Greenhouse and field evaluation of a novel HPPD-inhibiting herbicide, QYM201, for weed control in wheat

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QYM201, 1-(2-chloro-3-(3-cyclopropyl-5-hydroxy-1-methyl-1H-pyrazole-4-carbonyl)-6-(trifluoromethyl)phenyl)piperidin-2-one), is a newly developed HPPD- (4-hydroxyphenylpyruvate dioxygenase; EC 1.13.11.27) inhibiting herbicide for weed control. Experiments were carried out to determine the effect of QYM201 on weeds and its safety for wheat in the glasshouse and field. The results indicated that at doses of 90 and 135 g active ingredient (a.i.) ha\(^{-1}\), QYM201 was highly effective against both grass and broadleaf weeds, such as *Alopecurus aequalis* Sobol., *Alopecurus japonicus* Steud., and *Capsella bursa-pastoris* Medic. In a wheat hybrid tolerance experiment, QYM201 showed a high level of safety for most of the 17 tested wheat hybrids, and the SI values reached ≥5.7 in the selectivity index study. To determine application rules for QYM201, field experiments were conducted in 2016 and 2017. During this time, 90 to 270 g a.i. ha\(^{-1}\) post-emergence herbicide application (POST) was sufficient to supply satisfactory all-season control of *Alopecurus aequalis* Sobol., *Descurainia sophia* [L.] Schur., and *Malachium aquaticum* (L.) Fires. No damage to wheat plants was observed. In order to increase wheat yield and deliver effective weed control, a dosage of 90 to 180 g a.i. ha\(^{-1}\) is suggested. In conclusion, the herbicide QYM201 is safe to use in wheat fields to control winter weeds.

Winter wheat (*Triticum aestivum* L.) is the second most widely grown food crop in China, with a planting area of 24.1 million hectares and a production of 130.2 million tons in 2015\(^1\). Severe wheat yield losses can be caused by weeds with potential reductions up to 15%\(^2,3\). *Alopecurus japonicus* Steud., *Beckmannia syzigachne* [Steud.] Fern., *Alopecurus aequalis* Sobol., *Vicia sativa* L, *Capsella bursa-pastoris* Medic., *Descurainia sophia* [L.] Schur., and *Avena fatua* L are examples of common troublesome weeds in winter wheat fields\(^4\). Substantial yield reduction takes place when these weeds are not fully controlled.

Herbicides have been used for weed control in China since the early 1990s\(^5\); nowadays, chemical weed control still has an important role in producing high-yielding crops\(^6\). Herbicides with different modes of action can kill 90% to 99% of target weeds and are the most useful means of weed control developed\(^7–9\); however, this is not problem free. One case study reveals that more than 252 weed species have developed resistance to 23 different herbicides worldwide\(^10\). In China, almost 30 weed species have developed resistance to nearly 50 herbicides with more than 10 different sites of action so far\(^11\). Most recently, Zhu *et al.* reported that at least 12 weed species have been confirmed resistant to the main herbicides commonly used in wheat fields\(^11\). Specifically, in Jiangsu and Anhui provinces of China, *A. japonicus*, a widespread troublesome weed, has developed resistance to about 20 herbicides. These 20 herbicides include not only Acetyl-CoA carboxylase (ACCase) herbicides such as fenoxyprop-P-ethyl, pinoxaden, clodinafop-propargyl, and sethoxydim, but also include Acetolactate synthase (ALS) herbicides: pyribenoxim, imazapic, imazosulfuron, sulfosulfuron, penoxsulam, and pyroxasulfam\(^12\). Another problem is that some herbicides have a narrow weed spectrum and occasionally can cause damage to wheat plants; for example, Fluroxypyr is effective in controlling some broadleaf weeds but is ineffective against *C. bursa-pastoris* (L.) Medic. Mesosulfuron plus iodosulfuron can kill most weed species but sometimes damage wheat plants. Hence, the widespread use of Mesosulfuron and iodosulfuron has been limited in China. In another example, 2, 4-D butyl ester has become a commonly used herbicide in wheat fields for controlling broadleaf weeds in China, but it can cause damage to broadleaf crops due to spray drift and volatilization; this is particularly relevant with cotton\(^13,14\). In addition to the problems described above, extensive use of herbicides can also...
lead to an accelerated succession of weed communities. Therefore, herbicides with a new site of action, that have broad-spectrum weed control, high efficacy, and are safe to use on wheat are urgently needed.

QYM201, \(\text{C}_{20}\text{H}_{19}\text{ClF}_{3}\text{N}_{3}\text{O}_{3}\text{,} 1-(2\text{-chloro-3-(3-cyclopropyl-5-hydroxy-1-methyl-1H-pyrazole-4-carbonyl)-6-}
\text{(trifluoromethyl)phenyl)piperidin-2-one; Fig. 1),}\) is a novel HPPD-inhibiting herbicide that was developed by Qingdao Kingagroot Chemicals Co., Ltd. in 2011\(^{15}\). 4-hydroxyphenylpyruvate dioxygenase (HPPD) is a class of \(\alpha\)-keto acid-dependent non-heme iron (II) oxygenases which can be found in mammals, plants, and most microbes. HPPD catalyzes oxygenation of 4-hydroxyphenylpyruvate (HPP) to generate homogentisate (HG)\(^{16-19}\). The biosynthesis of prenylquinone and tocopherols is prevented once HPPD is inhibited in plants, which leads to a decrease in carotenoid biosynthesis, blocking of photosynthetic electron transfer chains, and photooxidation of chloroplasts\(^{20,21}\). Consequently, treated plants become bleached to death\(^{21}\). Therefore HPPD is selected as a target for herbicide development. To our knowledge, HPPD inhibitors have not been used in wheat fields anywhere in the world. Therefore, we suggest that QYM201 is a potentially beneficial herbicide for weed control, especially for resistant and harmful weeds in wheat fields.

In order to determine the spectrum of weed control, the safety to different wheat hybrids, and the selectivity of QYM201 among 3 commonly planted wheat hybrids and 4 common weeds, experiments were carried out in the greenhouse. In addition, field experiments were conducted to determine the effect of QYM201 on weed control in winter wheat fields with different rates of 6% QYM201 oil dispersion (OD) during the 2015–2016 and 2016–2017 growing seasons in Shandong province.

**Results**

**Greenhouse experiments.** Effectiveness of weed control. At all rates of application, QYM201 was effective on many of the tested weed species including grass weeds and broadleaf weeds. Treated weeds exhibited symptoms of bleach injury at 5 days after treatment (DAT), eventually undergoing necrosis and death at 20 DAT. At the dosage of 90 g a.i. ha\(^{-1}\), QYM201 was highly effective against 3 of the treated weeds, and dry weight inhibition of \(\text{A. aequalis, M. aquaticum, and D. sophia.}\) were up to 93, 91, and 92, respectively. Meanwhile dry weight inhibition of \(\text{A. japonicus, and L. arvense were 86 and 87, respectively.}\) Weed injury increased according to application rate - higher rates leading to greater injury. At a dosage of 135 g a.i. ha\(^{-1}\), 8 of the treated weeds were controlled by QYM201, with dry weight reductions ranging from 91% to 95% these weeds included \(\text{A. aequalis, A. japonicus, C. bursa-pastoris, M. aquaticum, V. didyma, P. kengiana, L. arvense, and D. sophia (Table 1).}\) However, even at high doses some weed species, such as \(\text{L. multiflorum, B. japonicus, A. squarrosa, and E. helioscopa,}\) showed only slight sensitivity to QYM201 with dry weight reductions of 21%, 23%, 20%, and 19%, respectively.

![Diagram of the chemical structure of QYM201](image.png)

**Chemical structure of the herbicide QYM201 used in this study.**

Wheat hybrid tolerance. QYM201 was safe for most of the treated wheat in the greenhouse experiment. When treated at 360 g a.i. ha\(^{-1}\), most of the tested wheat hybrids were tolerant to QYM201 with reductions of <7% and herbicide damage <20% (Table 2). However, Huamai 5, Yangfumai 4, and Yangmai 158 were sensitive to QYM201, showing dry weight reductions of 13, 12, and 17%, respectively. The damage caused by QYM201 to these 3 hybrids ranging from 12% to 17% (Table 2). Wheat hybrids Zhengmai 10, Hengguan 35, Haomai 1, and Xinong 979 became sensitive to QYM201 with dry weights inhibited by beyond 10%, while crop injury caused by the herbicide was up to 28% at a dose of 540 g a.i. ha\(^{-1}\) (Table 2). Meanwhile, there were obvious differences in sensitivity to QYM201 among the wheat hybrids. Most hybrids showed little if any reaction to the herbicide; Shannong 22, Jinan 17, Shannong 19, Zhengmai 9023, Yannong 19, Ningmai 24, Jimai 22, Liangxing 66, and Tainong 18 exhibited no obvious damage, and reductions in plant dry weights were <10%, with herbicide damage <20%. At the beginning of the treatment, some wheat plants showed some symptoms of whitening at 5 DAT, but subsequently all of them regained a normal appearance at approximately 12 DAT (Table 2).

**Selectivity index (SI).** In view of the wheat hybrid tolerance results, a dose-response study was performed to determine the SI values between 3 wheat hybrids (JM 22, LX 66, TN 18) and 4 weed species (\(\text{A. aequalis, A. japonicus, C. bursa-pastoris, and M. aquaticum.}\) GR\(_{50}\) values of the 3 wheat hybrids were 28.1, 58.9, 40.5, and 24.9, respectively (Table 3). The high GR\(_{50}\) values clearly indicated that QYM201 was safe for the 3 tested wheat hybrids and that the 4 weed species were also effectively controlled (Table 3). In addition, experimental results showed that \(\text{A. aequalis and M. aquaticum}\)
growing within 15 days after treatment (DAT). When treated at doses of 90–270 g a.i. ha\(^{-1}\), A. aequalis, A. japonicus and C. bursa-pastoris were more sensitive to QYM201 under post emergence herbicide applications (POST) than A. japonicus and C. bursa-pastoris (Table 3, Fig. 2). SI values from Table 3 indicate that QYM201 was safe for JM 22, LX 66, and TN 18 against weeds tested in this study with values ranging from 5.7 to 16.6.

**Field experiment.** Throughout the 2 years of field experiments, QYM201 performed with good efficacy against A. aequalis, D. sophia, and M. aquaticum (Table 4). The 3 weed species began turning white and stopped growing within 15 days after treatment (DAT). When treated at doses of 90–270 g a.i. ha\(^{-1}\), all weed densities decreased; moreover, control over A. aequalis, D. sophia, and M. aquaticum to levels of 90.6% to 100% was achieved in 45 DAT. Just as speculated, fenoxaprop-P-ethyl had almost no effect on M. aquaticum to levels of 90.6% to 100% was decreased; moreover, control over A. aequalis, D. sophia

Table 1. Dry weight inhibitions of trial weeds treated with QYM201 relative to the non-treated control in a greenhouse study 28 days after treatment (DAT). *Significant differences between the 2 rates at the 0.05 level according to Fisher’s protected LSD test. **Significant at P < 0.01; ***significant at P < 0.001; NS, not significant.

| Trial weeds                                      | Dry weight inhibition (SE) g a.i. ha\(^{-1}\) | F-statistic | P-value |
|-------------------------------------------------|---------------------------------------------|-------------|---------|
|                                                 | 90%                                         | 135%        |         |
| A. aequalis Seh. (Water foxtail)                 | 93 (0.4)                                    | 94 (0.3)    | NS      | 2.63 | 0.247 |
| A. japonicus Steud. (Japanese foxtail)           | 86 (0.2)                                    | 91 (0.5)**  | 485.04  | 0.002 |
| C. bursa-pastoris Medic (Shepherd’s purse)       | 85 (0.1)                                    | 91 (0.3)**  | 462.36  | 0.002 |
| M. aquaticum (L.) Fires (Crickweed)              | 91 (0.1)                                    | 94 (0.4)*   | 45.14   | 0.021 |
| V. didyma Tenore (Speedwell)                     | 86 (0.3)                                    | 91 (0.4)*   | 34.26   | 0.028 |
| B. szyszycznica Steud. Fern. (American slough grass) | 80 (0.2)                                    | 83 (0.0)**  | 181.21  | 0.006 |
| P. ochroleuca kengiana (Ohwi) (Hardgrass)       | 85 (0.1)                                    | 91 (0.6)*   | 46.13   | 0.021 |
| P. annua L. (Annual bluegrass)                   | 12 (0.7)                                    | 27 (0.7)*   | 60.32   | 0.016 |
| L. arvensis L. (Corns gromwell)                  | 87 (0.3)                                    | 93 (0.4)*   | 80.11   | 0.012 |
| D. sophia (L.) Scol. (Flaxweed)                 | 92 (0.0)                                    | 95 (0.2)**  | 646.02  | 0.002 |
| G. sibiricum L. Carolina cranebill herb          | 45 (0.6)                                    | 52 (0.8)    | NS      | 10.19 | 0.086 |
| C. arvense L. var. leersum (Gren. et Godr.) Rebb. (Catchweed) | 27 (0.2)                                    | 36 (0.6)*   | 52.92   | 0.018 |
| L. multiflorum Lam. (Italian ryegrass)           | 13 (0.1)                                    | 21 (1.0)*   | 30.74   | 0.031 |
| B. japonicus Thumb. (Japanese brome)             | 19 (0.2)                                    | 23 (0.7)*   | 28.96   | 0.033 |
| A. squarrosa L. Triticum tauschii               | 14 (0.1)                                    | 20 (1.0)*   | 26.49   | 0.036 |
| A. fatua L. (Wild oat)                          | 47 (0.7)                                    | 61 (1.0)**  | 531.37  | 0.002 |
| V. sativa L. (Vetch)                            | 44 (0.7)                                    | 53 (1.2)    | NS      | 6.74  | 0.122 |
| Euphorbia helioscopia L. (Sun spurge)            | 14 (1.0)                                    | 19 (1.4)**  | 160.45  | 0.006 |

The greenhouse bioassay results indicated that the weed control spectrum of QYM201 was broader than that of most commonly used herbicides in wheat fields; at all rates of application, QYM201 was able to control both grass weeds and broadleaf weeds. Post emergence applications of herbicides such as fluoroxypyr and tribenuron-methyl are highly efficient against a large number of broadleaf weeds but provide only limited control for grass weeds. Whereas fenoxaprop-P-ethyl and mesosulfuron-methyl are sufficiently effective against many grass weeds, they are not effective for broadleaf weeds. The ability of QYM201 to control both grass and broadleaf weeds may make it a preferred choice over any other ordinary herbicides for weed control in wheat fields. Importantly, we found that QYM201 was highly effective in its control of A. aequalis and A. japonicus, which are the most harmful weeds to wheat yield worldwide. The widespread application of herbicides has led to the rapid evolution of A. aequalis and A. japonicus herbicide tolerance throughout the world. In some areas of China, A. aequalis has developed resistance to ALS inhibitors and ACCase inhibitors, while A. japonicus has developed resistance to chlorosulfuron, fenoxaprop-P-ethyl, isoproturon, and/or to pinoxaden. Therefore, QYM201 will be helpful in controlling these resistant weeds. However, more attention should be given to preventing the development of resistance to QYM201.
development of resistance to QYM201, especially in *A. aequalis* or *A. japonicus*, by alternately using herbicides at different sites of action, promoting the diversity of crop cultivation, using biological controls, and the rational mixing of herbicides. However, the efficacy of QYM201 on a greater number of weed species that occur in wheat fields needs to be tested before recommendation of its widespread application.

In crop safety experiments, under all tested application rates, QYM201 was safe for most of the 17 tested hybrid wheat varieties. These results strongly suggested that QYM201 is an excellent alternative herbicide for controlling weeds in wheat fields. Moreover, the SI values were identified for JM22, LX66, TN18, and 4 common weeds that occur in wheat fields. It is well known that herbicides are more selective between crops and weeds when the SI value is greater than 1.0, and herbicides can be safely used in crops when the SI value increases over 2.0. In this study, we found that QYM201 was safe for JM22, LX66, and TN18 against *A. aequalis*, *A. japonicus*, *C. bursa-pastoris*, and *M. aquaticum* when POST was applied, with SI values from 5.7 to 16.6. However, the safety of QYM201 for use on other wheat hybrids should be assessed in further experiments in view of the complex distribution of wheat hybrids throughout different areas of China.

### Table 2.

Dry weight inhibitions (%) and visual injury ratings (%) of trial wheat hybrids treated with QYM201 as a POST relative to the non-treated control in a greenhouse study 28 days after treatment (DAT). *Significant differences between the 2 rates according to Fisher's protected LSD test. **Significant at P < 0.05; ***significant at P < 0.01; NS, not significant. Injury rating scale: 0% = no injury, 0~30% = cotyledon and a few functional leaves showed bleaching in addition to newly-emerged leaves, 30~60% = cotyledon, minority of functional leaves and newly-emerged leaves presented bleaching, 60~100% = most plants showed severe whitening symptoms and some even showed necrosis, 100% = plant death. ND, not determined.

| Trial plants | GR value (SE)a | SIb |
|--------------|---------------|-----|
|              | GR10 | GR50 | GR90 | JM 22 | LX 66 | TN 18 |
| Shannong 22  | 321.92 (0.3) | 0.003 | 10 (0.2) | 32 (1.0) | 366.57 | ND |
| Zhenmai 10   | 382.07 (0.2) | 0.003 | 2 (1.1) | 5 (0.8) | 4.99 | 0.155 |
| Jinan 17     | 21.29 (0.1) | 0.003 | 14 (0.7) | 30 (0.9) | 67.92 | 0.014 |
| Huamai 5     | 713.52 (1.0) | 0.003 | 11 (0.8) | 20 (1.2) | 87.35 | 0.011 |
| Shannong 19  | 1190.6 (2.0) | 0.003 | 17 (0.9) | 40 (1.1) | 223.06 | 0.004 |
| Jimai 22     | 930.4 (18.9) | 0.003 | 5 (1.7) | 10 (1.1) | 366.28 | ND |
| Liangxing 66 | 784.4 (12.8) | 0.003 | 16 (0.7) | 32 (0.9) | 49.50 | 0.155 |
| Tainong 18   | 1190.6 (21.6) | 0.003 | 22 (0.9) | 42 (1.2) | 70.69 | 0.011 |
| Jimai 22     | 1190.6 (21.6) | 0.003 | 22 (0.9) | 42 (1.2) | 70.69 | 0.011 |
| Liangxing 66 | 784.4 (12.8) | 0.003 | 16 (0.7) | 32 (0.9) | 49.50 | 0.155 |
| Tainong 18   | 1190.6 (21.6) | 0.003 | 22 (0.9) | 42 (1.2) | 70.69 | 0.011 |

Table 3. The doses of QYM201 causing 10% and 50% reduction of wheat dry weight and 50% and 90% of weeds’ dry matter, and the selectivity index (SI) values between 3 wheat hybrids and the 4 weed species 28 days after treatment (DAT) in greenhouse research. *GR, inhibitory concentration. SI, selectivity index values were calculated by equation 2. ND, not determined.

| Trial plants | GR value (SE)a | SIb |
|--------------|---------------|-----|
|              | GR10 | GR50 | GR90 | JM 22 | LX 66 | TN 18 |
| Alopecurus aequalis | 28.1 (3.2) | 0.80 (1.9) | 11.5 | 9.7 | 14.7 |
| Alopecurus japonicus | 58.9 (2.7) | 115.0 (2.6) | 8.1 | 6.8 | 10.4 |
| Capsella bursa-pastoris | 40.5 (0.8) | 137.5 (3.2) | 6.8 | 5.7 | 8.7 |
| Malachium aquaticum | 24.9 (1.4) | 71.5 (1.1) | 13.0 | 11.0 | 16.6 |
Figure 2. Percentage of dry weight residue of *A. aequalis*, *A. japonicus*, *M. aquaticum*, and *C. bursa-pastoris* as influenced by different doses of QYM201 at 28 days after treatment (DAT) in a greenhouse study. The regression lines were calculated using Equation 1.

### Table 4. Visual estimates of percentage control of weeds under different POST rates of QYM201 at Ta‘an, Shandong, China, in 2016 and 2017. aVisual estimates for weed control were recorded after 45 days of treatment, using a 0% (no weed control) to 100% (complete weed control) scale. bThe following different letters represent different significance at the \( P < 0.05 \) level according to Fisher’s protected LSD test.

| Treatments | Dose | Crop injurya,b | Wheat yieldb,c | Crop injurya,b | Wheat yieldb,c |
|------------|------|----------------|----------------|----------------|----------------|
|            | g a.i. ha\(^{-1}\) | 3 DAT | 5 DAT | 15 DAT | 30 DAT | 2016 | 2017 | 2016 | 2017 | 2016 | 2017 |
| QYM201     | 90   | 0.0 | 0.0 | 0.0 | 0.0 | 6136 (34)\(^{b}\) | 5930 (103)\(^{d}\) | 9.8 | 11.8 |
| QYM201     | 135  | 0.0 | 0.0 | 0.0 | 0.0 | 6321 (270)\(^{b}\) | 6099 (32)\(^{d}\) | 13.1 | 15.0 |
| QYM201     | 180  | 0.0 | 0.0 | 0.0 | 0.0 | 6411 (246)\(^{b}\) | 6231 (23)\(^{b}\) | 14.7 | 17.5 |
| QYM201     | 270  | 0.0 | 0.0 | 0.0 | 0.0 | 6529 (229)\(^{a}\) | 631 (146)\(^{a}\) | 16.8 | 19.0 |
| Fenoxapro-P-ethyl | 50 | 0.0 | 0.0 | 0.0 | 0.0 | 6089 (132)\(^{b}\) | 5885 (109)\(^{b}\) | 7.5 | 10.9 |
| Tribenuron-methyl | 22.5 | — | — | — | — | 6199 (36)\(^{b}\) | 6054 (39)\(^{b}\) | 10.9 | 14.1 |
| Hand-weeding | — | — | — | — | — | 6734 (214)\(^{b}\) | 6488 (84)\(^{a}\) | 20.5 | 22.3 |
| Weedy control | — | — | — | — | — | 5590 (250)\(^{c}\) | 5305 (90)\(^{c}\) | — | — |

Table 5. Visual estimates for wheat injury and wheat yields under different POST rates of QYM201 at Ta‘an, Shandong, China, in 2016 and 2017. aVisual estimates for crop injury were performed at 3, 5, 15, and 30 DAT, using a 0% (no crop injury) and 100% (plant death) scale. bDifferent significance between the wheat injuries or wheat yields of 2 years according to Fisher’s protected LSD test at the 0.05 level. cSignificant; NS, not significant. dThe following different letters represent different significance at the \( P < 0.05 \) level according to Fisher’s protected LSD test.
The 2-year field experiments demonstrated that the herbicide QYM201 had good efficacy against *A. aequalis*, *D. sophia*, and *M. aquaticum* with POST at doses of 90–270 g a.i. ha$^{-1}$. Previous field studies further indicate that QYM201 has potential as a POST for weed control. Cheng et al. report that weeds die more slowly than in the greenhouse, which was in accordance with our research. This might be owing to greater weed leaf-age and lower temperatures in the field. Furthermore, no obvious damage to wheat plants was observed during the 2 experimental years in any QYM201 treatments. Moreover, the effect of QYM201 on crop yield was characterized; results showed that wheat yields were higher in 2016 than in 2017 (Table 5). The differences between the data received might be owing to the lower weed density occurring in the experimental sites in 2016. Other factors such as different environmental conditions could also have caused these differences. Wheat yield was increased for all the QYM201 treatments; furthermore, the wheat yield at 270 g a.i. ha$^{-1}$ was not much different from that at 180 g a.i. ha$^{-1}$. According to our research, all of the facts indicate that the recommended dosage of QYM201 is 90 to 180 g a.i. ha$^{-1}$. Field results indicated that the hand-weeding plots had the highest yield among all the treatments; however, the cost of labor make this economically unattractive. It is commonly agreed that the combination of chemical measures with other agronomic methods may result in economical and effective control of weeds in wheat fields.

In summary, results from greenhouse and field studies indicated that QYM201 has good potential as an efficient broad-spectrum herbicide for controlling weeds in wheat fields. Under the challenge of controlling multiple herbicide resistance in weeds, the novel structure of this herbicide and its different mode of action could be an ideal option for weed control, especially for resistant weed species in wheat fields.

**Methods**

**Herbicide used.** QYM201 (Kingagroot, Qingdao, China) with 98% purity and 6% oil dispersion (OD) was provided by Qingdao Kingagroot Chemicals Co., Ltd. Control herbicides fenoxaprop-P-ethyl 69 g L$^{-1}$ and tribenuron-methyl 75% WDG were provided by Bayer Crop Science Co., Ltd. and Jiangsu Rotam Chemicals Co., Ltd., respectively. To obtain a series of concentrations, QYM201 98% technical material (TC) was dissolved in ethanol and diluted with 0.1% Tween-80 solutions. QYM201 6% OD and the 2 control herbicides were dissolved and diluted with deionized water.

**Greenhouse experiment.** Weed seeds of *A. aequalis*, *A. japonicus*, *V. didyma* Tenore, *D. sophia*, and *Beccmannia syzygachne* (Steud.) Fern were collected from Jiangsu province and the other 13 weed species were collected from Henan province, China, in 2014 (Table 1). All weed species seed germination rates were $>$85%. All wheat hybrids used in this study can be found in the agricultural seed market and they are listed in Table 2. Germination rates of all wheat seeds were $>$80%. All greenhouse conditions involved were similar to those in a previous experiment. Experiments were executed at Shandong Agricultural University, Taan, China. Weed and wheat seeds were immersed in a petri dish containing distilled water and placed in a 12 h photoperiod and 20°C growth chamber (Model RXZ, Ningbojiangnan Instrument Factory, Ningbo, China) to accelerate germination before planting. After visualization of seed radicles, 15–30 seeds were sown below the soil surface per plastic pot (160 mm diameter and 130 mm height). After weed emergence, the seedlings were thinned to 10 plants per plastic pot. At the 3–5 leaf stage the seedlings were treated with QYM201 using an auto spraying tower (Model ASS-4, National Agricultural Information Engineering and Technology Center of China) at a spray pressure of 0.275 MPa with 450 L ha$^{-1}$ spray volume. All greenhouse experiments had replications and were repeated once.

**Effectiveness of weed control.** All 18 tested weed species were treated with QYM201 at dosage rates of 90 and 135 g a.i. ha$^{-1}$, and an untreated control was designed for each weed species. After 28 days of treatment, the surviving weeds were cut off at the soil surface and placed in a labeled paper bag, put in an oven at 80°C for 72 h, and finally the dry weights were recorded. Other experimental conditions were consistent with those described above for the greenhouse experiment.

**Wheat hybrid tolerance.** All wheat hybrids were treated with QYM201 at 360 and 540 g a.i. ha$^{-1}$, and a non-treated control was also designed. After 28 days of treatment, wheat plants were cut off and put in an oven at 80°C for 72 h, and then dry weights were recorded. In addition, the degree of herbicide damage to wheat seedlings was also recorded and expressed as values from 0 to 100%: 0% indicated no damage and 100% indicated total death. Other experimental conditions were consistent with those described above for the greenhouse experiment.

**Selectivity index (SI).** The selectivity index refers to the ratio between the concentrations that caused 10% growth inhibition of crops and 90% growth inhibition in weeds. Three commonly cultivated wheat hybrids (*Jinmai 22* (JM 22), *Liangxing 66* (LX 66), and *Tainong 18* (TN 18)) in China and 4 widespread weeds (*A. aequalis*, *A. japonicus*, *C. bursa-pastoris*, and *M. aquaticum*) that occur in wheat fields were selected for testing. In order to obtain the SI values between wheat and weed species under QYM201 application, JM 22, LX 66, and TN 18 were treated at rates of 0, 270, 405, 607, 911, 1366, 2050, and 3075 g a.i. ha$^{-1}$; *A. aequalis* and *M. aquaticum* were treated with doses of 0, 15, 30, 45, 60, and 75 g a.i. ha$^{-1}$; and *M. aquaticum* was sprayed at concentrations of 0, 45, 60, 75, 90, and 135 g a.i. ha$^{-1}$; and *C. bursa-pastoris* was treated at rates of 0, 15, 60, 90, and 135 g a.i. ha$^{-1}$. These experiments were carried out simultaneously under the same experimental conditions. After 28 days of treatment, to record plant dry weights, shoots were harvested and put in an oven at 80°C for 72 h. Other conditions during the experiments were consistent with those described above.
Field experiment. Field experiments were conducted in 2016 and 2017 at Ningyang, Taian, which is situated in the northern winter wheat growing areas. The soil type was loam with 1.79% organic matter, pH 7.5, and a widely grown wheat hybrid Tainong 18 was tested in this study. On October 2, 2015, and October 9, 2016, winter wheat was chemically sown in rows at 15 cm intervals at a seeding rate of 225 kg ha$^{-1}$. The weed species that were common in this area during the 2 experimental years were A. aequalis, D. sophia, and M. aquaticum. The average densities for A. aequalis were 20 and 31 plants per m$^2$, 18 and 28 plants per m$^2$ for D. sophia, and 12 and 19 plants per m$^2$ for M. aquaticum, respectively, in 2016 and 2017. Before wheat sowing, diammonium phosphate was applied at a ratio of 450 kg ha$^{-1}$, and on March 3, 2016, and March 15, 2017, urea fertilizer was applied at a ratio of 375 kg ha$^{-1}$ at the wheat turning green stage. The monthly temperatures and precipitation at the site during the experimental period are shown in Table 6.

All treatments were arranged in a randomized complete block design and repeated 4 times. The area of each plot was 20 m$^2$ (4 m wide and 5 m long). This experiment contained a total of 8 treatments and there were 4 application rates of QYM201 (90, 135, 180, and 270 g a.i. ha$^{-1}$); a single concentration of fenoxaprop-P-ethyl (at a rate of 50 g a.i. ha$^{-1}$) and tribenuron-methyl (at a dose of 25 g a.i. ha$^{-1}$), respectively; a hand-weeded control (using hand hoes at 0, 15, 30, and 45 DAT) and an untreated control (Table 4). On March 21, 2016, and March 16, 2017, weeds were sprayed with herbicides at the 7 to 8 leaf stage. The average temperatures on the days of application were 13.2°C and 9.7°C, respectively. Herbicides were applied using a backpack sprayer (Bellspray Inc., Opelousa, LA) fitted with a single 8002 VS nozzle (Teejet Technologies, Wheaton, IL) in 450 L ha$^{-1}$ of water.

Visual estimates for crop injury were performed at 3, 5, 15, and 30 DAT, using a 0% (no crop injury) and 100% (plant death) scale. Visual estimates for weed control were recorded after 45 days of treatment, using a 0% (no weed control) to 100% (complete weed control) scale $^{30}$. In each test plot a random sample area of 0.33 m$^2$ was surveyed at 3 sample points. The number of healthy plants of 3 weed species at each sample point was investigated at 0, 15, 30, and 45 DAT, and the fresh weight of weeds was recorded while investigating the number of weeds at 45 DAT. At the time of wheat harvesting, 3 samples were taken per plot and weighed to evaluate the grain yield of each plot; the resulting wheat yield was expressed as kg/ha.

Statistical analysis. All greenhouse experiment data were subjected to Analysis of Variance (hereafter referred to as ANOVA; Version 22.0; IBM Corporation, Armonk, NY). Data were pooled because there was no significant ($P > 0.05$) interaction with the 2 replicate treatments, and means were separated using Fisher’s protected LSD tests at the 0.05 level. All regression analyses were performed using SigmaPlot software (Version 13.0; Systat Software Inc., CA, USA). To evaluate weed control and assess the dose of QYM201 required for 90% weed control, regression of weed dry matter over herbicide dose was performed using the 4 parameter log-logistic model described by Seefeldt et al.$^{1,41}$:

$$y = c + (d - c)/(1 + \exp[b(\log x - \log GR_{50})])$$

(1)

where $b$ is the slope of the line, $c$ is the lower limit, $d$ is the upper limit, $x$ is the herbicide dose, $GR_{50}$ is the dose giving 50% response, and $y$ is the growth response (percentage of the untreated control).

$GR_{50}$, $GR_{90}$, and $GR_{90}$ values were calculated according to regression parameters.$^{41}$ The SI values of QYM201 were calculated by the following equation:

$$SI_{(10,90)} = \frac{GR_{10(crop)}}{GR_{90(weed)}}$$

(2)

where $GR_{10}$ is the dose of wheat growth reduction by 10%, and $GR_{90}$ is the dose of weeds growth reduction by 90%.

Field experiment data were subjected to ANOVA, and means were separated using Fisher’s protected LSD tests at the 0.05 level. Treatment interactions of the 2 years were not significant ($P > 0.05$), therefore the data were pooled by the year.

Data Availability
All data generated or analyzed in this study are included in the Supplementary Information files.

References
1. NBSC (National Bureau of Statistics of China). National data. http://data.stats.gov.cn/easyquery.htm?cn=C01, Accessed date: 31 January 2017 (2017).
2. Zhang, C. et al. Current advances in research on herbicide resistance. Scientia Agricultura Sinica 42, 1274–1289 (2009).
3. Tu, H. L. The succession of weed population in five crops in Sustainable weed management in the 21st Century (ed. Sun, D. C.) 5–9 (Guangxi Nationality Press, 1999).
4. Zhang, Z. P. Development of chemical weed control and integrated weed management in China. Weed Biol. Manag. 3, 197–203 (2003).
5. Su, S. New herbicides, formulation and combination product. Modern Agrochemicals 6, 1 (2007).
6. Baghestani, M. A., Zand, E., Soufi, M. A. & Rahimian, M. H. Morphological and physiological characteristics which enhance competitiveness of winter wheat (Triticum aestivum) against C. sativum. Weed Sci. 1, 111–126 (2005).
7. Delyé, C., Jasienski, M. & Le Corre, V. Deciphering the evolution of herbicide resistance in weeds. Trends Genet. 29, 649–658 (2013).
8. Mallory-Smith, C. A. & Retzinger, E. J. Revised classification of herbicides by site of action for weed resistance management strategies. Weed Technol. 17, 605–619 (2003).
9. Wakabayashi, K. & Böger, P. Target sites for herbicides entering the 21st century. Pest Manag. Sci. 58, 1149–1154 (2002).
10. Heap, I. International survey of herbicide resistant weeds. http://www.weedscience.com, Accessed date: 31 January 2017 (2017).
11. Zhu, J. et al. Weed research status, challenges, and opportunities in China. Crop Protection., https://doi.org/10.1016/j.cropro.2018.02.001 (2018).
12. Feng, Y. J., Gao, Y., Zhang, Y., Dong, L. Y. & Li, J. Mechanisms of resistance to pyroxasulam and ACCase inhibitors in Japanese Foxtail (Alopecurus japonicus). Weed Sci. 64, 695–704 (2016).
13. Li, X., Li, B., Su, L. & Suo, Z. Study on weed control efficacy and wheat injures of 2, 4-D butylate. J. Hebei Agric. Sci. 2, 38–42 (2002).
14. Yang, C. K., He, X. G. & Li, H. B. Drift injury of 2, 4-D butyl ester and remedial measures to cotton. Hubei Plant Prot. 1, 35–36 (2005).
15. Anonymous. KingAgroot. http://www.kingagroot.com/product_sanzuo.html (2017).
16. Pelttari, K. E. The mode of action of oxaxifluor: a case study of an emerging target site in Herbicides and their mechanisms of action (eds. Cobb, A. H. & Kirkwood, R. C.) 121–238 (Sheffield Academic, 2000).
17. Hira, K., Uchida, A. & Ohno, R. Major synthetic routes for modern herbicide classes and agrochemical characteristics in Herbicide classes in development: mode of action, targets, genetic engineering, chemistry (eds Böger, P., Wakabayashi, K. & Hira, K.) 179–289 (Springer, 2002).
18. Matringe, M., Saillard, A., Pelissier, B., Rolland, A. & Zink, O. p-Hydroxyphenylpyruvate dioxygenase inhibitor-resistant plants. Pest Manag. Sci. 61, 269–276 (2005).
19. Mitchell, G. et al. Mesotrinone: a new selective herbicide for use in maize. Pest Manag. Sci. 57, 120–128 (2001).
20. Norris, S. R., Barrette, T. R. & DellaPenna, D. Genetic dissection of carotenoid synthesis in arabidopsis defines plastocyanine as an essential component of phytone desaturation. Plant Cell 7, 2139–2149 (1995).
21. Böger, P. Carotenoid biosynthesis inhibitor herbicides-mode of action and resistance mechanism. Pesticide Outlook 9, 29–35 (1998).
22. Schonhammer, A., Freitag, J. & Koch, H. Topramezone - ein neuer Herbizidwirkstoff zur hochselektiven Hirse- und Unkrautbekämpfung in Mais [Topramazon - A newly highly selective herbicide compound for control of warm season grasses and dicytledonous weeds in maize]. J. Plant Dissec. Proct. (Suppl. 20), 1023–1031 (2006).
23. Yang, G. Q. et al. Efficacy experiment on several kinds of broadleaf herbicide in wheat field. Beijing Agric 21, 41–42 (2009).
24. ICAMA (Institute for Control of Agrichemicals, Ministry of Agriculture). The Bulletins of the Pesticide Registration in China. China Agriculture Press, Beijing, China. p. 166 (1988).
25. Guo, W. et al. Fenoxaprop-ethyl and mesosulfuron-methyl resistance status of shortawn foxtail (Alopecurus aequalis Sobol.) in eastern China. Pestic. Biochem. Physiol. 148, 126–132 (2018).
26. Guo, W. et al. Multiple resistance to ACCase and AHAS-inhibiting herbicides in shortawn foxtail (Alopecurus aequalis Sobol.) from China. Pestic. Biochem. Physiol. 124, 66–72 (2015).
27. Xia, W. et al. Molecular basis of ALS- and/or ACCase-inhibitor resistance in shortawn foxtail (Alopecurus aequalis Sobol.). Pestic. Biochem. Physiol. 122, 76–80 (2015).
28. Li, Y. et al. Studies on resistance of weeds Backmannia Syzigachne and Alopecurus japonicus to herbicide chlorosulfuron. Jiangsu Journal of Agricultural Sciences 12, 34–38 (1996).
29. Li, Y., Wu, J., Wang, Q. & Liu, L. Resistance of Alopecurus japonicus on chlorosulfuron, isoproturon and fenoxaprop-p-ethyl. Jiangsu Journal of Agricultural Science 21, 293–287 (2005).
30. Mohamed, I. A., Li, R., You, Z. & Li, Z. Japanese foxtail (Alopecurus japonicus) resistance to fenoxaprop and pinoxaden in China. Weed Sci. 60, 167–171 (2012).
31. Cong, C. et al. Evaluation of weed efficacy and crop safety of fluorochloridone in China. Weed Technol. 28, 721–728 (2014).
32. Beckie, H. J. & Harker, K. N. Our top 10 herbicide-resistant weed management practices. Pest Manag. Sci. 73, 1045–1052 (2017).
33. Tind, T., Mathiesen, T. J., Jensen, J. E., Ritz, C. & Streibig, J. C. Using a selectivity index to evaluate logarithmic spraying in grass seed crops. Pest Manag. Sci. 65, 1257–1262 (2009).
34. Bartley, M. R. Assessment of herbicide selectivity in Herbicide bioassays (eds. Streibig, J. C. & Kudsk, P.) 57–74 (CRC Press, 1993).
35. Cheng, X. et al. Weed control efficacy and winter wheat safety of a novel herbicide HW02. Crop Prot. 43, 246–250 (2013).
36. Gianessi, L. P. The increasing importance of herbicides in worldwide crop production. Pest Manag. Sci. 69, 1099–1105 (2013).
37. Mulder, T. A. & Doll, J. D. Integrating reduced herbicide use with mechanical weeding in corn (Zea mays). Weed Technol. 7, 382–389 (1993).
38. Zhao, N. et al. Greenhouse and field evaluation of oxaxifluor for weed control in maize in China. Scientific Reports. 7, 12809 (2017).
39. Yuan, G. et al. Molecular basis for resistance to ACCase-inhibiting herbicides in Psodosclerochola kengiana populations. Pestic. Biochem. Physiol. 119, 9–15 (2015).
40. Tind, T., Mathiesen, T. J., Jensen, J. E. & Erhardt, T. On the mechanism of action and selectivity of the corn herbicide topramezone: a new inhibitor of 4-hydroxyphenylpyruvate dioxygenase. Pest Manag. Sci. 63, 429–439 (2007).
41. Seefeldt, S. S., Jensen, J. E. & Fuerst, E. P. Log-logistic analysis of herbicide dose-response relationships. Weed Technol. 9, 218–227 (1995).

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Author Contributions
F.Z., H.W. and J.W. designed and performed the greenhouse studies. F.Z. performed the field experiments and data analysis. F.Z. and W.L. wrote the paper. All authors edited and reviewed the manuscript.
**Additional Information**

**Competing Interests:** The authors declare no competing interests.

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