0.9999          | 87.0   |
| Dried ginseng   | \( y = 66,912,235.11 \times + 20,781.54 \) | 0.9996          | 91.7   |
| Red ginseng     | \( y = 3,967,045.54 \times - 588.30 \)         | 0.9999          | 5.4    |
| Ginseng plant   | \( y = 101461225.21 \times + 1330231.11 \)       | 0.9912          | 98.1   |
| Ginseng soil    | \( y = 85006757.21 \times + 653659.39 \)         | 0.9967          | 99.2   |

Note: ME, Matrix effects.

The accuracy and precision of the method were verified using an addition-recovery test. According to the above method, the added amounts of fresh ginseng and soil were 0.01, 0.05, and 0.5 mg/kg, and those of dry ginseng, red ginseng, and plants were 0.01, 0.05, 0.5, and 50 mg/kg, respectively. This method was repeated five times. The results are presented in Table 2. The sensitivity and accuracy of the method met the requirements and were suitable for the residue analysis of mandipropamid in ginseng.

Table 2 The addition recovery rate, RSD, LOQ, and LOD in ginseng
### Table 3. Spiked level of mandipropamid and its recovery in ginseng matrices

| Matrix         | Spiked level (mg/kg) | Average Recovery (%) | RSD (%) | LOQ (mg/kg) | LOD (mg/kg) |
|----------------|----------------------|----------------------|---------|-------------|-------------|
| Fresh ginseng  | 0.01                 | 89.9                 | 10.1    | 0.01        | 0.002       |
|                | 0.05                 | 87.4                 | 4.0     |             |             |
|                | 0.5                  | 96.3                 | 1.7     |             |             |
| Dried ginseng  | 0.01                 | 96.1                 | 1.3     |             |             |
|                | 0.05                 | 99.0                 | 1.8     |             |             |
|                | 0.5                  | 101.6                | 2.8     |             |             |
|                | 50                   | 95.7                 | 1.4     |             |             |
| Red ginseng    | 0.01                 | 92.6                 | 3.6     |             |             |
|                | 0.05                 | 98.7                 | 3.1     |             |             |
|                | 0.5                  | 100.0                | 1.4     |             |             |
|                | 50                   | 101.0                | 2.7     |             |             |
| Ginseng plant  | 0.01                 | 89.6                 | 2.4     |             |             |
|                | 0.05                 | 99.1                 | 2.4     |             |             |
|                | 0.5                  | 94.2                 | 1.9     |             |             |
|                | 50                   | 95.8                 | 2.2     |             |             |
| Ginseng soil   | 0.01                 | 97.3                 | 1.1     |             |             |
|                | 0.05                 | 93.7                 | 1.2     |             |             |
|                | 0.5                  | 96.8                 | 1.5     |             |             |

Note: RSD, relative standard deviation; LOQ, limit of quantitation; LOD, limit of detection.

### 3.2 The degradation dynamics of mandipropamid in ginseng plant and soil

According to the design of the field experiment, samples were collected to assess the degradation dynamics of mandipropamid in ginseng plants and soil in Fusong County, Jilin Province, Huanren Manchu Autonomous County of Liaoning Province, and Baishan City of Jilin Province were collected. As detected using the 2.3-2.4 methods, the degradation of mandipropamid conformed to first-order kinetics. The content of mandipropamid in ginseng plant and soil 2 h after application was that of the original residues, and as time passed, the residue concentration of mandipropamid gradually decreased. The results are shown in Figure 1–2 and Table 3. The half-life of mandipropamid in ginseng plant was 13.8 (Fusong), 28.0 (Huanren), and 13.9 d (Baishan). The original residue amounts of mandipropamid in ginseng plant were 5.24 (Fusong), 3.22 (Huanren), and 4.42 mg/kg (Baishan). The half-life of mandipropamid in ginseng plant was 9.8 (Fusong), 16.0 (Huanren), and 27.4 d (Baishan). The original residue amount of mandipropamid in ginseng plants was 0.039 (Fusong), 0.054 (Huanren), and 0.068 mg/kg (Baishan). The difference in the original residues may be due to multiple factors, such as plant growth status and weather conditions (temperature, humidity, wind speed, etc.) at the test point during spraying. The results showed that the half-life of mandipropamid in ginseng plants was not significantly different in Fusong and Baishan, whereas that in Huanren was significantly higher than that in Fusong and Baishan, mainly due to plant size, sparseness, and metabolic capacity, which may also be affected by factors such as plant variety and weather conditions (Bai et al., 2020). The half-life of mandipropamid in ginseng soil was different in Fusong, Huanren, and Baishan. Since the ginseng soil was artificially mixed with soil, its organic matter content varied between locations. The organic acid content of Baishan soil was 4%, that of Fusong soil was 4.3%, that of Huanren soil was 4.4%, and Baishan soil had the lowest organic matter content. This may be responsible for the half-life of mandipropamid in Baishan soil, which was significantly higher than that of the other two locations, possibly because of to the effects of factors such as the types of microorganisms in the soil, temperature and humidity of the environment, and duration of sunshine.
Table 3 The degradation dynamics of mandipropamid in ginseng plant and soil

| Matrix       | Location   | Equation         | Coefficient ($R^2$) | Half-life ($T_{1/2}$) |
|--------------|------------|------------------|---------------------|-----------------------|
| Ginseng plant| Fusong     | $C_t = 4.9394e^{-0.046t}$ | 0.9377              | 13.8                  |
|              | Huanren    | $C_t = 2.7426e^{-0.019t}$ | 0.8217              | 28.0                  |
|              | Baishan    | $C_t = 3.9597e^{-0.042t}$ | 0.9043              | 13.9                  |
| Ginseng soil | Fusong     | $C_t = 0.0235e^{-0.019t}$ | 0.6379              | 9.8                   |
|              | Huanren    | $C_t = 0.0423e^{-0.028t}$ | 0.9024              | 16.0                  |
|              | Baishan    | $C_t = 0.0499e^{-0.014t}$ | 0.7488              | 27.4                  |

3.3 Final residues of mandipropamid in ginseng

Based on the design of the field experiment, the final residues of mandipropamid in fresh ginseng, dried ginseng, red ginseng, ginseng plant, and ginseng soil in Fusong County, Jilin Province, Huanren Manchu Autonomous County in Liaoning Province, Baishan City in Jilin Province, Ji’an City in Jilin Province, and Yanbian City in Jilin Province were collected. The results obtained using the above-described methods are shown in Table 4. The residual amounts of mandipropamid were as follows: fresh ginseng, <0.01–0.185; dried ginseng, <0.01–0.265; red ginseng, 0.085–1.544; ginseng plant, 0.075–4.800; and ginseng soil, <0.01–0.014 mg/kg. The final residual amount of mandipropamid in ginseng showed an insignificant decreasing trend with time, which may be affected by the application time, crop varieties, weather, and other factors. The STMR of mandipropamid was <0.01, 0.019, and 0.295 mg/kg in fresh, dried, and red ginseng, respectively. The HRs of mandipropamid in fresh, dried, and red ginseng were 0.185, 0.265, and 1.544 mg/kg, respectively. At present, China has not established the maximum residue limit (MRL) of mandipropamid in ginseng, partly because of the lack of mandipropamid residue and digestion data available for ginseng. The results of this study provide a basis for the rational use of mandipropamid in ginseng and help establish the MRL of mandipropamid in ginseng.

Table 4 Final residues of mandipropamid in ginseng with different application dosages and times
## 3.4 Dietary risk assessment

### 3.4.1 Chronic dietary exposure risk assessment

The chronic dietary exposure risk assessment is based on the Chinese dietary structure, combined with the registered crops and corresponding STMRi values and the daily allowable intake of mandipropamid to calculate the RQ for evaluation. At present, mandipropamid has been registered in China for tomato, pepper, lychee, potato, grape, ginseng, and watermelon. According to the principle of maximum risk, the largest MRL value in the food group was selected for evaluation, and the largest MRL value was selected according to the following priority order: China>CAC>United States>EU>South Korea>Japan>Australia, according to the “National Food Safety Standard Maximum Residue Limits of Pesticides in Food” (National Health Commission of the People's Republic of China, 2019). The ADI of mandipropamid is 0.2 mg/kg bw.

The maximum STMRi value of mandipropamid in fresh, dried, and red ginseng was selected as the reference limit for chronic dietary risk assessment. Ginseng is classified as soy sauce, and the STMRi of mandipropamid in red ginseng is regarded as the residue of soy sauce. The results are shown in Table 5, where the median RQ value is 2.9%, which is far less than 100%, indicating that the chronic dietary risk of mandipropamid use on ginseng is acceptable, and the recommended dose will not cause unacceptable risks to Chinese consumers.

Table 5 The Chinese dietary pattern and risk probability of mandipropamid in ginseng

| Matrix          | Does (g a.i./ha) | Times | PHI | Residue data (n = 3) (Mean value, mg/kg) | STMR (mg/kg) | STMR (mg/kg) |
|-----------------|------------------|-------|-----|-----------------------------------------|--------------|--------------|
| Fresh ginseng   | 210.6            | 1     | 14  | < 0.01(6), 0.034, 0.035, 0.067, 0.185     | <0.01        | 0.185        |
|                 |                  |       | 21  | < 0.01(8), 0.033, 0.033                   |              |              |
|                 |                  |       | 28  | < 0.01(7), 0.016, 0.068, 0.069            |              |              |
| Dried ginseng   | 210.6            | 1     | 14  | < 0.01, 0.012, 0.012, 0.017, 0.019, 0.099, 0.100, 0.222, 0.231 | 0.019        | 0.265        |
|                 |                  |       | 21  | 0.011, 0.011, 0.015, 0.024, 0.024, 0.031, 0.035, 0.157, 0.157 |
|                 |                  |       | 28  | 0.006, 0.007, 0.016, 0.017, 0.018, 0.021, 0.021, 0.211, 0.265 |
| Red ginseng     | 210.6            | 1     | 14  | 0.085, 0.091, 0.092, 0.100, 0.236, 0.243, 0.255, 0.303, 1.896, 1.901 | 0.295        | 1.544        |
|                 |                  |       | 21  | 0.164, 0.179, 0.182, 0.289, 0.300, 0.310, 0.380, 0.390, 1.534, 1.544 |
|                 |                  |       | 28  | 0.112, 0.116, 0.133, 0.146, 0.457, 0.462, 0.479, 0.487, 1.432, 1.452 |
| Ginseng plant   | 210.6            | 1     | 14  | 0.075, 0.078, 0.223, 0.235, 1.250, 1.255, 1.632, 1.662, 4.643, 4.800 | 0.729        | 4.800        |
|                 |                  |       | 21  | 0.177, 0.192, 0.500, 0.623, 0.689, 0.694, 0.938, 0.973, 2.005, 2.007 |
|                 |                  |       | 28  | 0.389, 0.466, 0.466, 0.476, 0.578, 0.763, 0.847, 0.872, 1.604, 1.635 |
| Ginseng soil    | 210.6            | 1     | 14  | < 0.01(10)                               | 0.01         | 0.014        |
|                 |                  |       | 21  | < 0.01(8), 0.014, 0.014                   |              |              |
|                 |                  |       | 28  | < 0.01(8), 0.012, 0.012                   |              |              |
| Food classification | Fi (kg) | Residue data (mg/kg) | Sources | NEDI (mg) | ADI/mg | RQ % |
|---------------------|--------|----------------------|---------|-----------|--------|------|
| Tubers              | 0.0495 | 0.01                 | China   | 7.86×10⁻⁶ | 0.2×63 | 2.9  |
| Dark vegetables     | 0.0915 | 3                    | China   | 4.36×10⁻³ |        |      |
| Fruits              | 0.0457 | 2                    | China   | 1.45×10⁻³ |        |      |
| Soy sauce           | 0.009  | 0.295                | STMR    | 4.21×10⁻⁵ |        |      |
| Total               | 1.0286 | 5.86×10⁻³             |         |           |        |      |

Note: Fi, Fi, dietary reference intake for a certain kind of food of healthy Chinese people; STMR is the supervised trials median residue of mandipropamid with a pre-harvest interval RQ, chronic dietary exposure risk probability.

3.4.2 Acute dietary exposure risk assessment

According to the JMPR report (He, 2008), it is not necessary to establish an acute reference dose for mandipropamid, and short-term intake of mandipropamid is unlikely to cause health problems to the public. Therefore, this study did not conduct an acute dietary risk assessment of mandipropamid in fresh, dried, and red ginseng.

4 Conclusion

In this study, an HPLC-MS/MS method was established for the detection of mandipropamid in ginseng, and the degradation dynamics, residue dissipation, and dietary risk assessment of mandipropamid in ginseng were studied under field application. This method has good precision and accuracy. The residues in fresh ginseng, dried ginseng, red ginseng, ginseng plant, and ginseng soil were <0.01–0.185, <0.01–0.265, 0.085–1.544, 0.075–4.800, and <0.01–0.014 mg/kg, respectively. The half-lives of mandipropamid in ginseng plant and soil were 13.8–28.0 and 9.8–27.4 d, respectively. According to the final residual test results, after one application, the chronic dietary risk of mandipropamid in ginseng was an RQ value of 2.9%, which was far less than 100%, indicating that there was no significant potential risk of mandipropamid in ginseng at the recommended dose. This study provides a basis for the rational use of mandipropamid in ginseng, as well as a reference for the establishment of MRL of mandipropamid in ginseng.

Declarations

Authors Contributions Zhiguang Hou performed interpretation, Writing, Review and Editing.

Xingang Hou performed the data analyses and manuscript preparation and wrote the manuscript.

Liping Wei performed the experiments of field experiments and sample collection section.

Zhanwen Cao performed the experiments of field experiments and sample collection section.

Zhou Lu performed the analysis with constructive discussions.

Hanju Liu performed the experiments of field experiments and sample collection section.

Zhongbin Lu contributed to the conception of the study and provided assistance through all the experiments.

Funding Partial funding was received from the Agricultural Industry Standard of the Chinese Ministry of Agriculture (2018) (grant no.: 181721301092371097) and the Special Fund for Ginseng Industry Development of Jilin Province (2015) (grant no.: 201501).

Data availability All data generated or analyzed during this study are included in this published article [and its supplementary information files]
Compliance with ethical standards

Ethics approval and consent to participate  Not applicable

Consent for publication  Not applicable

Competing interests  The authors declare that they have no competing interests

References

1. Bai, A., Chen, A., Chen, W., et al., 2020. Study on degradation behaviour, residue distribution, and dietary risk assessment of propiconazole in celery and onion under field application [J]. J. Sci. Food Agric. https://doi.org/10.1002/jsfa.10817.
2. Chen, J., Tian, B.H., Lai, R.L., et al., 2021. Field efficacy of new mixtures of oxathiapiprolin-mandipropamid 26% SC against to late blight [J]. Agrochemicals 60(02), 154-156.
3. Dong, K. J., Jeong, W. M., Goo, Y. M., et al., 2020. Study on residual characteristics of mandipropamid and metalaxyl-M in Cnidium officinale Makino [J]. The Korean Journal of Pesticide Science, 2020, 24(2), 172-179.
4. Fang, Q., Wu, R., Hu, G., et al., 2019. Dissipation behavior, residue distribution and risk assessment of three fungicides in pears [J]. J. Sci. Food Agric. 100(4).
5. Fan, S., Zhang, Z., Su, H., et al., 2020. Panax ginseng clinical trials: Current status and future perspectives [J]. Biomed. Pharmacother. 132, 110832.
6. Farha, W., Rahman, M.M., El-Aty, A.A., et al., 2016. Analysis of mandipropamid residual levels through systematic method optimization against the matrix complexity of sesame leaves using HPLC/UVD [J]. Biomed. Chromatogr. 30(7), 990-995.
7. He, Y., 2008. Mandipropamid; Department of Science and Education, Ministry of Agriculture, China [Online]. Available at: http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/lpe/lpe-m/en/
8. Kwon, C.H., Chang, M.I., Im, M.H., et al., 2008. Determination of mandipropamid residues in agricultural commodities using high-performance liquid chromatography with mass spectrometry [J]. Analytical Science & Technology 21(6), 518-525.
9. Liu, D., Wang, X.M., Hou, Z.G., et al., 2016. Toxicological test and field efficacy of fungicides to Pseudoperonospora cubensis [J]. Agrochemicals 55(05), 377-379+386.
10. Malhat, F.M., Abdallah, H., 2012. Dissipation and residues of mandipropamid in grape using QuEChERS methodology and HPLC-DAD [J]. Isrn Analytical Chemistry 2012(1), 5.
11. Ministry of Agriculture and Rural Affairs of the People's Republic of China, NY/788-2018 Guideline for the testing of pesticide residues in corps [Z]. 2018.
12. National Health Commission of the People's Republic of China, National food safety standard—Maximum residue limits for pesticides in food: GB 2763-2019 [S]. 2019.
13. Park, T.Y., Hong, M., Sung, H., et al., 2017. Effect of Korean red ginseng in chronic liver disease [J]. J. Ginseng Res. 2017, 41(4), 450-455.
14. Vargas-Pérez, M., González, F.J.E., Frenich, A. G., 2020. Dissipation and residue determination of fluopyram and its metabolites in greenhouse crops [J]. Journal of the. Science of. Food and Agriculture. 2020, 100(13).
15. Siegenthaler, T.B., Hansen, Z., 2021. Sensitivity of Phytophthora capsici from Tennessee to mefenoxam, fluopicolide, oxathiapiprolin, dimethomorph, mandipropamid, and cyazofamid [J]. Plant Dis. https://doi.org/10.1094/PDIS-08-20-1805-RE.
16. Tang, Z.-H., Wang, et al., 2011. Baseline and differential sensitivity to mandipropamid among isolates of Peronosphythora litchii, the causal agent of downy blight on litchi[J]. Crop Protection Guildford, 2011, 3: 354-359.
17. Xu, G., Jia, X., Zhang, H., et al., 2020. Enantioselective fate of mandipropamid in grape and during processing of grape wine [J]. Environ. Sci. Pollut. Res. 27(32), 40148-40155.
18. Yang, S.H., Lee, J.I., Choi, H., 2020. Dissipation characteristics of mandipropamid and thiamethoxam for establishment of pre-harvest residue limits in lettuce [J]. J. Appl. Biol. Chem. 63(3), 267-274.
19. Zhang, B., Zhao, W., Zhang, Y. L., et al., 2015. Control effect of five kinds of preparations and combinations of cucumber downy mildew and its evaluation [J]. Agrochemical, 2015,54(06), :456-457+468.
20. Hu, Zhang, H., Xiang, et al., 2014. Enantioselective determination of carboxyl acid amide fungicide mandipropamid in vegetables and fruits by chiral LC coupled with MS/MS [J]. J. Sep. Sci. 37(3), 211-218.

21. Zhang, N., Huang, X., Guo, Y.L., et al., 2021. Evaluation of storage period of fresh ginseng for quality improvement of dried and red processed varieties [J]. J. Ginseng Res. https://doi.org/10.1016/j.jgr.2021.06.007.

Figures

![Figure 1](image)

**Figure 1**

The degradation dynamics curve of mandipropamid in ginseng plant
Figure 2

The degradation dynamics curve of mandipropamid in ginseng soil