Establishment of Toxicity and Susceptibility Baseline of Broflanilide for Aphis gossypii Glove

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Simple Summary: The control of Aphis gossypii has relied on the application of insecticides, but the resistance to insecticides has become a key factor in the successful management of A. gossypii. It is a critical measure to introduce a novel insecticide with a different action mode in the resistance management. We found that broflanilide has high insecticidal activity against A. gossypii. Broflanilide susceptibility was determined in field populations of A. gossypii from main cotton planting areas of China. Meanwhile, the susceptible baseline of the cotton aphid to broflanilide was established. These results suggested that the cotton aphid possessed high susceptibility to broflanilide. The susceptible baseline provides a comparative basis for the future resistance monitoring in the management of cotton aphids.

Abstract: The Aphis gossypii is an important pest that can damage cotton plants and can cause a huge economic loss worldwide. Chemical control is a main method to manage this pest, but the cotton aphid resistance to insecticides has become a severe problem in the management of the cotton aphid. It is important to introduce a novel insecticide for rotational application with other insecticides. Broflanilide, as a meta-diamide insecticide with a special mode of action, showed high efficiency against lepidopterous larvae. However, we found that broflanilide possessed high insecticidal activity against the sap-sucking pest A. gossypii. The susceptibility of A. gossypii to broflanilide from 20 field populations in main cotton planting areas of China in 2021 was determined by the leaf-dipping method. LC50 values of broflanilide to A. gossypii ranged from 0.20 µg mL⁻¹ to 1.48 µg mL⁻¹. The susceptible baseline of A. gossypii to broflanilide was established with the LC50 value of 0.41 µg mL⁻¹ and might be used to calculate the resistance ratio (RR) of cotton aphid population in broflanilide resistance monitoring. The RR value of field populations in China was from 0.49 to 3.61 in 2021. It suggested that the broflanilide may be a potential agent in the resistance management of A. gossypii to insecticides. These results are significantly useful for the rational chemical control of cotton aphids.

Keywords: Aphis gossypii; broflanilide; susceptibility baseline; resistance monitoring

1. Introduction

Broflanilide is a novel insecticide with a typical meta-diamide [3-benzamido-N-(4-(perfluoro propane-2-yl) phenyl) benzamide] structure. It is categorized as a member of a new group (Group 30) by the Insecticide Resistance Action Committee (IRAC) [1]. Broflanilide is metabolized to the active desmethyl-broflanilid in insect pests, which is a noncompetitive antagonist to act on the third transmembrane domain of γ-aminobutyric acid receptor (GABAR) [2,3]. Broflanilide was effective against larvae of Lepidoptera and Coleoptera, thrips and sanitary pests, as well as Myzus persicae (Hemiptera: Aphididae) and Aphis fabae (Hemiptera: Aphididae) [4–8]. Broflanilide has exhibited low toxicity to the major natural enemy Cyrtorhinus lividipennis (Hemiptera: Miridae) in paddy fields [9].
found that broflanilide possessed high activity against *A. gossypii*, which has developed very high resistance to neonicotinoid and pyrethroid insecticides in China [10–13].

The cotton aphid, *A. gossypii* Glover (Hemiptera: Aphididae), is a sap-sucking pest that threatens a wide range of crops, including pepper, tomato, eggplant, watermelon, cucumber, squash, pumpkin, citrus fruit, potato, and cotton [14]. It can damage the hosts by direct sap-feeding plant tissue nutrition and indirectly through the transmission of plant pathogens [15]. The control of cotton aphids is largely dependent on the use of insecticides. The cotton aphid has evolved high level of resistance to many insecticides, including organophosphates [10,16], carbamates [17], pyrethroids [11], and neonicotinoids [18,19], because of their continuous use for a long time.

Organophosphates and carbamates were widely used to control cotton aphids in 1960s–1980s in China, but the cotton aphid evolved 23 and 148 fold resistance to two organophosphate insecticides, parathion and demeton, in North China in 1964 [20]. The resistance of cotton aphids to omethoate increased to 60–80 times in four regions of Shandong province in 2004 compared with 22–37 times in 1985 [17]. The cotton aphid resistance to omethoate in six areas of Xinjiang reached 2137–9501 fold in 2018 [21]. In 1999, the cotton aphid evolved 18–34 times resistance to a carbamate insecticide, carbosulfan, in Shandong province [17]; however, the resistance of the cotton aphid from Xinjiang reached 148.0 times in 2018 [21]. Pyrethroid insecticides were used for the control of cotton aphids since the mid-1980s, but the resistance of the cotton aphid to pyrethroids was rapidly detected [20]. In 1985, the cotton aphid developed 3228 and 241 fold resistance to deltamethrin and fenvalerate [20]; by 2013, the field populations of the cotton aphid evolved more than 1000 times resistance to beta-cypermethrin in China [11]. In 2018, the cotton aphid developed 353–4932 times resistance to beta-cypermethrin in cotton fields of Xinjiang [21]. At present, neonicotinoid insecticides are widely applied for the control of cotton aphids; however, *A. gossypii* also evolved high resistance to neonicotinoids including imidacloprid, acetamiprid, and thiamethoxam, and the resistance ratio reached more than 471.2-fold in Shandong and Shanxi provinces and the field population in Xinjiang developed 1095 times resistance [21,22].

The insecticide resistance has become a critical problem for the successful management of cotton aphids. The application of the insecticides with new structural types is one of the important measures for the control of *A. gossypii* and resistance management in fields. The broflanilide displayed a high efficiency against 20 field populations of the cotton aphid in 2021. We established the susceptible baseline of *A. gossypii* to broflanilide as a reference for future resistance monitoring.

2. Materials and Methods

2.1. Insects

The field populations of *A. gossypii* were collected from 20 main cotton planting areas of China from July to September in 2021. More than 2000 apterous aphids were randomly collected according to a five-point sampling method from 20–30 cotton plants at each sample site to ensure that the samples were representative. The information and geographic distribution of the field populations collecting information are shown in Figure 1 and Table 1. Neonicotinoids (imidacloprid, acetamiprid, and thiamethoxam), pyrethroids (beta-cypermethrin and deltamethrin), and a sulfoximine insecticide (sulfoxaflor) have been used in these regions for the control of cotton aphid. These cotton aphid populations were transferred to the laboratory and reared on cotton seedlings (*Gossypium hirsutum* L. var. Xinmian No. 1) without pesticide exposure. All field populations were reared in insectaria under the controlled conditions with 22 ± 1 °C, 60–70% of relative humidity, and 16:8 h (L:D) of photoperiod. The aphid populations were raised for at least 3 generations in the insectaria and used for subsequent experiments.
Figure 1. Geographical distribution of Aphis gossypii samples in China.

2.2. Chemicals

Broflanilide was obtained from Badische Anilin-und-Soda-Fabrik (BASF, Beijing, China) with 98% purity. Analytical grade acetone (>99.5% purity) and agar strips (>99% purity) were purchased from Sinopharm Chemical Reagent Co., Ltd. (Beijing, China), and Triton X-100 was obtained from Sigma-Aldrich Co. (Saint Louis, MO, USA).

2.3. Toxicity Bioassays

The toxicity of broflanilide to the cotton aphid was determined by the leaf-dipping method as previously described [23] with slight modifications. We used a two-step dilution method. First, the stock solution of broflanilide (5000 μg mL⁻¹) was prepared with acetone for easy dilution with water. The desired concentrations (0, 0.1, 0.2, 0.4, 0.8, 1.6, 6.4, 10.0 μg mL⁻¹) were obtained by diluting the above stock solution with the distilled water with 0.05% triton-X 100 before bioassay. Fresh cotton leaves were cut into 21 mm-diameter leaf discs with punch, and then these leaf discs were immersed in the above diluted solutions for 15 s. The leaf discs only treated with 0.05% (v/v) Triton-X 100 water were used as the corresponding control. The treated leaf discs were placed indoors to dry, and then the dried leaf discs were put into 12-well cell plates that contained 2.5 mL of 1.85%
(w/v) agar. Healthy apterous adult aphids were gently transferred into 12-well cell plates from cotton seedlings using a soft small brush, and then the plate was sealed with Chinese art paper to prevent aphids from escaping, three replicates per concentration and at least 25 aphids in each well. The 12-well cell plates were placed under the same condition as the aphid culture. The number of live and dead aphids was scored after 72 h exposure. The aphid was considered dead if it could not move by the touch of a soft small brush.

Table 1. Information of *Aphis gossypii* field populations used for bioassay in China.

| Populations | Location (City, Province) | Longitude and Latitude | Collecting Date   |
|-------------|---------------------------|-----------------------|-------------------|
| CZ          | Cangzhou, Hebei           | 116.87° E, 38.31° N   | 3 September 2021  |
| HS          | Hengshui, Hebei           | 115.58° E, 37.55° N   | 21 July 2021      |
| NF          | Kaifeng, Henan            | 114.35° E, 34.79° N   | 10 September 2021 |
| NY          | Nanyang, Henan            | 112.54° E, 33.00° N   | 2 September 2021  |
| BZ          | Binzhou, Shandong         | 118.02° E, 37.43° N   | 6 August 2021     |
| YC          | Yuncheng, Shanxi          | 111.00° E, 35.02° N   | 5 August 2021     |
| KEL         | Kuerle, Xinjiang          | 86.39° E, 40.59° N    | 30 July 2021      |
| ALE10       | Alaer10, Xinjiang         | 81.24° E, 40.56° N    | 30 July 2021      |
| ALE16       | Alaer16, Xinjiang         | 80.84° E, 40.50° N    | 30 July 2021      |
| BL          | Bole, Xinjiang            | 82.05° E, 44.85° N    | 13 July 2021      |
| CA          | Changji, Xinjiang         | 87.31° E, 44.01° N    | 13 July 2021      |
| KC          | Kuche, Xinjiang           | 83.05° E, 42.08° N    | 30 July 2021      |
| KT          | Kuitun, Xinjiang          | 84.90° E, 44.43° N    | 13 July 2021      |
| SW          | Shawan, Xinjiang          | 85.62° E, 44.33° N    | 13 July 2021      |
| SY          | Shaya, Xinjiang           | 82.92° E, 41.25° N    | 30 July 2021      |
| SHZ         | Shihzei, Xinjiang         | 86.08° E, 44.31° N    | 13 July 2021      |
| TMSK        | Tumushuke, Xinjiang       | 79.21° E, 40.00° N    | 30 July 2021      |
| TLF         | Tulufan, Xinjiang         | 89.19° E, 42.94° N    | 17 September 2021 |
| WS          | Wusu, Xinjiang            | 84.68° E, 44.44° N    | 13 July 2021      |
| YL          | Yili, Xinjiang            | 81.32° E, 43.92° N    | 17 September 2021 |

2.4. Data Analysis

Probit analysis was used to calculate the slope of the regress curve, LC\(_{50}\) and LC\(_{90}\), and 95% confidence limits by POLO Plus 2.0 software [24], and the Chi-square (χ\(^2\)) values and degrees of freedom (df) were obtained from this software. The p-value was calculated by the CHIDIST function of Excel 2019 using Chi-square values and degrees of freedom.

The bioassay data of all aphid populations were pooled for the establishment of the susceptible baseline of *A. gossypii* to broflanilide, and the susceptible baseline was used to calculate the resistance ratio by LC\(_{50}\) of field population/susceptible baseline.

3. Results

3.1. The Toxicity of Broflanilide to Field Populations of *Aphis gossypii*

Broflanilide exhibited high toxicity against all field populations of *A. gossypii* with LC\(_{50}\) values of 0.20–1.48 µg mL\(^{-1}\) and LC\(_{90}\) values of 0.70–4.90 µg mL\(^{-1}\) (Table 2). The slope ranged from 1.24 ± 0.12 to 6.59 ± 1.10 for field populations of *A. gossypii* (Table 2). It suggested that there was higher susceptible consistency among individuals of cotton aphid population. The ALE10 population was the most susceptible to broflanilide with the LC\(_{50}\) value of 0.20 µg mL\(^{-1}\), and the population with the largest LC\(_{50}\) value was from KC, LC\(_{50}\) value of 1.48 µg mL\(^{-1}\). The difference of LC\(_{50}\) values between ALE10 and KC populations was 7.4 times.

3.2. Susceptible Baseline of *Aphis gossypii* to Broflanilide

The curve of dose-mortality that was used to calculate the susceptible baseline of *A. gossypii* to broflanilide showed an S-shaped distribution (Figure 2A). The toxicity regression analysis showed the R\(^2\) = 0.96 (p < 0.001) and slope =1.86 (Figure 2B), which indicated a high linear relationship between concentration logarithm and mortality probability value.
Table 2. Toxicity of broflanilide to *Aphis gossypii* field populations.

| Populations | Slope ± SE a | LC50 (95%CL) b µg mL⁻¹ | RR c | LC90 (95%CL) b µg mL⁻¹ | χ²(df) d | p Value |
|-------------|--------------|-------------------------|------|-------------------------|----------|---------|
| ALE10       | 1.58 ± 0.20  | 0.20 (0.09–0.32)        | 0.49 | 1.28 (0.87–2.13)        | 16.03 (12) | 0.19    |
| ALE16       | 1.24 ± 0.12  | 0.44 (0.28–0.66)        | 1.07 | 4.77 (2.95–9.21)        | 14.04 (12) | 0.30    |
| BL          | 1.91 ± 0.20  | 0.45 (0.30–0.62)        | 1.10 | 2.13 (1.57–3.16)        | 17.74 (14) | 0.22    |
| BZ          | 3.02 ± 0.33  | 0.76 (0.60–0.92)        | 1.85 | 2.02 (1.64–2.69)        | 18.41 (16) | 0.30    |
| CJ          | 2.90 ± 0.37  | 0.51 (0.38–0.63)        | 1.24 | 1.41 (1.15–1.84)        | 12.01 (16) | 0.74    |
| CZ          | 2.42 ± 0.25  | 0.37 (0.27–0.46)        | 0.90 | 1.25 (0.97–1.75)        | 14.25 (12) | 0.29    |
| HS          | 4.46 ± 0.69  | 0.36 (0.26–0.45)        | 0.88 | 0.70 (0.56–0.90)        | 15.72 (16) | 0.47    |
| KC          | 2.47 ± 0.42  | 1.48 (0.97–1.96)        | 3.61 | 4.90 (3.60–8.30)        | 14.35 (14) | 0.42    |
| KEL         | 4.37 ± 0.75  | 0.55 (0.45–0.64)        | 1.34 | 1.09 (0.91–1.46)        | 11.56 (12) | 0.48    |
| KY          | 1.71 ± 0.23  | 0.25 (0.12–0.40)        | 0.61 | 1.40 (0.88–3.00)        | 15.31 (10) | 0.12    |
| KT          | 3.92 ± 0.47  | 1.10 (0.89–1.30)        | 2.68 | 2.34 (1.94–3.04)        | 15.21 (14) | 0.36    |
| NY          | 2.74 ± 0.46  | 0.46 (0.27–0.63)        | 1.12 | 1.35 (1.00–2.10)        | 16.03 (14) | 0.31    |
| SHZ         | 2.19 ± 0.49  | 0.68 (0.14–1.12)        | 1.66 | 2.61 (1.78–5.05)        | 18.47 (13) | 0.14    |
| SW          | 6.56 ± 1.10  | 0.89 (0.74–1.01)        | 2.17 | 1.39 (1.20–1.80)        | 14.93 (13) | 0.31    |
| SY          | 1.97 ± 0.38  | 0.42 (0.14–0.65)        | 1.02 | 1.90 (1.31–4.12)        | 18.96 (13) | 0.12    |
| TLF         | 2.02 ± 0.26  | 0.34 (0.23–0.44)        | 0.83 | 1.45 (1.11–2.08)        | 10.64 (13) | 0.64    |
| TMSK        | 3.21 ± 0.70  | 0.67 (0.31–0.89)        | 1.63 | 1.67 (1.30–2.81)        | 15.62 (12) | 0.21    |
| WS          | 2.08 ± 0.34  | 0.60 (0.32–0.86)        | 1.46 | 2.47 (1.88–3.42)        | 10.15 (13) | 0.68    |
| YC          | 2.37 ± 0.33  | 0.41 (0.24–0.57)        | 1.00 | 1.42 (1.05–2.14)        | 17.94 (15) | 0.27    |
| YL          | 3.69 ± 0.57  | 0.43 (0.31–0.53)        | 1.05 | 0.95 (0.78–1.22)        | 7.96 (13)  | 0.85    |
| SBL c       | 2.12 ± 0.08  | 0.41 (0.37–0.44)        | 1.00 | 1.63 (1.52–1.78)        | 168.12 (174) | 0.61  |

a SE, Standard Error. b CL, 95%, Confidence Limits of 95%. c RR, Resistance Ratio = LC50 of filed populations/susceptible baseline. d χ²(df), Chi-square (χ²) and degrees of freedom (df). e SBL, Susceptible Baseline of *Aphis gossypii* to broflanilide.

Figure 2. The dose-mortality curve and toxicity regression of broflanilide against cotton aphids. (A): The dose-mortality curve of broflanilide to *Aphis gossypii*. The concentration logarithm as X-axis and mortality as Y-axis. (B): The toxicity regression curve of broflanilide to *Aphis gossypii*. The concentration logarithm as X-axis and mortality probability value as Y-axis. The correlation coefficient is 0.96 (p < 0.001).

We established that the susceptible baseline of *A. gossypii* to broflanilide for the LC₅₀ value of 0.41 µg mL⁻¹, and the LC₉₀ was 1.63 µg mL⁻¹ and slope was 2.12 ± 0.08 (Table 2). The susceptible baseline was used to calculate the resistance ratio (RR) of cotton aphid populations to broflanilide. All field populations in 2021 were susceptible to broflanilide, and the RR ranged from 0.49 to 3.61.

4. Discussion

The application of chemical insecticides is an indispensable measure in the practice of cotton pest management. The resistance of cotton aphids to traditional insecticides (organophosphorus, carbamate, pyrethroid, and neonicotinoid insecticides) has become a constraint in the control of cotton aphids [10,13,19]. It is an essential way for pest management to rotate application among different action modes of insecticides.
Broflanilide has a novel mode of action, classified as a new member of group 30 (mode of action: GABA-gated chloride channel allosteric modulator) [1,25]. As an antagonist of GABAR, broflanilide exhibited high biological activity against various insect species such as Helicoverpa armigera (Lepidoptera: Noctuidae), Spodoptera exigua (Lepidoptera: Noctuidae) [26], Spodoptera Litura (Lepidoptera: Noctuidae) [27], and Anopheles arabiensis (Diptera: Culicidae) [28], which also seriously affected the growth and development of some pests [29,30]. Interestingly, broflanilide possessed low toxicity to some natural enemies such as C. lividipennis and Typhlodromips swirskii (Acari: Phytoseiidae) and have low residue in the environment [9,31,32].

In this study, broflanilide showed high biological activity to A. gossypii with the LC$_{50}$ values ranging from 0.20 to 1.48 µg mL$^{-1}$ for all field populations in cotton production areas of China. Broflanilide has similar toxicity to A. fabae and Mythimna separata (Lepidoptera: Noctuidae) with the LC$_{50}$ of 0.15 µg mL$^{-1}$ and 0.64 µg mL$^{-1}$, respectively [7]. Xu et al. (2020) determined that broflanilide at 10 µg mL$^{-1}$ could result in 100% mortality of the M. persicae, and the LC$_{50}$ values of broflanilide against the Plutella xylostella (Lepidoptera: Plutellidae), S. exigua, and Chilo suppressalis (Lepidoptera: Crambidae) were only 0.13, 0.92, and 1.23 µg mL$^{-1}$, respectively [8]. Tang et al. (2021) determined the susceptibility of H. armigera and S. exigua collected from Hunan province to broflanilide, and the LC$_{50}$ values were 0.038–0.068 µg mL$^{-1}$ and 0.039–0.087 µg mL$^{-1}$ [26]. The lethal activity of broflanilide against third-instar larvae and adults of S. litura were 0.13 mg kg$^{-1}$ (LD$_{50}$) and 3.59 µg mL$^{-1}$ (LC$_{50}$), respectively [27].

The susceptible baseline of broflanilide against A. gossypii was established by pooling the bioassay data of all field populations with the LC$_{50}$ of 0.41 µg mL$^{-1}$. According to research reports, LC$_{50}$ values of the susceptible baseline for A. gossypii were 0.50 µg mL$^{-1}$ for beta-cypermethrin and 1.1 µg mL$^{-1}$ for deltamethrin [11]. LC$_{50}$ values of sulfoxaflor and imidacloprid against the susceptible strain were 0.64 µg mL$^{-1}$ and 0.32 µg mL$^{-1}$, respectively [31,33]. Shi et al. (2022) also used the mean LC$_{50}$ value (0.149 µg mL$^{-1}$) of 16 field populations as the susceptible baseline of A. gossypii to afidopyropen [34]. Our results demonstrated that A. gossypii has a high susceptibility to broflanilide, which is similar to the susceptible baseline of the insecticides mentioned above.

A. gossypii has developed high resistance to some commonly used insecticides, such as pyrethroids and neonicotinoids [10–12]. Detoxifying enzymes including esterases and cytochrome P450 monoxygenases (P450) and point mutations in sodium channels have been demonstrated to contribute A. gossypii resistance to pyrethroids [11,35]. Both the enhancement of P450 activity and target mutations in the nicotinic acetylcholine receptors were involved in A. gossypii resistance to neonicotinoids [19,36]. Broflanilide, as a noncompetitive antagonist of targeting on GABAR, displayed high efficiency to field populations of A. gossypii, although A. gossypii has developed high resistance to pyrethroids and neonicotinoids in cotton fields. Similarly, A. arabiensis was susceptible to broflanilide, but it possessed high resistance to pyrethroids [28]. In addition, the P. xylostella has developed 1143-fold resistance to abamectin [37], and H. armigera evolved 20.36 and 39.12 fold resistance to chlorantraniliprole and benzoate, but broflanilide still showed high insecticidal activities against their larvae [26]. This indicated that broflanilide did not exhibit the cross-resistance with other insecticides mentioned above.

5. Conclusions

Broflanilide exhibited good biological activity against A. gossypii, which provides a potential alternative for the control of cotton aphids. These results are useful for the chemical control of A. gossypii in cotton fields.
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References

1. IRAC. Mode of Action Classification Scheme (Version 10.3, June 2022). Available online: http://www.irac-online.org (accessed on 7 September 2022).

2. Nakao, T.; Banba, S.; Nomura, M.; Hirase, K. Meta-diamide insecticides acting on distinct sites of RDL GABA receptor from those for conventional noncompetitive antagonists. Insect Biochem. Mol. Biol. 2013, 43, 366–375. [CrossRef] [PubMed]

3. Ozoe, Y.; Kita, T.; Ozoe, F.; Nakao, T.; Sato, K.; Hirase, K. Insecticidal 3-benzamido-N-phenylbenzamides specifically bind with high affinity to a novel allosteric site in house fly GABA receptors. Pestic. Biochem. Physiol. 2013, 107, 285–292. [CrossRef] [PubMed]

4. Bai, X.N.; Li, Y.S.; Yang, M.; Wang, Y.Y. New pesticides registered in China in 2020. Agrochemicals 2021, 60, 79–82.

5. Li, Y. Pesticide registration and new pesticides registered in China in 2020. World Pestic. 2021, 43, 10–15.

6. Ngufor, C.; Govoetchan, R.; Fongnikin, A.; Vigninou, E.; Syme, T.; Akogbeto, M.; Rowland, M. Efficacy of broflanilide (vectron T500), a new meta-diamide insecticide, for indoor residual spraying against pyrethroid-resistant malaria vectors. Sci. Rep. 2021, 11, 7976. [CrossRef]

7. Liu, A.P.; Huang, M.Z.; Wu, M.F.; Long, C.Y.; Wang, H.F.; Ren, Y.G.; Huang, Z.C.; Li, J.M.; Zhang, P.; Liu, X.P. Synthesis and biological activity of broflanilide. Fine Chem. Intermed. 2020, 50, 16–20.

8. Xu, J.B.; Liu, S.W.; Guo, C.X.; Xu, L.B.; Ban, L.F.; Wu, H.F. Synthesis and insecticidal activity of broflanilide. Agrochemicals 2020, 59, 11–14.

9. Xu, S.; Wu, Y.J.; Li, B.T.; Shi, X.G.; Xiong, Z.H. Toxicity of broflanilide on major rice pests and its influence on natural enemies in paddy fields. Acta Phytophylacica Sin. 2019, 46, 574–581.

10. An, J.J.; Gao, Z.L.; Dang, Z.H.; Zhao, Y.J.; Dou, Y.N.; Yan, X.; Hua, J.N.; Pan, W.L.; Guo, J.L.; Li, Y.F. Resistance dynamic of different Aphis gossypii populations in Hebei province to six insecticides. Chin. J. Pestic. Sci. 2021, 23, 1123–1131.

11. Chen, X.W.; Tie, M.Y.; Chen, A.Q.; Ma, K.S.; Li, F.; Liang, P.Z.; Liu, Y.; Song, D.L.; Gao, X.W. Pyrethroid resistance associated with M918L mutation and detoxifying metabolism in Aphis gossypii from Bt cotton growing regions of China. Pest Manag. Sci. 2017, 73, 2353–2359. [CrossRef]

12. Wang, Z.J.; Liang, C.R.; Shang, Z.Y.; Yu, Q.T.; Xue, C.B. Insecticide resistance and resistance mechanisms in the melon aphid, Aphis gossypii, in Shandong, China. Pestic. Biochem. Physiol. 2021, 172, 104768. [CrossRef] [PubMed]

13. Subbaratnam, G.V.; Radhika, P. Global view of insecticide resistance management in cotton aphid review. Pest Manag. Econ. Zool. 2005, 13, 163–183.

14. Somar, R.O.; Zamani, A.A.; Alizadeh, M. Joint action toxicity of imidacloprid and pymetrozine on the melon aphid, Aphis gossypii. Crop Prot. 2019, 124, 104850. [CrossRef]

15. Ebert, T.A.; Cartwright, B. Biology and ecology of Aphis gossypii Glover (Homoptera: Aphididae). Southwest. Entomol. 1997, 22, 116–153.

16. Fukuto, T.R. Mechanism of action of organophosphorous and carbamate insecticides. Environ. Health Perspect. 1990, 87, 245–254. [CrossRef] [PubMed]

17. Wang, K.Y.; Guo, Q.L.; Xia, X.M.; Wang, H.Y.; Liu, T.X. Resistance of Aphis gossypii (Homoptera: Aphididae) to selected insecticides on cotton from five production regions in Shandong, China. J. Pestic. Sci. 2007, 32, 372–378. [CrossRef]

18. Koo, H.N.; An, J.J.; Park, S.E.; Kim, J.I.; Kim, G.H. Regional susceptibilities to 12 insecticides of melon and cotton aphid, Aphis gossypii (Hemiptera: Aphididae) and a point mutation associated with imidacloprid resistance. Crop Prot. 2014, 55, 91–97. [CrossRef]
19. Bass, C.; Denholm, I.; Williamson, M.S.; Nauen, R. The global status of insect resistance to neonicotinoid insecticides. *Pestic. Biochem. Physiol.* 2015, 121, 76–87. [CrossRef]

20. Sun, Y.Q.; Feng, G.L.; Yuan, J.G.; Gong, K.Y. Insecticide resistance of cotton aphid in North China. *Entomol. Sin.* 1994, 1, 242–250. [CrossRef]

21. Patima, W.; Guo, P.P.; Ma, S.J.; Gao, X.W.; Zhang, L.J.; Zhang, S.; Ma, D.Y. Resistance of different field populations of *Aphis gossypii* to ten insecticides in Xinjiang. *Plant Prot.* 2019, 45, 273–278. [CrossRef] [PubMed]

22. Chen, X.; Tang, C.; Ma, K.; Xia, J.; Song, D.; Gao, X.W. Overexpression of multiple cytochrome P450 genes associated with sulfoxaflor resistance in *Aphis gossypii* Glover collected from Bt cotton fields in China. *Pest Manag. Sci.* 2020, 76, 1371–1377. [CrossRef] [PubMed]

23. Moores, G.D.; Gao, X.W.; Denholm, I.; Devonshire, A.L. Characterization of insensitive acetylcholinesterase in insecticide-resistant cotton aphids, *Aphis gossypii* Glover (Hemiptera: Aphididae). *Pestic. Biochem. Physiol.* 1996, 56, 102–110. [CrossRef]

24. LeOra. Polo-Plus, POLO for Windows LeOra Software. 2002. Available online: www.LeOra-Software.com (accessed on 17 January 2018).

25. Nakao, T.; Banba, S. Broflanilide: A meta-diamide insecticide with a novel mode of action. *Bioorg. Med. Chem.* 2016, 24, 372–377. [CrossRef] [PubMed]

26. Shi, D.D.; Liang, P.Z.; Zhang, L.; Lv, H.X.; Gao, X.W.; You, H.; Li, J.H.; Ma, K.S. Susceptibility baseline of *Spodoptera exigua* with sulfoxaflor resistance in *Aphis gossypii* Glover. *Crop Prot.* 2020, 124, 105017. [CrossRef]

27. Shen, N.; Liu, H.Y.; Mou, T.Y.; Ma, Y.B.; Li, Y.; Song, Z.J.; Tang, T.; Han, Z.J.; Zhao, C.Q. Novel meta-diamide insecticide, broflanilide, suppresses the population of common cutworm *Spodoptera litura* via its lethal and sublethal effects. *Pest Manag. Sci.* 2022, 78, 1081–1089. [CrossRef]

28. Snetselaar, J.; Rowland, M.W.; Manunda, B.J.; Kisengwa, E.M.; Small, G.J.; Malone, D.J.; Mosha, F.W.; Kirby, M.J. Efficacy of indoor residual spraying with broflanilide (tenebenal), a novel meta-diamide insecticide, against pyrethroid-resistant anopheline vectors in northern Tanzania: An experimental hut trial. *PLoS ONE* 2021, 16, e0248026. [CrossRef] [PubMed]

29. Jia, Z.Q.; Zhan, E.L.; Zhang, S.G.; Jones, A.K.; Zhu, L.; Wang, Y.N.; Huang, Q.T.; Han, Z.J.; Zhao, C.Q. Sublethal doses of broflanilide prevents molting in the fall armyworm, *Spodoptera frugiperda* via altering molting hormone biosynthesis. *Pestic. Biochem. Physiol.* 2022, 181, 105017. [CrossRef]

30. Jia, Z.Q.; Zhan, E.L.; Lian, S.G.; Wang, Y.; Song, P.P.; Jones, A.K.; Han, Z.J.; Zhao, C.Q. Broflanilide prolongs the development of fall armyworm *Spodoptera frugiperda* by regulating biosynthesis of juvenile hormone. *Entomol. Gen.* 2022, 42, 761–769. [CrossRef]

31. Shen, N.; Li, Y.; Leviticus, K.; Chang, X.L.; Tang, T.; Cui, L.; Han, Z.J.; Zhao, C.Q. Effect of broflanilide on the phytophagous mite *Tetranychus urticae* and the predatory mite *Typhlodromips swirskii*. *Pest Manag. Sci.* 2021, 77, 2964–2970. [CrossRef]

32. Xie, G.; Zhou, W.W.; Jin, M.X.; Yu, A.L.; Rao, L.; Jia, H.R.; Luo, J.; He, Y.C.; Li, B.T. Residues analysis and dissipation dynamics of broflanilide in rice and its related environmental samples. *Int. J. Anal. Chem.* 2020, 14, 8845387. [CrossRef]

33. Ma, K.S.; Tang, Q.L.; Zhang, B.Z.; Liang, P.; Wang, B.M.; Gao, X.W. Overexpression of multiple cytochrome P450 genes associated with sulfoxaflor resistance in *Aphis gossypii* Glover. *Pestic. Biochem. Physiol.* 2019, 157, 204–210. [CrossRef] [PubMed]

34. Shi, D.D.; Liang, P.Z.; Zhang, L.; Lv, H.X.; Gao, X.W.; You, H.; Li, J.H.; Ma, K.S. Susceptibility baseline of *Aphis gossypii* Glover (Hemiptera: Aphididae) to the novel insecticide afidopyropen in China. *Crop Prot.* 2022, 151, 105834. [CrossRef]

35. Rinkevich, F.D.; Du, Y.Z.; Dong, K. Diversity and convergence of sodium channel mutations involved in resistance to pyrethroids. *Pestic. Biochem. Physiol.* 2013, 106, 93–100. [CrossRef] [PubMed]

36. Shi, X.G.; Zhu, Y.K.; Xia, X.M.; Qiao, K.; Wang, H.Y.; Wang, K.Y. The mutation in nicotinic acetylcholine receptor beta 1 subunit may confer resistance to imidacloprid in *Aphis gossypii* (Glover). *J. Food Agric. Environ.* 2012, 10, 1227–1230.

37. Sun, X.; Wei, R.; Li, L.H.; Zhu, B.; Liang, P.; Gao, X.W. Resistance and fitness costs in diamondback moths after selection using broflanilide, a novel meta-diamide insecticide. *Insect Sci.* 2022, 29, 188–198. [CrossRef]