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ARTICLE

# Drug repurposing strategy II: from approved drugs to agri-fungicide leads

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## Abstract

Epidemic diseases of crops caused by fungi deeply affected the course of human history and processed a major restriction on social and economic development. However, with the enormous misuse of existing antimicrobial drugs, an increasing number of fungi have developed serious resistance to them, making the diseases caused by pathogenic fungi even more challenging to control. Drug repurposing is an attractive alternative, it requires less time and investment in the drug development process than traditional R&D strategies. In this work, we screened 600 existing commercially available drugs, some of which had previously unknown activity against pathogenic fungi. From the primary screen at a fixed concentration of 100 μg/mL, 120, 162, 167, 85, 102, and 82 drugs were found to be effective against *Rhizoctonia solani, Sclerotinia sclerotiorum, Botrytis cinerea, Phytophthora capsici, Fusarium graminearum* and *Fusarium oxysporum*, respectively. They were divided into nine groups lead compounds, including quinoline alkaloids, benzimidazoles/carbamate esters, azoles, isothiazoles, pyrimidines, pyridines, piperidines/piperazines, ionic liquids and miscellaneous group, and simple structure-activity relationship analysis was carried out. Comparison with fungicides to identify the most promising drugs or lead structures for the development of new antifungal agents in agriculture.

## Introduction

Plant diseases and pests lead to reduced yields and quality of crops [1–3], which have a major impact on economic development and food security [4]. Research revealed that more than 19,000 species of fungi could cause plant diseases and some of them could be dormant in dead plants until opportunities were conducive to their proliferation [5]. It is estimated that the average annual economic loss caused by plant pathogenic fungi exceeds $200 billion [6]. *Fusarium* is one of the most important plant pathogenic fungi, for example, *Fusarium graminearum* and *Fusarium oxysporum* cause head blight and root rot. They can produce mycotoxins such as monothiocarbates and fumonisin [7, 8]. *Rhizoctonia solani*, *Sclerotinia sclerotiorum*, *Botrytis cinerea* and *Phytophthora capsici* host a wide range of more than 200 crops, including fruits and vegetables [9, 10]. Thus the loss of crops caused by fungi had become a severe issue that cannot be ignored.

Currently, there are several approaches to control plant diseases, such as breeding of resistant varieties, biological control and chemical control. However, the breeding also has many drawbacks, including lengthy breeding cycles, lack of varieties and geographical limitations of breeds [11]. Although biological control is advocated, the development process of biopesticides is slow and easy to deposit, so it is difficult to be widely applied in agricultural production at present [12, 13]. Thus, agrochemicals are still the primary form of control [14]. However, an expanding number of these weed, plant disease and pest insects are no longer effectively controlled by many of the existing agrochemical tools, a trend also observed in the medical community with the rise of antibiotic resistance [15, 16]. In particular, the

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development of resistance to critical fungicides against major crop fungal diseases, such as benzimidazoles and strobilurins, has had a significant impact on the fungicide market and the discovery of agrochemicals [17]. Therefore, it is necessary to develop novel, practical and resistant fungicidal agents to control plant diseases.

Drug development is an expensive, time-consuming and risky process [18]. In general, it can take up to 20 years for a drug from initial discovery to market. The development process can cost up to $2 billion, with only a 5% chance of successfully completing clinical trials and reaching the market [19, 20]. Likewise, an agrochemical takes 10–12 years from discovery to market and costs an estimated $286 million to develop [15, 21, 22]. Thus, it poses challenges to the development of novel pesticides. Drug repositioning or finding novel indications for known drugs is a way to reduce the time and cost of drug discovery as the toxicity, pharmacokinetic and biological activity of these drugs are well defined. In the medical field, many drugs have been successfully applied through repositioning [23–26]. As such, it has proven to be a preferred and advantageous alternative strategy for the more rapid discovery of new applications for drugs [27].

On this basis, 600 approved drugs with different structures and functions against *Rhizoctonia solani, Sclerotinia sclerotiorum, Botrytis cinerea, Phytophthora capsici, Fusarium graminearum and Fusarium oxysporum* were screened in this study and served as a theoretical basis for pesticide development.

## Materials and methods

### Fungal strains

Six phytopathogenic fungi, named *R. solani*, *S. sclerotiorum*, *B. cinerea*, *P. capsici*, *F. graminearum* and *F. oxysporum* were isolated, purified and identified from susceptible plants cultivated at the Gansu Academy of Agricultural Sciences, China.

### Approved drugs

The 600 approved drugs were purchased from commercial suppliers. Drugs were delivered in centrifugal tube (100 μg $ml^{-1}$, dissolved in DMSO) and kept at −80 °C until use.

### Screening Assay

In vitro, the antifungal activity of the drugs was initially evaluated using mycelial growth inhibition assay [6] with some modifications. The dissolved drug was added to the PDA medium so that the concentration of PDA containing the drug was 100 μg/mL. Zero point five percent DMSO (v/v) was added to the PDA medium as a blank control. The six plant pathogenic fungi were used to evaluate the antifungal activity of the samples. Take the disc (5.00 mm diameter) from the edge of the mycelia of the active colony with a hole punch, and then pick it to the center of the drug-containing plate with the inoculating needle. Lastly, the plates were incubated upside down in the dark at 26 °C. Three replicates per treatment. The diameter of the inhibition zone (mm) was measured by the cross method using digital calipers, and the growth inhibition rate of the samples on the fungal mycelium was calculated according to the following formula.

$$\text{Mycelial growth inhibition}(\%) = \frac{C - T}{C - 5} \times 100$$

The C and T are the average diameter of fungal colonies in the control and treated groups, respectively.

On the basis of the initial screening for antifungal activity, the highly active drugs were selected for virulence effect determination. The PDA medium was diluted to different solution concentrations (50 μg $ml^{-1}$, 25 μg $ml^{-1}$, 10 μg $ml^{-1}$, etc.), and the plates were incubated upside down in the dark at 26 °C. The inhibition rate as above, and the antifungal activity was indicated as $EC_{50}$.

### Statistical Analysis

The statistical analysis was conducted by SPSS 24.0. The $EC_{50}$ values were derived from the parameters in the regression curves.

## Results

The preliminary screening of 600 approved drugs against six phytopathogenic fungi at 100 μg $ml^{-1}$ showed that 120, 162, 167, 85, 102 and 82 drugs against *R. solani, S. sclerotiorum, B. cinerea, P. capsici, F. graminearum* and *F. oxysporum*, respectively, inhibiting the growth of mycelium of by more than 70% (Fig. 1) . To further determine the antifungal activity of these drugs, they were evaluated using the $EC_{50}$. We considered drugs with $EC_{50}$ less than 25 μg $ml^{-1}$ as candidates. Their original uses and toxicity are shown in Table 1 (https://pubchem.ncbi.nlm.nih.gov/, November 2022). As drug repurposing has gained tremendous popularity in the pharmaceutical field, we divided the candidate drugs into 9 lead series and conducted a brief discussion of structure and activity.

### Fungicides against plant pathogenic fungi

Plant pathogens can cause crop yield reduction and quality deterioration, and control of plant diseases is still dominated

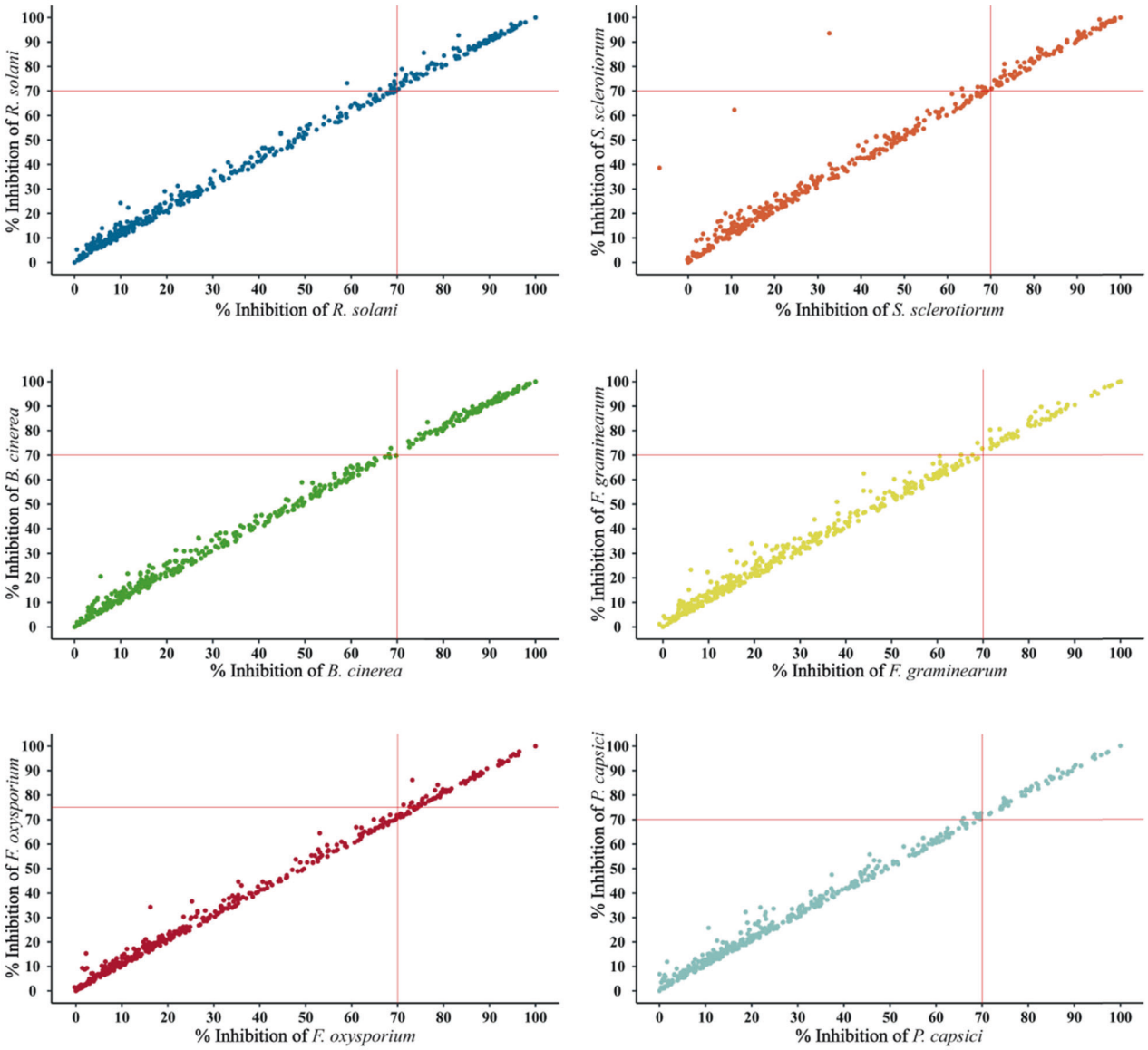



**Fig. 1** A total of 600 drugs were tested against pathogenic fungi at 100 μg/mL

by chemical fungicides. We evaluated the in vitro activity of the fungicide in Fig. 2. Carbendazim and thiophanate-methyl were broad-spectrum fungicides belonging to the benzimidazole and substituted benzene fungicides respectively, with $EC_{50}$ values in the range of 0.14–22.12 μg $ml^{-1}$ for pathogenic fungi. They had excellent activity against *S. sclerotiorum*, with $EC_{50}$ was 0.68 and 0.53 μg $ml^{-1}$, respectively. Difenoconazole is a sterol demethylation inhibitor with systemic, prophylactic and therapeutic effects. It had relatively potent activity against five pathogens except for *R. solani*, especially *F. oxysporum*, with an $EC_{50}$ of 0.04 μg $ml^{-1}$. Boscalid was a novel nicotinamide fungicide with positive action against *R. solani*, *S. sclerotiorum*, *B. cinerea* and *F. graminearum*, with $EC_{50} < 2$ μg $ml^{-1}$. Azoxystrobin and kresoxim-methyl were strobilurin fungicides with good activity against *S. sclerotiorum* with $EC_{50}$ of 4.9 and 4.66 μg $ml^{-1}$, respectively. Pyrimethanil and thirluzamide belong to the genus of methyl pyrimidine and benzamides, respectively. They were potent pesticides against *B. cinerea* and *R. solani* with $EC_{50}$ was 3.89 and 0.054 μg $ml^{-1}$, respectively. We evaluated the different classes of fungicides against plant pathogens to provide a basis for the activity level of the drugs screened for this study.

## Quinoline alkaloids

Alkaloids are a class of alkaline nitrogen-containing organic compounds in plants, marine organisms, microorganisms and insects. They have a wide range of biological activities such as

**Table 1** Active drugs"hits"identified from initial screening anti-plant pathogenic fungi[a]

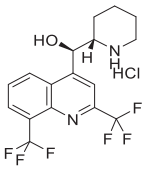
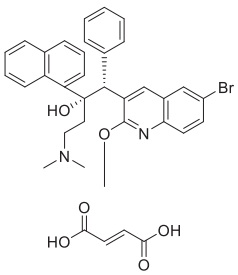
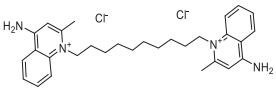
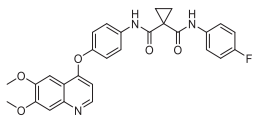
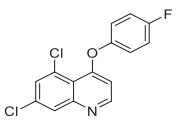
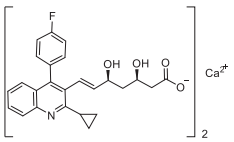
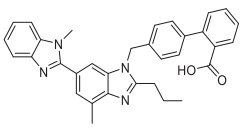
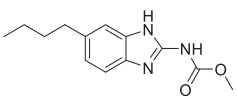
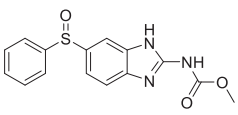
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Mefloquine hydrochloride |  | Anti-malarial | Rat: $LD_{50}$ = 880 mg/kg (oral) | >25 | >25 | **14.55** | >25 | >25 | >25 |
| 2 | Bedaquiline (fumarate) |  | Antituberculotic | Mouse and rat: single oral doses of 800 mg/kg | >25 | **6.81** | **9.45** | >25 | >25 | >25 |
| 3 | Dequalinium chloride |  | Antiseptic | Mouse: $LD_{50}$ = 70 mg/kg (subcutaneous) | >25 | **9.52** | >25 | >25 | >25 | >25 |
| 4 | Cabozantinib |  | Antineoplastic | - | **0.032** | >25 | >25 | >25 | >25 | >25 |
| 5 | Quinoxyfen |  | Fungicides (powdery mildew) | Mouse: $LD_{50}$ > 500 mg/kg (oral) | **2.21** | >25 | >25 | >25 | >25 | >25 |
| 6 | Pitavastatin hemicalcium |  | Lipid-lowering agents | Rat: LDLo = 500 mg/kg (oral) | >25 | >25 | **0.75** | **6.92** | **0.78** | **0.32** |
| 7 | Telmisartan |  | Antihypertensive | Mouse: $LD_{50}$ = 200 mg/kg (intravenous) | >25 | **5.81** | **2.19** | >25 | **4.80** | **3.27** |
| 8 | Parbendazole |  | Anthelmintic | Mouse: $LD_{50}$ = 1700 mg/kg (oral) | **0.051** | **0.16** | >25 | >25 | >25 | >25 |
| 9 | Oxfendazole |  | Anthelmintic | Rat: $LD_{50}$ > 6400 mg/kg; Mouse: $LD_{50}$ > 6400 mg/kg | **1.08** | **10.38** | >25 | >25 | >25 | >25 |

**Table 1** (continued)

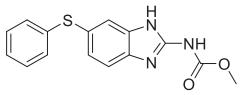
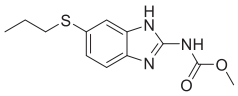
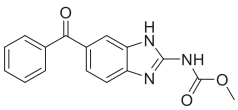
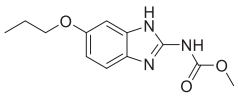
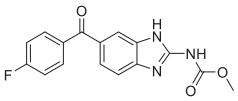
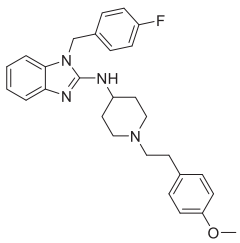
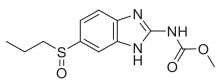
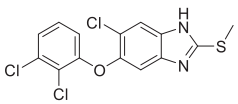
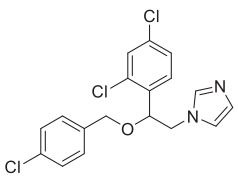
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 10 | Fenbendazole |  | Anthelmintic | Rat: $LD_{50}$ > 10 gm/kg (oral); Rat: $LD_{50}$ > 2 gm/kg (subcutaneous) | **0.007** | **0.097** | >25 | >25 | >25 | >25 |
| 11 | Albendazole |  | Anthelmintic | Rat: $LD_{50}$ = 2400 mg/kg (oral); Rat: $LD_{50}$ = 256 mg/kg (intravenous) | **0.12** | **0.11** | >25 | >25 | **2.84** | >25 |
| 12 | Mebendazole |  | Anthelmintic | Rat: $LD_{50}$ = 714 mg/kg (oral); Mouse: $LD_{50}$ = 620 mg/kg (oral) | **0.011** | **0.52** | >25 | >25 | >25 | >25 |
| 13 | Oxibendazole |  | Anthelmintic | Mouse: LDLo = 32 gm/kg (oral) | **0.43** | **0.103** | >25 | >25 | >25 | >25 |
| 14 | Flubendazole |  | Anthelmintic | Rat: $LD_{50}$ = 2560 mg/kg (oral); Mouse: $LD_{50}$ > 2560 mg/kg (oral) | >25 | **0.36** | >25 | >25 | >25 | >25 |
| 15 | Astemizole |  | Antihistaminic | Mouse: $LD_{50}$ = 2052 mg/kg | >25 | >25 | >25 | **22.05** | >25 | >25 |
| 16 | Albendazole S-oxide |  | Anthelmintic | Mouse: $LD_{50}$ > 800 mg/kg (oral) | **11.78** | **9.35** | >25 | >25 | >25 | >25 |
| 17 | Triclabendazole |  | Anthelmintic | Rat: $LD_{50}$ > 8 gm/kg (oral); Rat: $LD_{50}$ > 4 gm/kg (skin) | **4.39** | **4.85** | **6.92** | **11.26** | **28.90** | **21.15** |
| 18 | Econazole |  | Antifungal drug | Mice: $LD_{50}$ = 462 mg/kg (oral); Rats: $LD_{50}$ = 668 mg/kg (oral) | **13.75** | **0.25** | **0.034** | **0.093** | **0.094** | **0.01** |

**Table 1** (continued)

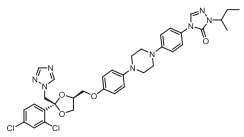
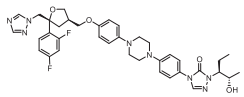
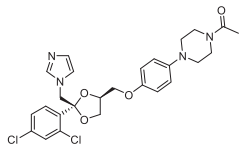
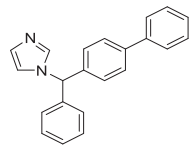
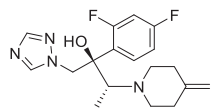
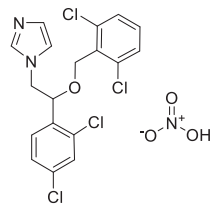
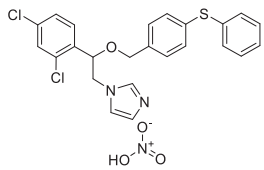
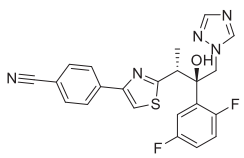
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 19 | Itraconazole |  | Antifungal drug | Mouse: $LD_{50}$ > 320 mg/kg (oral); Dog: $LD_{50}$ > 200 mg/kg (oral) | **>25** | **0.024** | **0.025** | >25 | **0.044** | **0.024** |
| 20 | Posaconazole |  | Antifungal drug | Clinical trials: some patients received posaconazole up to 1600 mg/day with no adverse events noted | **>25** | **0.053** | **0.061** | >25 | **0.165** | **0.11** |
| 21 | Ketoconazole |  | Antifungal drug | Rat: $LD_{50}$ = 227 mg/kg (oral) | >25 | **0.15** | **0.34** | **2.34** | **0.26** | **0.12** |
| 22 | Bifonazole |  | Antifungal drug | Rat: $LD_{50}$ = 1463 mg/kg (oral); Mouse: $LD_{50}$ = 2629 mg/kg (oral) | **4.86** | **4.58** | **1.26** | **0.54** | **0.18** | **0.17** |
| 23 | Efinaconazole |  | Antifungal drug | Rat: daily doses of up to 30 (males) and 40 (females) mg/kg (generally well tolerated) | **1.51** | **0.095** | **0.058** | **0.15** | **0.035** | **0.026** |
| 24 | Isoconazole nitrate |  | Antifungal drug | Rat: $LD_{50}$ = 5600 mg/kg (oral); Rat: $LD_{50}$ >10 gm/kg (subcutaneous) | **7.42** | **0.066** | **0.101** | **1.17** | **0.28** | **0.021** |
| 25 | Fenticonazole nitrate |  | Antifungal drug | Rat: $LD_{50}$ > 3 mg/kg (oral); Rat: $LD_{50}$ >750 gm/kg (subcutaneous) | **7.23** | **0.12** | **0.054** | **0.37** | **0.15** | **0.056** |
| 26 | Isavuconazole |  | Antifungal drug | Rats:At doses up to 90 mg/kg/day (oral:not affect the fertility) | >25 | **0.76** | **0.043** | **0.35** | **0.14** | **0.015** |

**Table 1** (continued)

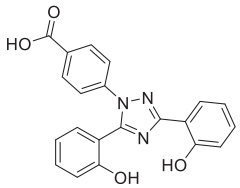
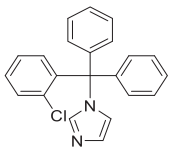
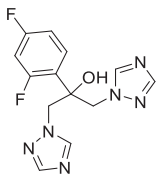
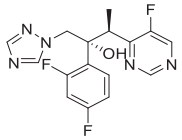
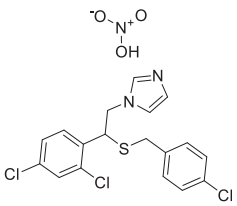
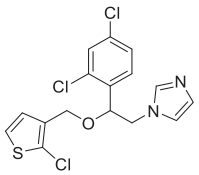
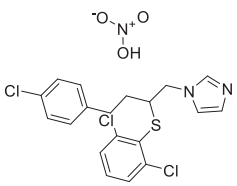
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 27 | Deferasirox |  | Iron chelating agent | - | **17.94** | >25 | **4.73** | >25 | >25 | >25 |
| 28 | Clotrimazole |  | Antifungal drug | Rat (male): $LD_{50}$ = 708 mg/kg (oral); Mouse (male): $LD_{50}$ = 923 mg/kg (oral) | **0.61** | **0.17** | **0.32** | **0.48** | **0.08** | **0.061** |
| 29 | Fluconazole |  | Antifungal drug | Rat: $LD_{50}$ = 1271 mg/kg (oral); Rat: $LD_{50}$ > 941 mg/kg (intraperitoneal) | >25 | >25 | **11.16** | >25 | >25 | **3.77** |
| 30 | Voriconazole |  | Antifungal drug | Mouse: $LD_{50}$ = 223.07 mg/kg (intravenous) | **1.64** | **0.26** | **0.12** | **0.79** | **0.078** | **0.032** |
| 31 | Sulconazle nitrate |  | Antifungal drug | Rat: $LD_{50}$ = 1741 mg/kg (oral); Rat: $LD_{50}$ = 735 mg/kg (intraperitoneal) | **2.47** | **0.14** | **0.057** | **1.30** | **0.12** | **0.014** |
| 32 | Vagistat |  | Antifungal drug | Mouse: $LD_{50}$ = 1870 mg/kg (oral); Mouse: $LD_{50}$ = 508 mg/kg (intraperitoneal) | **6.45** | **0.079** | **0.058** | **0.96** | **0.31** | **0.015** |
| 33 | Butoconazole nitrate |  | Antifungal drug | Rat: $LD_{50}$ = 1720 mg/kg (oral); Rat: $LD_{50}$ = 940 mg/kg (intraperitoneal) | **5.12** | **0.20** | **0.29** | **3.00** | **0.11** | **0.019** |

**Table 1** (continued)

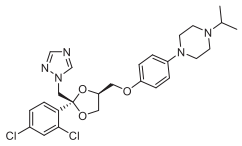
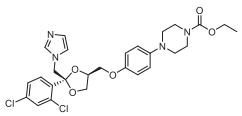
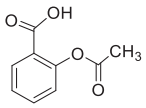
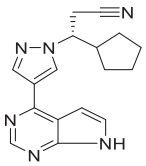
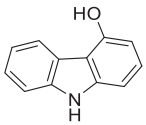
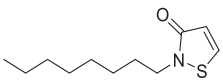
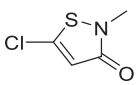
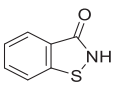
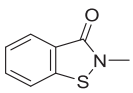
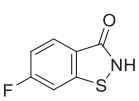
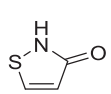
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 34 | Terconazole |  | Antifungal drug | Rat (male): $LD_{50}$ = 1741 mg/kg (oral); Rat (female): $LD_{50}$ = 849 mg/kg (oral) | >25 | **9.99** | **9.74** | >25 | **20.35** | **0.37** |
| 35 | Elubiol |  | Antifungal drug | - | **19.61** | **0.051** | **0.11** | **2.82** | **0.11** | **0.025** |
| 36 | Luliconazole |  | Antifungal drug | In clinical trials, no serious toxicity was reported | **8.83** | **0.003** | **0.001** | **0.003** | **0.005** | **0.001** |
| 37 | Ruxolitinib |  | Antineoplastic | Rat: $LD_{50}$ = 250 mg/kg (oral) | >25 | >25 | **10.79** | >25 | **24.42** | >25 |
| 38 | 4,5-Dichloro-2-octyl-isothiazolone |  | Fungicide (mould) | Toxicity of poisoning | **0.58** | **0.80** | **0.63** | **0.27** | **2.45** | **2.64** |
| 39 | Octyl-2*H*- isothiazol-3-one |  | Fungicide (mould) | Rat: $LD_{50}$ = 550 mg/kg (oral); Rat: LC > 2 gm/m$^3$ (inhalation) | **1.29** | **0.17** | **0.13** | **0.28** | **0.55** | **1.10** |
| 40 | Isothiazolinone chloride |  | Fungicide (mould) | - | **17.92** | >25 | >25 | >25 | >25 | >25 |
| 41 | 1,2-Benzisothiazol-3(2*H*)-one |  | Fungicide (mould) | Rat: $LD_{50}$ = 1020 mg/kg (oral); Mouse: $LD_{50}$ = 1150 mg/kg (oral) | **3.51** | **2.12** | **3.40** | **2.96** | >25 | >25 |
| 42 | Methyl-1,2-benzothiazol-3(2*H*)- one |  | Fungicide (mould) | Water flea: $EC_{50}$ = 0.92 ppm; Freshwater green algae: $EC_{50}$ = 0.92 ppm | **5.84** | **13.53** | **20.22** | **16.86** | **19.00** | >25 |
| 43 | Fluoro-1,2-benzoisothiazol- 3(2*H*)-one |  | Fungicide (mould) | - | **8.94** | **7.70** | **10.71** | **10.58** | **24.39** | >25 |
| 44 | Isothiazol-3-one |  | Pharmaceutical intermediates | - | **7.95** | **6.21** | **9.45** | **9.90** | **27.41** | **19.43** |

**Table 1** (continued)

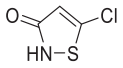
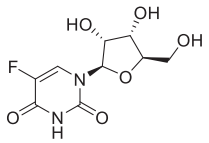
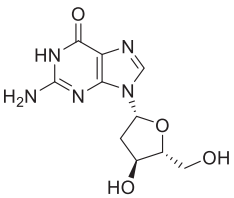
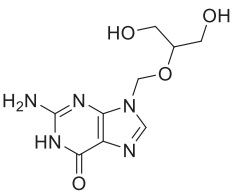
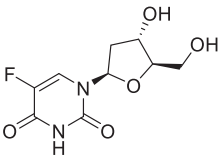
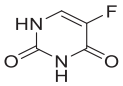
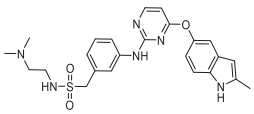
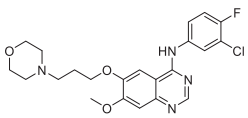
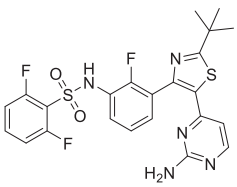
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 45 | 5-Chloro-3-hydroxyisothiazole |  | Pharmaceutical intermediates | - | **0.98** | **1.98** | **3.80** | **4.06** | **3.29** | **3.70** |
| 46 | 5-Fluorouridine |  | Pharmaceutical intermediates | Rat: $LD_{50}$ = 400 mg/kg (intraperitoneal); Mouse: $LD_{50}$ = 160 mg/kg (intraperitoneal) | >25 | **0.49** | **0.83** | **17.26** | >25 | >25 |
| 47 | 2'-Deoxyguanosine |  | Pharmaceutical intermediates | Rat: $LD_{50}$ > 800 mg/kg (intraperitoneal) | >25 | **15.13** | >25 | >25 | >25 | >25 |
| 48 | Ganciclovir |  | Antiviral | Mouse: $LD_{50}$: > 2 g/kg (oral): | >25 | **7.56** | >25 | >25 | >25 | >25 |
| 49 | Floxuridine |  | Antineoplastic | Rat: $LD_{50}$ = 215 mg/kg (oral) | >25 | **2.43** | **1.12** | >25 | >25 | >25 |
| 50 | 5-Fluorouracil |  | Antineoplastic | Mice: $LD_{50}$=230 mg/kg (oral) | >25 | >25 | **6.33** | **9.46** | >25 | >25 |
| 51 | Sulfatinib |  | Antineoplastic | - | >25 | >25 | **3.37** | >25 | >25 | >25 |
| 52 | Gefitinib |  | Antineoplastic | Low toxicity | >25 | >25 | **13.52** | >25 | >25 | >25 |
| 53 | Dabrafenib |  | Antineoplastic | Rats: $LD_{50}$ > 2000 mg/kg | >25 | **2.31** | **0.63** | >25 | >25 | >25 |

**Table 1** (continued)

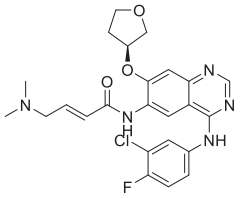
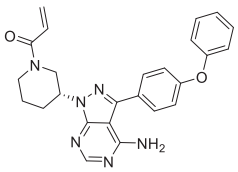
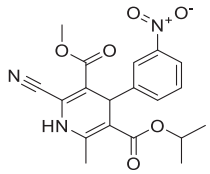
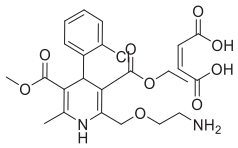
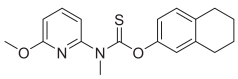
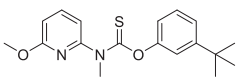
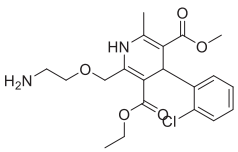
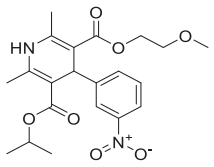
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 54 | Afatinib |  | Antineoplastic | - | >25 | >25 | **5.00** | >25 | >25 | >25 |
| 55 | Ibrutinib |  | Antineoplastic | - | >25 | **5.53** | **2.29** | >25 | **14.02** | **9.11** |
| 56 | Nilvadipine |  | The treatment of hypertension | Rat: $LD_{50}$ = 1560 mg/kg (oral); Rat: $LD_{50}$ > 1 gm/kg (subcutaneous) | >25 | **6.46** | **5.74** | >25 | **20.44** | >25 |
| 57 | Amlodipine maleate |  | The treatment of hypertension | - | >25 | >25 | **12.43** | >25 | >25 | >25 |
| 58 | Liranaftate |  | Antifungal drug | Rat: $LD_{50}$ > 2 gm/kg (oral); Rat: $LD_{50}$ > 2 gm/kg (intraperitoneal) | **0.048** | **0.168** | **0.004** | **0.19** | **0.031** | **0.27** |
| 59 | Pyributicarb |  | Herbicides | Rat: $LD_{50}$ > 5 gm/kg (oral); Rat: $LD_{50}$ > 5 gm/kg (intraperitoneal) | **0.22** | **2.07** | **0.089** | **0.12** | **0.30** | **1.93** |
| 60 | Amlodipine |  | The treatment of hypertension | Women: LDLo = 1400 ug/kg (oral) | >25 | >25 | **10.53** | >25 | >25 | >25 |
| 61 | Nimodipine |  | Treatment of cerebrovascular | Rat: $LD_{50}$ = 2738 mg/kg (oral); Mouse: $LD_{50}$ = 940 mg/kg (oral) | >25 | >25 | **10.27** | >25 | >25 | >25 |

**Table 1** (continued)

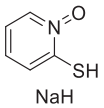
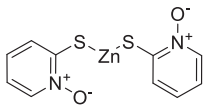
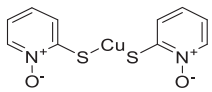
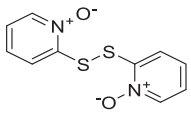
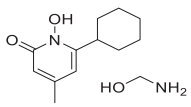
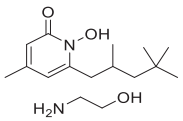
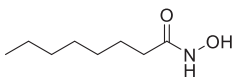
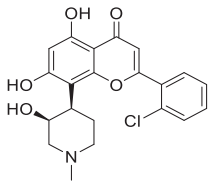
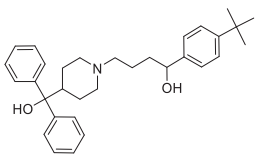
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 62 | Sodium pyrithione |  | Antimicrobial agents | Mouse: $LD_{50}$ = 265 mg/kg (intraperitoneal); Rat: $LD_{50}$ = 385 mg/kg (intraperitoneal) | **5.45** | **1.42** | **2.26** | **4.72** | **10.72** | **2.83** |
| 63 | Zinc pyrithione |  | Antimicrobial agents | - | **7.79** | **0.43** | **7.97** | **0.97** | **3.80** | **2.25** |
| 64 | Copper pyrithione |  | Fungicides | Fathead minnow: LC50 = 4.3 ppb; Crassostrea virginica: $EC_{50}$ = 9.2 ppb | **6.73** | **0.36** | **2.55** | **1.13** | **5.28** | **28.54** |
| 65 | Bispyrithione |  | Pesticide intermediates | - | **3.31** | **3.17** | **2.03** | **0.37** | **25.55** | **1.39** |
| 66 | Ciclopirox ethanolamine |  | Antifungal agent | Rat: $LD_{50}$ = 2350 mg/kg (oral); Rat: $LD_{50}$ > 2500 mg/kg (subcutaneous); | **14.68** | **1.95** | **5.37** | **10.93** | **14.08** | **18.66** |
| 67 | Piroctone olamine |  | Anti-dandruff agent | Mouse: $LD_{50}$ = 5 gm/kg (oral) Rat: $LD_{50}$ = 8100 mg/kg (oral) | **18.77** | **7.29** | >25 | **19.28** | **17.77** | **17.08** |
| 68 | Caprylohydroxamic acid |  | Preservatives | Rat: $LD_{50}$ = 10700 mg/kg (oral); Mouse: $LD_{50}$ = 8820 mg/kg (oral) | **27.75** | **16.12** | **7.08** | >25 | >25 | >25 |
| 69 | Flavopiridol |  | Anti-cancer | - | **17.83** | **22.72** | **12.81** | >25 | >25 | >25 |
| 70 | Terfenadine |  | Antihistamines | Rat: $LD_{50}$ = 5 gm/kg (oral); Rat: $LD_{50}$ >1250 mg/kg (subcutaneous) | >25 | **14.52** | **12.38** | **23.03** | >25 | >25 |

**Table 1** (continued)

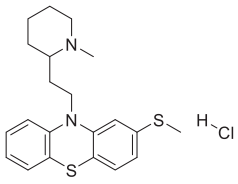
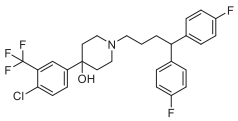
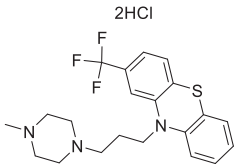
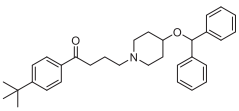
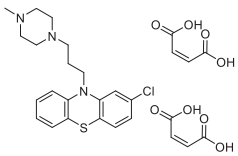
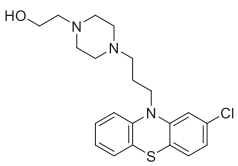
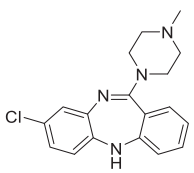
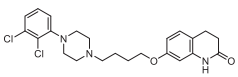
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 71 | Thioridazine hydrochloride |  | Antipsychotic | Rat: $LD_{50}$ = 1060 mg/kg (oral); Rat: $LD_{50}$ = 71 mg/kg (intravenous) | >25 | **21.62** | >25 | >25 | **18.49** | **15.90** |
| 72 | Penfluridol |  | Antipsychotic | Mouse: $LD_{50}$ = 87 mg/kg (oral); Rat: $LD_{50}$ = 160 mg/kg (oral) | >25 | **6.95** | **13.53** | **17.32** | >25 | >25 |
| 73 | Trifluoperazine |  | Antipsychotic | Mouse: $LD_{50}$ = 1350 mg/kg (oral); Mouse: $LD_{50}$ = 120 mg/kg (intraperitoneal) | **3.66** | **13.20** | **4.12** | **6.17** | **8.59** | **8.19** |
| 74 | Ebastine |  | Antihistamines | Rat: $LD_{50}$ > 4 gm/kg (oral); Rat: $LD_{50}$ = 496 mg/kg (intraperitoneal) | **21.04** | **17.05** | **13.82** | >25 | **19.64** | >25 |
| 75 | Prochlorperazine maleate |  | Antipsychotic | Rat: $LD_{50}$ = 750 mg/kg (oral) Rat: $LD_{50}$ = 320 mg/kg (subcutaneous) | **14.84** | **20.95** | **17.53** | >25 | >25 | **12.31** |
| 76 | Perphenazine |  | Antipsychotic | Rat: $LD_{50}$ = 318 mg/kg (oral); Rat: $LD_{50}$ = 146 mg/kg (intraperitoneal) | **16.19** | **14.46** | **18.21** | >25 | **13.70** | **15.60** |
| 77 | Clozapine |  | Antipsychotic | Rat: $LD_{50}$ = 251 mg/kg (oral); Rat: $LD_{50}$ = 251 mg/kg (subcutaneous) | >25 | >25 | **23.13** | >25 | >25 | >25 |
| 78 | Aripiprazole |  | Antipsychotic | - | >25 | **20.25** | **17.55** | **24.71** | **17.91** | **24.92** |

**Table 1** (continued)

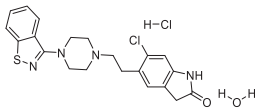
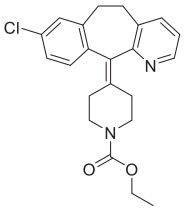
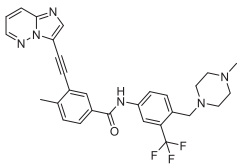
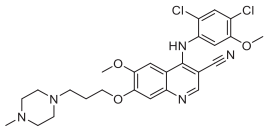
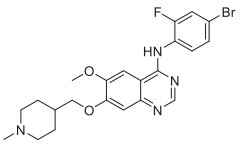
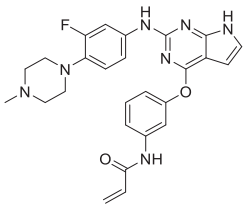
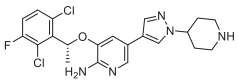
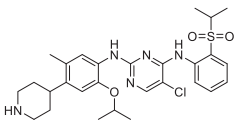
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 79 | Ziprasidone hydrochloride |  | Antipsychotic | - | >25 | **22.96** | >25 | >25 | >25 | >25 |
| 80 | Loratadine |  | Antihistamines | Rat: $LD_{50}$ > 5000 mg/kg (oral) | **6.19** | >25 | **24.53** | >25 | >25 | **12.18** |
| 81 | Ponatinib |  | Antiangiogenic; antineoplastic | Toxicity of poisoning | **0.017** | >25 | **11.47** | >25 | >25 | >25 |
| 82 | Bosutinib |  | Antineoplastic | - | >25 | **7.69** | **13.86** | >25 | >25 | >25 |
| 83 | Vandetanib |  | Antineoplastic | Low toxicity | >25 | >25 | **17.32** | **13.34** | >25 | >25 |
| 84 | Avitinib |  | Antineoplastic | - | >25 | **11.21** | **11.80** | **49.36** | >25 | >25 |
| 85 | Crizotinib |  | Antineoplastic | - | >25 | **11.85** | **10.59** | >25 | >25 | >25 |
| 86 | Ceritinib |  | Antineoplastic | - | >25 | >25 | **19.57** | >25 | >25 | >25 |

**Table 1** (continued)

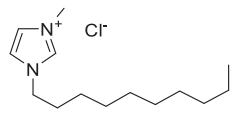
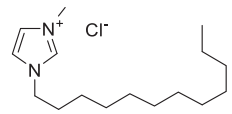
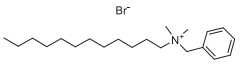
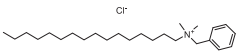
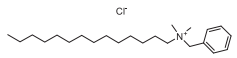
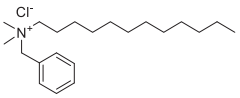
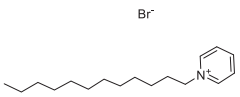
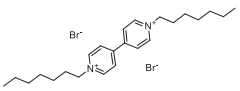
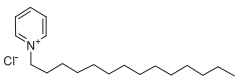
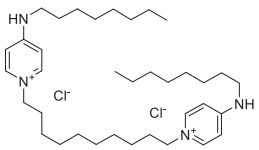
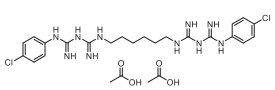
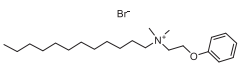
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 87 | Decyl-3-methylimidazolium chloride |  | Chemical intermediates | - | >25 | **22.95** | >25 | >25 | >25 | >25 |
| 88 | 1-Dodecyl-3-methylimidazolium chloride |  | Chemical intermediates | - | >25 | **6.12** | >25 | >25 | >25 | >25 |
| 89 | Dodecyl dimethyl benzyl ammonium bromide |  | Disinfectant; preservative | Rat: $LD_{50}$ = 230 mg/kg (oral); Mouse: $LD_{50}$ = 277 mg/kg | >25 | **5.80** | **8.85** | >25 | >25 | >25 |
| 90 | Cetalkonium chloride |  | Preservatives | Rat: $LD_{50}$ > 500 mg/kg (oral) | >25 | **8.63** | >25 | >25 | >25 | >25 |
| 91 | Myristalkonium chloride |  | Germicide and algicide | Mouse: $LD_{50}$ = 919 mg/kg (oral); Mouse: $LD_{50}$ = 18 mg/kg (intravenous) | >25 | **14.28** | **9.06** | >25 | >25 | >25 |
| 92 | Benzododecinium chloride |  | Preservatives | Rat: $LD_{50}$ = 400 mg/kg (oral); Rat: $LD_{50}$ = 100 mg/kg (intraperitoneal) | >25 | >25 | **11.40** | >25 | >25 | >25 |
| 93 | 1-Dodecylpyridinium bromide |  | Surfactant | - | >25 | **15.34** | **2.63** | **16.69** | >25 | >25 |
| 94 | 1,1'-Di-n-heptyl-4,4'-bipyridinium dibromide |  | Calcium release inhibitors | - | >25 | >25 | **17.80** | >25 | >25 | >25 |
| 95 | 1-Tetradecylpyridinium chloride |  | Surfactant | - | >25 | **23.77** | **11.35** | >25 | >25 | >25 |
| 96 | Octenidine dihydrochloride |  | Antibacterial agents | - | >25 | **17.57** | **5.36** | >25 | >25 | >25 |
| 97 | Chlorhexidine diacetate |  | Cationic broad-spectrum antimicrobial | Mouse: $LD_{50}$= 2 gm/kg (oral); Mouse: $LD_{50}$= 38 mg/kg (intraperitoneal) | **12.14** | **6.66** | **3.35** | **10.13** | **11.19** | **3.65** |
| 98 | Domiphen bromide |  | Disinfectants | Guinea pig:lowest published lethal dose: 10 mg/kg | **22.25** | **6.42** | **9.96** | **21.27** | >25 | >25 |

**Table 1** (continued)

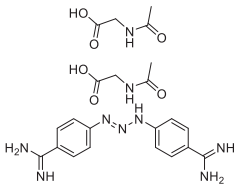
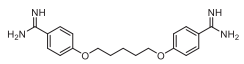
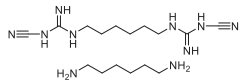
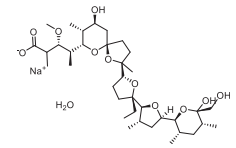
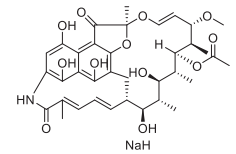
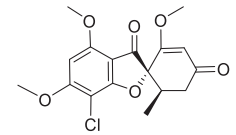
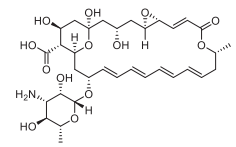
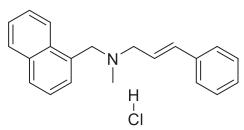
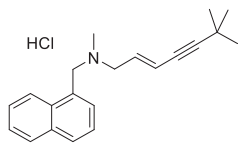
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 99 | Diminazene aceturate |  | Antiparasitic agent; trypanocidal drug | - | >25 | **6.22** | **3.07** | **3.18** | >25 | >25 |
| 100 | Pentamidine |  | Antiinfective agent | Mouse: $LD_{50}$= 50 mg/kg (intraperitoneal) | >25 | **5.86** | **3.89** | >25 | >25 | >25 |
| 101 | Enebicyanog |  | Fungicides and preservatives | - | **2.89** | **0.91** | **0.62** | **20.94** | >25 | >25 |
| 102 | Monensin sodium salt |  | Antiprotozoal agent | - | **8.80** | **0.076** | **0.11** | >25 | **0.67** | **0.36** |
| 103 | Rifamycin sodium |  | Antibiotics | Rat: $LD_{50}$= 2680 mg/kg (oral); Mouse: $LD_{50}$= 2120 mg/kg (oral) | **23.18** | **18.91** | **7.53** | >25 | >25 | >25 |
| 104 | (+)-Griseofulvin |  | Antibiotics | Rat: $LD_{50}$ >10 gm/kg (oral); Rat: $LD_{50}$ = 400 mg/kg (intravenous) | **2.77** | **13.20** | **0.31** | **6.17** | **2.26** | **3.88** |
| 105 | Natamycin |  | Antiseptic; antifungal | Rat: $LD_{50}$ = 2730 mg/kg (oral); Rat: $LD_{50}$ = 190 mg/kg (subcutaneous) | **0.51** | **1.18** | **0.84** | **2.18** | **2.32** | **0.63** |
| 106 | Naftifine hydrochloride |  | Antifungal | - | >25 | **12.47** | **1.68** | **13.68** | **9.40** | **12.78** |
| 107 | Terbinafine hydrochloride |  | Antifungal | Rat: $LD_{50}$ > 2 gm/kg (skin) | **18.05** | **0.80** | **0.11** | **0.17** | **0.26** | **0.51** |

**Table 1** (continued)

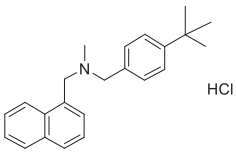
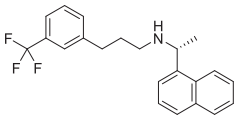
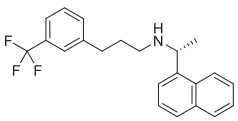
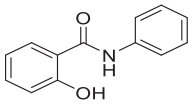
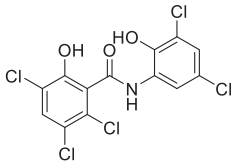
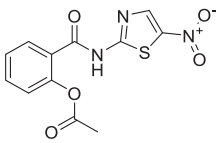
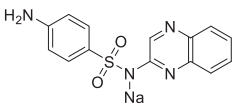
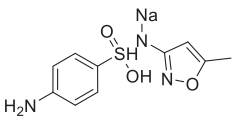
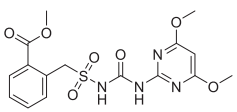
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 108 | Butenafine hydrochloride |  | Antifungal | Rat: $LD_{50}$ > 4 gm/kg (oral) Rat: $LD_{50}$ > 100 gm/kg (intravenous) | **2.75** | **0.22** | **0.07** | **0.08** | **0.29** | **0.85** |
| 109 | Tolnaftate |  | Antifungal | Mouse: $LD_{50}$ = 4800 mg/kg (intravenous); Mouse: $LD_{50}$ = 120 mg/kg (intraperitoneal) | **0.36** | **7.90** | **0.07** | >25 | **0.47** | >25 |
| 110 | Cinacalcet |  | A calcimimetic and a P450 inhibitor | - | **9.89** | **20.12** | **10.83** | **15.25** | **13.37** | **10.41** |
| 111 | Salicylanilide |  | Fungicides (cosmetics) | Mouse: $LD_{50}$ = 2400 mg/kg (oral); Mouse: $LD_{50}$ > 500 mg/kg (intraperitoneal) | **24.43** | >25 | **21.90** | **21.77** | **14.62** | **11.64** |
| 112 | Oxyclozanide |  | Anthelmintic | Rat: $LD_{50}$ = 1 gm/kg (oral) | **0.71** | **0.50** | **0.09** | >25 | >25 | >25 |
| 113 | Nitazoxanide |  | Anthelmintic | Mouse: $LD_{50}$ = 1350 mg/kg (oral); Rat: $LD_{50}$ > 10 gm/kg (oral) | >25 | **1.42** | **1.15** | >25 | >25 | >25 |
| 114 | Sulfaquinoxaline sodium |  | Anthelmintic | - | >25 | >25 | >25 | **14.47** | >25 | >25 |
| 115 | Sulfisomezole sodium |  | Antibiotics | - | >25 | >25 | **14.20** | >25 | **14.71** | >25 |
| 116 | Bensulfuron-methyl |  | Herbicides | Rat: $LD_{50}$ > 5 gm/kg (oral); Rat: $LD_{50}$ > 2 gm/kg (skin) | >25 | **12.67** | **12.40** | **17.36** | >25 | >25 |

**Table 1** (continued)

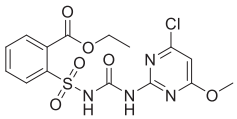
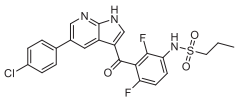
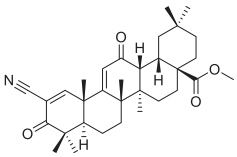
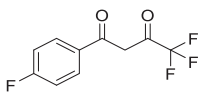
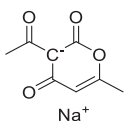
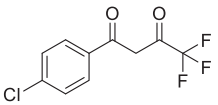
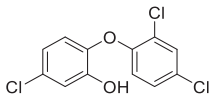
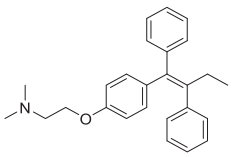
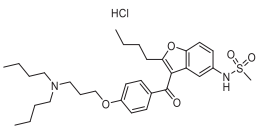
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 117 | Chlorimuron-ethyl |  | Herbicides | Rat: $LD_{50}$ = 4102 mg/kg (oral) | >25 | **13.09** | **11.68** | >25 | >25 | >25 |
| 118 | Vemurafenib |  | Antineoplastic | Rat: up to 250 mg/kg/day (no evidence of teratogenicity) | **0.42** | >25 | >25 | >25 | >25 | >25 |
| 119 | Bardoxolone methyl |  | Antineoplastic; anti-inflammatory | - | **0.56** | >25 | **1.72** | >25 | >25 | >25 |
| 120 | 4,4,4-Trifluoro-1- (4-fluorophenyl)butane-1,3-dione |  | Pharmaceutical intermediates | - | **6.45** | **13.12** | **4.76** | **6.43** | **31.06** | **31.75** |
| 121 | Sodium dehydroacetate |  | Food additives; preservatives | - | **18.02** | **8.91** | **16.21** | **6.59** | **7.95** | **24.01** |
| 122 | (4-Chloropheny)- 4,4,4-trifluoro-1,3-butanedione |  | Pharmaceutical intermediates | - | **2.64** | **3.28** | **1.69** | **1.90** | **9.51** | **10.36** |
| 123 | Triclosan |  | Preservatives; fungicides | Rat: $LD_{50}$ = 3700 mg/kg | **7.88** | **10.03** | **2.24** | **3.15** | **4.39** | **4.96** |
| 124 | Tamoxifen |  | Antineoplastic | Rat: $LD_{50}$ = 4100 mg/kg (oral); Rat: $LD_{50}$ = 700 mg/kg (intraperitoneal) | >25 | **11.04** | **7.37** | >25 | >25 | >25 |
| 125 | Dronedarone hydrochloride |  | Anti-arrhythmic | - | >25 | **4.74** | **10.21** | >25 | >25 | **20.85** |

**Table 1** (continued)

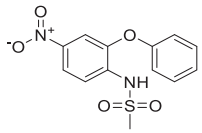
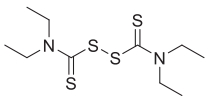
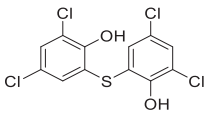
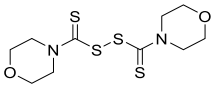
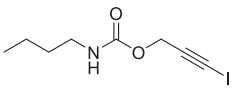
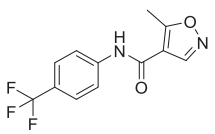
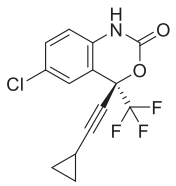
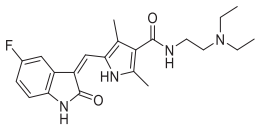
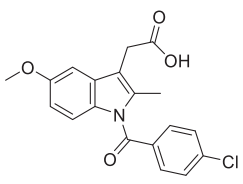
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 126 | Nimesulide |  | Non-steroidal anti-inflammatory | Mouse: $LD_{50}$ = 216 mg/kg (intraperitoneal); Mouse: $LD_{50}$ = 392 mg/kg (oral) | >25 | >25 | **1.24** | >25 | >25 | >25 |
| 127 | Disulfiram |  | Antineoplastic | Rats: $LD_{50}$ = 8.6 g/kg (oral) | **20.28** | **15.95** | >25 | >25 | >25 | >25 |
| 128 | Bithionol |  | Anthelmintic | Mouse: $LD_{50}$ = 760 mg/kg (oral); Mouse: $LD_{50}$ = 760 mg/kg (intraperitoneal) | >25 | >25 | >25 | >25 | >25 | **10.35** |
| 129 | JX06 |  | Selective covalent inhibitors | Mouse: $LD_{50}$ = 3250 mg/kg (oral) | **21.28** | >25 | >25 | >25 | >25 | >25 |
| 130 | Iodopropynyl butylcarbamate |  | Fungicides (wood) | Rat: $LD_{50}$ = 1.5 g/kg (oral) | **0.12** | **0.14** | **0.11** | **0.55** | **0.47** | **0.45** |
| 131 | Leflunomide |  | Non-steroidal anti-inflammatory | Mouse: $LD_{50}$ = 445 mg/kg (oral); Mouse: $LD_{50}$ = 185 mg/kg (intraperitoneal) | >25 | >25 | **15.21** | >25 | >25 | >25 |
| 132 | Efavirenz |  | Antivirals | Cynomolgus monkeys:dosages of 60 mg/kg daily (substantial malformations) | **8.43** | **6.78** | >25 | **27.13** | **16.77** | **16.93** |
| 133 | Sunitinib |  | Anti-tumour | Rat, mouse, and dog: 500 mg/kg (The maximally tolerated dose for when given orally) | >25 | >25 | **21.87** | >25 | >25 | >25 |
| 134 | Indometacin |  | Non-hormonal anti-inflammatory | Rats: $LD_{50}$ = 2.42 mg/kg (oral) | **13.85** | >25 | **4.46** | >25 | **22.52** | >25 |

**Table 1** (continued)

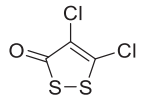
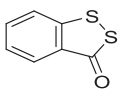
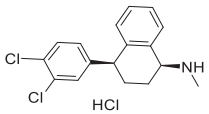
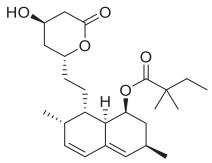
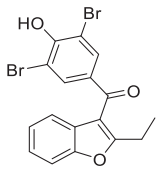
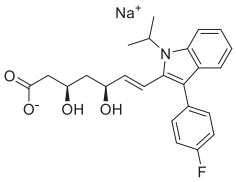
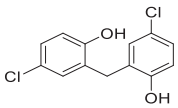
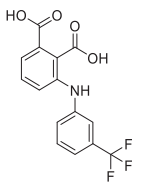
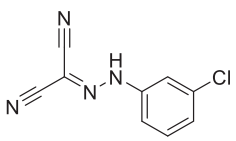
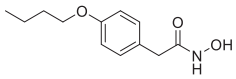
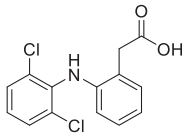
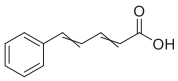
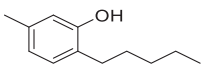
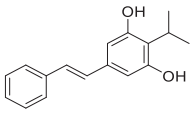
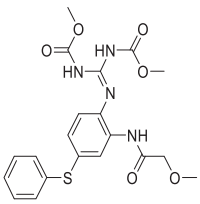
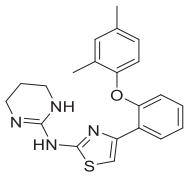
| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 135 | Dichloro-1,2-dithiacyclopentenone |  | Fungicides (multi-disciplinary) | Mouse: $LD_{50}$ = 13 mg/kg (intravenous) | **3.69** | **6.32** | **6.66** | **5.27** | **5.76** | **6.26** |
| 136 | 3*H*-1,2-Benzodithiol-3-one |  | Pharmaceutical intermediates | - | >25 | **22.43** | **18.95** | >25 | >25 | >25 |
| 137 | Sertraline hydrochloride |  | Antidepressants | Mouse: LDLo = 336 mg/kg (oral); Women: TDLo = 7 mg/kg/2W-I (oral) | **17.48** | **17.71** | **8.64** | **34.65** | **20.60** | **14.19** |
| 138 | Simvastatin |  | Lipid-lowering drugs | Mouse: $LD_{50}$ = 798 mg/kg (intraperitoneal); Mouse: $LD_{50}$ = 3 gm/kg (oral) | **15.43** | **9.21** | **8.15** | >25 | **7.16** | >25 |
| 139 | Benzbromarone |  | Lowering uric acid | Rat: $LD_{50}$ = 1230 mg/kg (subcutaneous); Rat: $LD_{50}$ = 248 mg/kg (oral); Mouse: $LD_{50}$ = 618 mg/kg (oral) | >25 | **10.75** | **1.95** | **12.48** | **9.18** | >25 |
| 140 | Fluvastatin sodium salt |  | Lipid-lowering drugs | - | >25 | **0.52** | **0.21** | >25 | **0.62** | **2.55** |
| 141 | Dichlorophen |  | Anti-microbial agents | Rat:$LD_{50}$ = 1683 mg/kg (oral) | **4.52** | **7.88** | **7.55** | **5.24** | **7.55** | **7.04** |
| 142 | Flufenamic acid |  | Anti-inflammatory | Mouse: $LD_{50}$ = 490 mg/kg (oral); Mouse: $LD_{50}$ = 620 mg/kg (subcutaneous) | **8.37** | **15.28** | **4.56** | **45.27** | **24.54** | **14.25** |
| 143 | Carbonyl cyanide 3-chloro- phenylhydrazone |  | A geroprotector; an antibacterial agent and an ionophore | Rat: LDLo = 50 mg/kg (subcutaneous); Mouse: LDLo = 8 mg/kg (intraperitoneal) | **0.53** | **0.57** | **0.38** | **4.33** | **6.07** | **4.69** |

**Table 1** (continued)

| No. | Compound name | Chemical structure | Main use | Toxicity | $EC_{50}$ (μg/mL) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 144 | Bufexamac |  | Non-steroidal anti-inflammatory | Rat: $LD_{50}$ = 3370 mg/kg (oral); Mouse: $LD_{50}$ = 1195 mg/kg (oral) | >25 | **21.95** | >25 | >25 | >25 | >25 |
| 145 | Diclofenac |  | Anti-inflammatory drugs | Mouse: $LD_{50}$ = 170 mg/kg (oral) | **6.63** | **13.34** | **3.18** | >25 | >25 | >25 |
| 146 | Phenylpenta-2,4-dienoic acid |  | Light sensitive compound | - | >25 | **17.94** | >25 | >25 | >25 | >25 |
| 147 | Amylmetacresol |  | Antiseptic; antifungal | Rat: $LD_{50}$ = 1500 mg/kg (oral) | **11.58** | **18.79** | **7.29** | **8.81** | >25 | >25 |
| 148 | Tapinarof |  | Antifungal drug | - | **9.55** | **12.32** | **14.99** | **11.95** | **14.20** | **14.44** |
| 149 | Febantel |  | Anthelmintic | Rat: $LD_{50}$ = 10605 mg/kg (oral); Mouse: $LD_{50}$ > 10 gm/kg (oral) | **0.15** | >25 | >25 | >25 | >25 | >25 |
| 150 | Abafungin |  | Antifungal drug | - | **3.05** | **0.39** | **18.66** | **3.37** | **0.47** | **1.80** |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

lowering blood pressure, anti-tumor, central nervous system, lowering blood glucose, lowering blood lipids, insect repellent and anti-microbial [28–32]. Therefore they show potential for application in medical treatment and agricultural insecticide. In previous studies, our team designed and synthesized a variety of quinoline alkaloid derivatives based on different structures of natural product alkaloids, and tested their activity against plant pathogenic fungi [33–40] (Table 2), which provided a theoretical basis and laid a solid foundation for the development and application of alkaloids. To further obtain a broader spectrum of effective anti-phytopathogenic fungal alkaloids, the 28 drugs with different biological functions were repositioned (Table 3), and 6 compounds with better anti-phytopathogenic fungal activities were obtained, as shown in Table 1 and Fig. 3. Among them, pitavastatin calcium had a relatively broad spectrum of activity against pathogenic fungi, particularly against *B. cinerea, P. capsici* and *F. oxysporum*, with $EC_{50}$ of less than 1 μg $ml^{-1}$. However, cabozantinib showed more excellent activity against *R. solani*, with $EC_{50}$ of 0.032 μg $ml^{-1}$, which may be the introduction of 1-methoxy-4-methylbenzene into the quinoline structure to enhance the antifungal activity. In addition, dequalinium chloride, mefloquine hydrochloride and bedaquiline showed potential against *B. cinerea* or *S. sclerotiorum*. Therefore, the quinoline alkaloids designed and

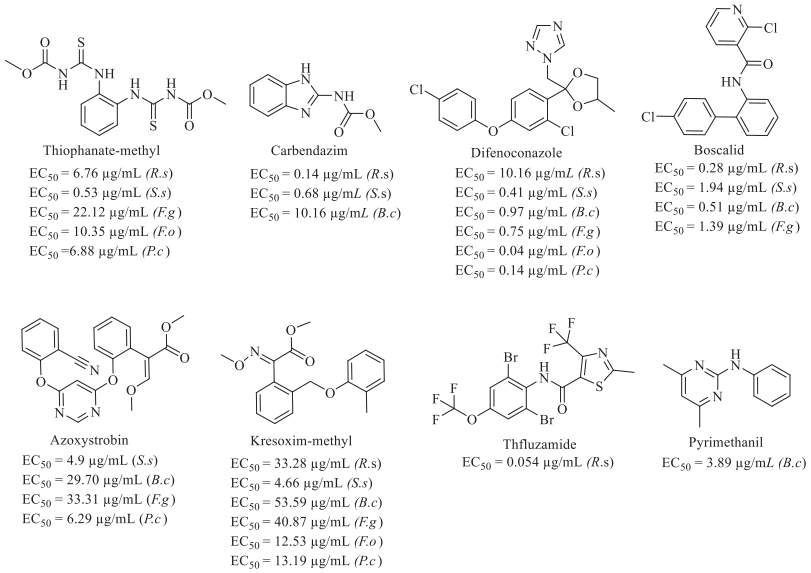



**Fig. 2** The $EC_{50}$ of fungicides against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

synthesized in our laboratory, as well as the repositioning of other functional alkaloids, we found that alkaloids have great potential in the field of agricultural disease control.

## Benzoimidazole/carbamate drugs

Benzimidazoles and their derivatives are an essential group of active agents in pesticides and pharmaceuticals with broad-spectrum biological activities, such as anticancer [41], antibacterial [42], antiviral [43] and antiparasitic [44]. Likewise, carbamates are a group of insecticides with outstanding bioactivity, which have properties such as rapid decomposition, short residual period and low bioaccumulation [45, 46]. On this basis, we screened 26 drugs against pathogenic fungi, as shown in Table 4, and screened out 11 drugs with excellent action, as shown in Table 1 and Fig. 4, which laid the foundation for searching for lead compounds with good activity.

The structure-activity relationship showed that drugs attached to the benzene ring to n-butyl had positive activity against *R. solani* and *S. sclerotiorum* with $EC_{50}$ of 0.051 μg $ml^{-1}$ and 0.16 μg $ml^{-1}$, respectively, while replacing the C atom in n-butyl with an S atom (fenbendazole) or O atom (oxibendazole) had an insignificant effect on activity. However, the S-atom in n-butyl was replaced by sulfur monoxide (albendazole S-oxide), significantly less active against both pathogens. The acetophenone structure (mebendazole) exhibited positive inhibition activity against *R. solani* and *S. sclerotiorum*. But the introduction of an F-atom into the acetophenone structure (flubendazole) significantly reduced the inhibition activity against *R. solani* ($EC_{50} > 25$ μg $ml^{-1}$). Surprisingly, the substitution of the acetophenone with the phenyl sulfane moiety (fenbendazole) showed significant inhibitory activity against *R. solani* and *S. sclerotiorum* with $EC_{50}$ of 0.007 μg $ml^{-1}$ and 0.097 μg $ml^{-1}$ respectively. However, the replacement of the S atom by the sulfoxide resulted in significantly reduced activity against both pathogens. By comparing the activity of benzimidazole/carbamate against plant pathogens, we found that iodopropynyl butylcarbamate was effective in expanding the antifungal spectrum and had promising activity against pathogenic fungi. Thus the repositioning of benzoimidazoles/carbamates can be an effective way to expand their application areas.

## Azole drugs

Azoles drugs have a wide range of applications in agriculture and medicine, such as low cost, availability and bioavailability, making azoles drugs of choice treating of fungal infections in most HIV/AIDS patients [47]. In agricultural production, triazole fungicides are mainly used to control plant fungal diseases caused by rust and mulberry powdery mildew pathogens due to their high efficiency and low toxicity [48]. The results indicate that azoles have broad antifungal activity as an essential backbone, which offers the possibility of developing new drugs. We screened 46 azole drugs (Table 5) against plant pathogens and obtained 16 drugs with optimal activity, as shown in Table 1 and Fig. 5.

The activity of bifonazole and clotrimazole showed that clotrimazole was more active than bifonazole against *R. solani* and *S. sclerotiorum*, which may be related to 1-benzyl-1*H*-imidazole. Econazole, vagistat, isoconazole nitrate and fenticonazole nitrate shared the basic structure (1-(2-(2,4-dichlorophenyl)-methoxy-2-ethyl)−1*H*-imidazole) and had comparable activity against all pathogens. All the compounds showed excellent activity against *P. capsici* with $EC_{50} < 0.06$ μg $ml^{-1}$, indicating that this basic structure played a vital role in anti-pathogenic fungi. Replacing the O atom in the basic structure above with an S atom (sulconazle

**Table 2** The $EC_{50}$ of quinoline alkaloids designed and synthesized in our laboratory against plant pathogenic fungi[a]

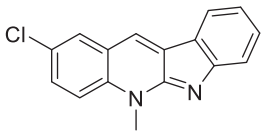
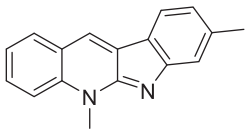
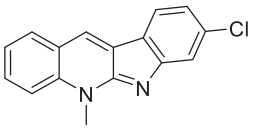
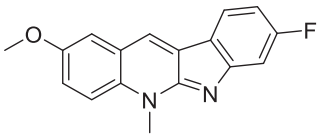
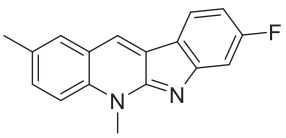
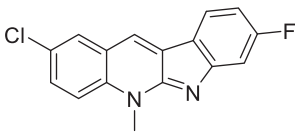
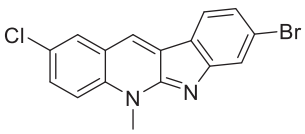
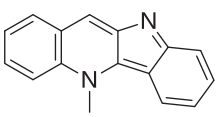
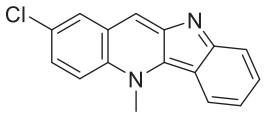
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 1 |  | 11.79 | 5.03 | 0.08 | 0.94 | - | - | 0.98 | [33] |
| 2 |  | 14.04 | 1.07 | 0.09 | 2.80 | - | - | 0.83 | [33] |
| 3 |  | 4.93 | 2.80 | 0.07 | 1.92 | - | - | - | [33] |
| 4 |  | 5.29 | 1.93 | 0.16 | 1.63 | - | - | - | [33] |
| 5 |  | 5.36 | 2.68 | 0.14 | 1.48 | - | - | - | [33] |
| 6 |  | 0.75 | 2.77 | 0.10 | 6.51 | - | - | - | [33] |
| 7 |  | å 30 | 8.44 | 0.09 | 19.50 | - | - | - | [33] |
| 8 |  | - | - | 0.050 | | - | - | - | [34] |
| 9 |  | - | - | 0.037 | | - | - | - | [34] |

**Table 2** (continued)

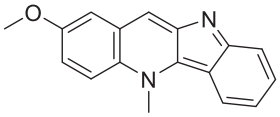
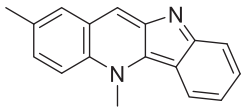
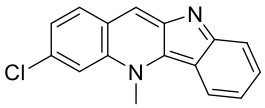
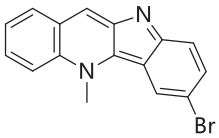
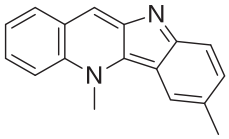
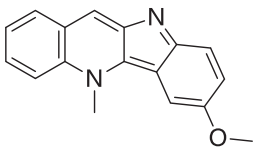
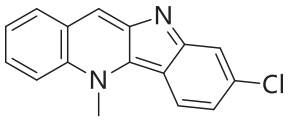
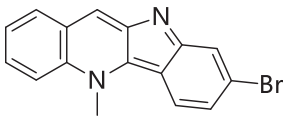
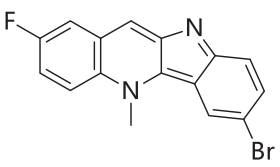
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 10 |  | - | - | 0.027 | | - | - | - | [34] |
| 11 |  | - | - | 0.034 | | - | - | - | [34] |
| 12 |  | - | - | 0.040 | | - | - | - | [34] |
| 13 |  | - | - | 0.061 | | - | - | - | [34] |
| 14 |  | - | - | 0.055 | | - | - | - | [34] |
| 15 |  | - | - | 0.086 | | - | - | - | [34] |
| 16 |  | - | - | 0.037 | | - | - | - | [34] |
| 17 |  | - | - | 0.032 | | - | - | - | [34] |
| 18 |  | - | - | 0.035 | | - | - | - | [34] |

**Table 2** (continued)

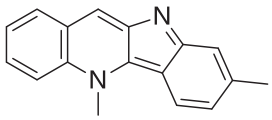
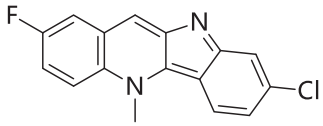
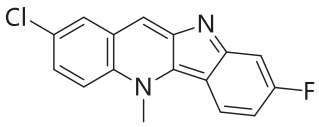
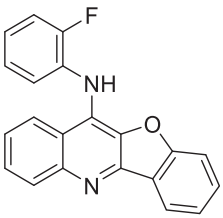
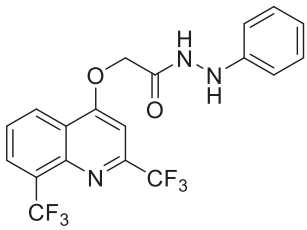
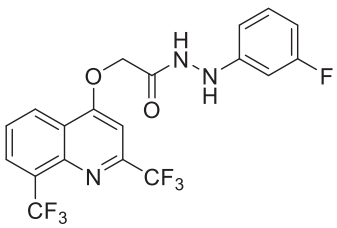
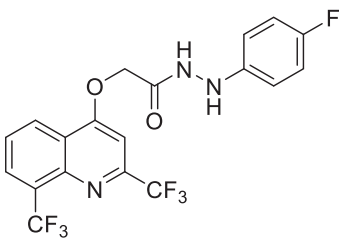
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 19 |  | - | - | 0.047 | | - | - | - | [34] |
| 20 |  | - | - | 0.068 | | - | - | - | [34] |
| 21 |  | - | - | 0.071 | | - | - | - | [34] |
| 22 |  | - | - | 1.32 | | - | - | - | [34] |
| 23 |  | 1.52 | 1.79 | 1.33 | 8.37 | - | - | - | [35] |
| 24 |  | 2.59 | 1.98 | 7.91 | 2.60 | - | - | - | [35] |
| 25 |  | 2.64 | 1.20 | 0.76 | 3.55 | - | - | - | [35] |

**Table 2** (continued)

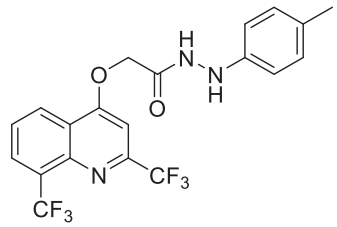
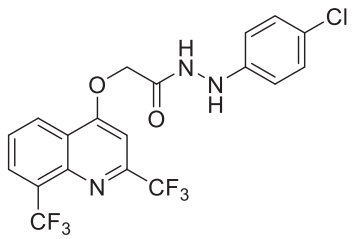
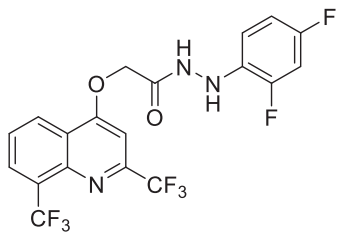
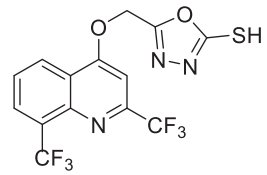
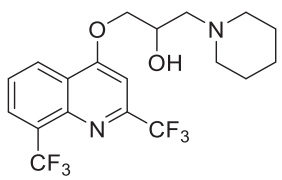
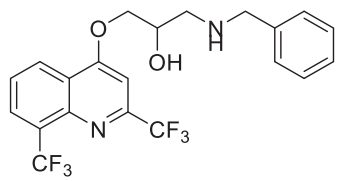
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 26 |  | 5.41 | 1.16 | 1.88 | 15.72 | - | - | - | [35] |
| 27 |  | 3.58 | 1.16 | 0.73 | 5.90 | - | - | - | [35] |
| 28 |  | 1.84 | 0.52 | 0.50 | 21.37 | - | - | - | [35] |
| 29 |  | >40 | 0.83 | 1.99 | 32.06 | - | - | - | [35] |
| 30 |  | - | - | 8.42 | 27.79 | - | - | - | [36] |
| 31 |  | 9.45 | 13.29 | 6.03 | 15.38 | - | - | - | [36] |

**Table 2** (continued)

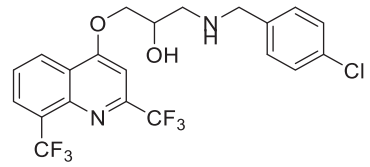
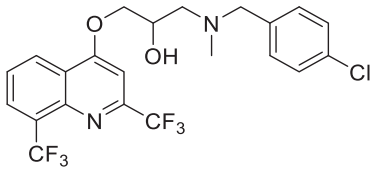
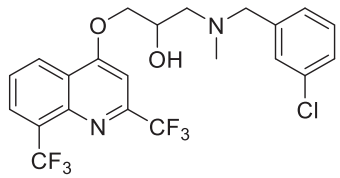
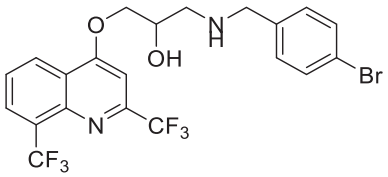
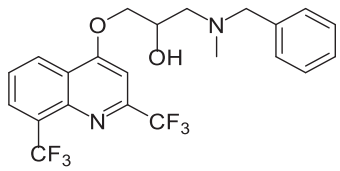
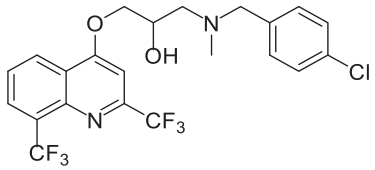
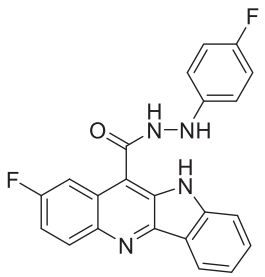
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 32 |  | - | - | 6.01 | 15.93 | - | - | - | [36] |
| 33 |  | - | - | 4.53 | 14.76 | - | - | - | [36] |
| 34 |  | - | - | 6.93 | 17.37 | - | - | - | [36] |
| 35 |  | - | - | 7.24 | 19.60 | - | - | - | [36] |
| 36 |  | - | - | 9.16 | 34.92 | - | - | - | [36] |
| 37 |  | 8.95 | 10.31 | | | - | - | - | [36] |
| 38 |  | 2.28 | 2.74 | 9.61 | 2.21 | - | - | - | [37] |

**Table 2** (continued)

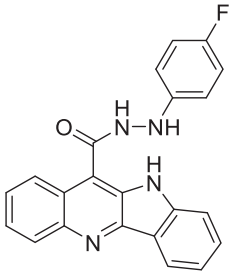
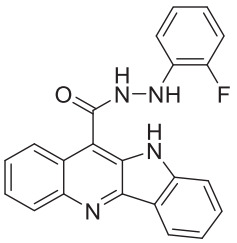
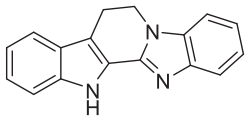
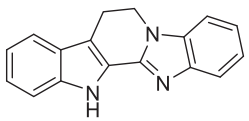
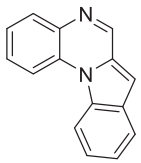
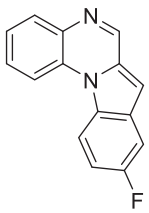
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 39 |  | 2.85 | 0.78 | 3.62 | 1.59 | - | - | - | [37] |
| 40 |  | 2.71 | - | 4.37 | 5.11 | - | - | - | [37] |
| 41 |  | - | - | 1.32 | - | - | - | - | [37] |
| 42 |  | 1.97 | 2.87 | 5.97 | - | 12.72 | - | - | [38] |
| 43 |  | 1.770 | - | - | 5.959 | - | - | - | [39] |
| 44 |  | 0.098 | - | - | - | - | - | - | [39] |

**Table 2** (continued)

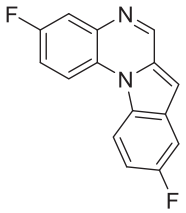
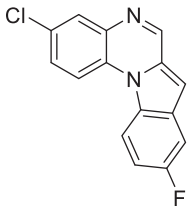
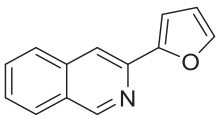
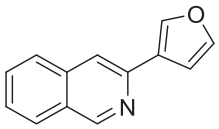
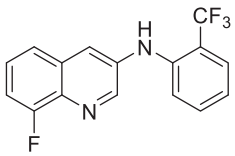
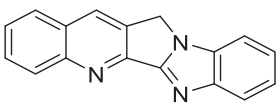
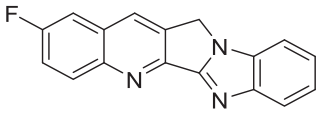
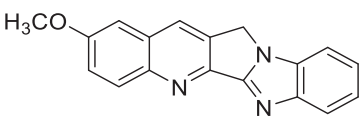
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 45 |  | 0.065 | - | - | - | - | - | - | [39] |
| 46 |  | 0.073 | - | - | - | - | - | - | [39] |
| 47 |  | 5.550 | 30.920 | 24.049 | 12.282 | 11.076 | 9.281 | - | [39] |
| 48 |  | 5.708 | 20.971 | 21.871 | 27.733 | 19.796 | 12.512 | - | [39] |
| 49 |  | 3.915 | 1.569 | 4.999 | 0.249 | 0.246 | 0.505 | - | [39] |
| 50 |  | - | - | 0.103 | - | - | - | - | [40] |
| 51 |  | - | - | 0.146 | - | - | - | - | [40] |
| 52 |  | - | - | 0.321 | - | - | - | - | [40] |

**Table 2** (continued)

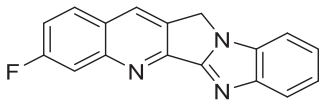
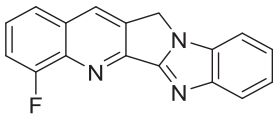
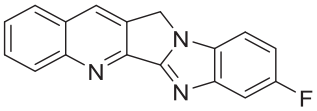
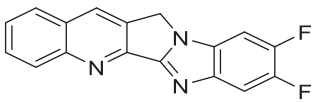
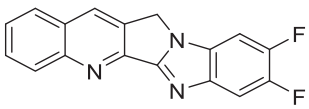
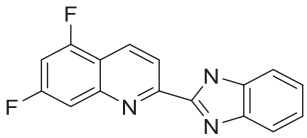
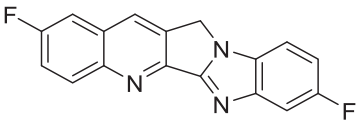
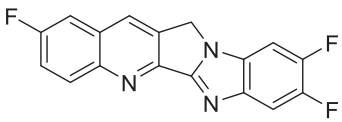
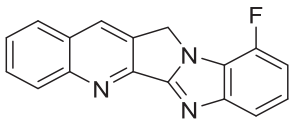
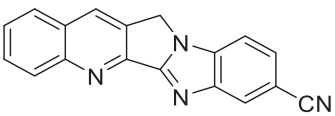
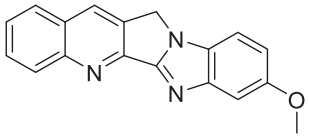
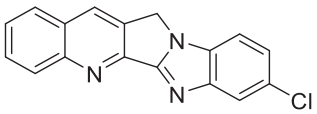
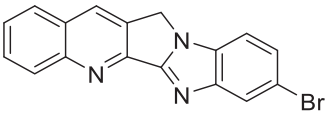
| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 53 |  | - | - | 0.069 | - | - | - | - | [40] |
| 54 |  | - | - | 0.036 | - | - | - | - | [40] |
| 55 |  | - | - | 0.050 | - | - | - | - | [40] |
| 56 |  | - | - | 0.066 | - | - | - | - | [40] |
| 57 |  | - | - | 0.093 | - | - | - | - | [40] |
| 58 |  | - | - | 0.191 | - | - | - | - | [40] |
| 59 |  | - | - | 0.042 | - | - | - | - | [40] |
| 60 |  | - | - | 0.229 | - | - | - | - | [40] |
| 61 |  | - | - | 0.047 | - | - | - | - | [40] |
| 62 |  | - | - | 0.133 | - | - | - | - | [40] |

**Table 2** (continued)

| No. | Chemical structures | $EC_{50}$(μg/mL) | | | | | | | References |
|---|---|---|---|---|---|---|---|---|---|
| | | *R. s* | *S. s* | *B. c* | *F. g* | *M. o* | *P. c* | *M. m* | |
| 63 |  | - | - | 0.108 | - | - | - | - | [40] |
| 64 |  | - | - | 0.245 | - | - | - | - | [40] |
| 65 |  | - | - | 0.397 | - | - | - | - | [40] |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*; *M.o*, *Magnaporthe oryzae*; *M.m*, *Mycosphaerella melonis*

nitrate) had little effect on the activity against the plant pathogens, suggesting that the basic structure was still the key to activity. Voriconazole, efinaconazole and isavuconazole had similar basic structures, but efinaconazole showed better activity than the other two drugs with $EC_{50}$ of 0.095 μg $ml^{-1}$ and 0.035 μg $ml^{-1}$ against *S. sclerotiorum* and *F. oxysporum*, respectively. The activity of ketoconazole against plant pathogens was significantly higher than that of terconazole, and the $EC_{50}$ was in the range of 0.12–2.34 μg $ml^{-1}$, which showed that 1-methyl-1*H*-imidazole was more effective than 1-methyl-1*H* − 1,2,4-triazole in this type of drug. However, not all drugs containing 1-methyl-1*H* − 1,2,4-triazole structures were less active against pathogens than 1-methyl-1*H*-imidazole. Itraconazole and posaconazole showed the strongest inhibitory activity against pathogens with $EC_{50} < 0.17$ μg $ml^{-1}$. In summary, the azole backbone is the main active group against plant pathogenic fungi with a view to repositioning old drugs for plant disease control.

## Isothiazolinone drugs

Isothiazolinone is a major industrial bactericide, antiseptic and anti-enzyme agent, with outstanding inhibition of mold, algae and other microorganisms [49]. Recently, a series of derivatives with anti-tuberculosis and lipase inhibitors have been designed and synthesized [50, 51]. We selected 26 isothiazolinones (Table 6) for screening against phytopathogenic fungi and obtained 8 drugs with good activity, which were briefly analysed in Table 1 and Fig. 6.

The 5-chloro-3-hydroxyisothiazole was the introduction of a Cl atom to the isothiazol-3-one structure, which significantly increased the activity against plant fungi with an $EC_{50}$ in the range of 0.98–4.06 μg $ml^{-1}$, but the introduction of a methyl group to 5-chloro-3-hydroxyisothiazole decreased the antifungal activity. The introduction of a Cl atom and octane on the 5-chloro-3-hydroxyisothiazole structure resulted in increasing activity against phytopathogenic fungi with an $EC_{50}$ in the range of 0.27–2.64 μg $ml^{-1}$. However, 2-octyl-2*H*-isothiazol-3-one showed comparable activity against plant pathogens compared to 4,5-dichloro-2-octyl-isothiazolone. Therefore, the introduction of octane in this structure may enhance the activity of phytopathogenic fungi, compared to 1,2-benzisothiazol-3(2*H*)-one, 2-methyl-1,2-benzothiazol-3(2*H*)-one and 6-fluoro-1,2-benzoisothiazol-3(2*H*)-one showed reduced antifungal activity, indicating that the introduction of substituents in this structure (benzoisothiazole) reduced the antifungal activity. Overall, the isothiazolinone structure is a potential lead compound against phytopathogenic fungi.

## Pyrimidine drugs

Pyrimidine derivatives play an important role in insecticide, fungicide, weed control, antiviral, anticancer, etc. [52, 53], and have been the focus of attention of major pesticide companies in the world. In this study, we screened 65 drugs (Table 7) against agropathogenic fungi and obtained 10 highly active drugs, as shown in Table 1 and Fig. 7.

**Table 3** In vitro antifungal activities (inhibition rate/%) of the quinoline alkaloids against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Quinine sulfate dihydrate | 100 | 12.85 ± 1.52 | 2.54 ± 1.47 | 20.62 ± 1.48 | 8.99 ± 0.94 | 12.65 ± 0.62 | 10.38 ± 1.66 |
| 2 | Hydroquinidine | 100 | 59.34 ± 1.66 | 14.43 ± 1.39 | 24.9 ± 1.37 | 22.31 ± 0.46 | 18.48 ± 0.52 | 16.97 ± 0.11 |
| 3 | Hydroquinidine 4-chlorobenzoate | 100 | 68.33 ± 0.43 | 81.23 ± 1.88 | 88.05 ± 1.74 | 28.96 ± 1.98 | 75.01 ± 0.4 | 70.48 ± 0.82 |
| 4 | Hydroquinine | 100 | 4.11 ± 1.30 | 7.55 ± 0.10 | 18.14 ± 1.85 | 12.60 ± 1.41 | 20.11 ± 2.05 | 16.88 ± 0.99 |
| 5 | Quinine hydrochloride dihydrate | 100 | 0 ± 0 | 0 ± 0 | 36.25 ± 1.69 | 6.19 ± 0.55 | 21.35 ± 0.51 | 17.87 ± 1.52 |
| 6 | Synephrine | 100 | 6.04 ± 0.32 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 20.33 ± 1.39 | 8.95 ± 0.56 |
| 7 | *N*-Benzylcinchoninium chloride | 100 | 11.11 ± 2.39 | 0 ± 0 | 10.52 ± 0.67 | 0 ± 0 | 18.63 ± 1.04 | 24.22 ± 1.89 |
| 8 | *N*-Benzylquininum chloride | 100 | 17.96 ± 0.42 | 0 ± 0 | 11.84 ± 1.57 | 13.68 ± 1.98 | 31.34 ± 1.05 | 0 ± 0 |
| 9 | *N*-Benzylcinchonidinium chloride | 100 | 13.45 ± 2.54 | 0 ± 0 | 5.48 ± 2.51 | 0 ± 0 | 28.23 ± 2.15 | 11.99 ± 1.34 |
| 10 | Cinchonine hydrochloride | 100 | 15.79 ± 2.26 | 0 ± 0 | 8.8 ± 0.45 | 0 ± 0 | 32.26 ± 0.48 | 18.13 ± 0.67 |
| 11 | Quinine dihydrochloride | 100 | 17.36 ± 0.79 | 0 ± 0 | 9.83 ± 0.63 | 0 ± 0 | 18.15 ± 1.97 | 17.45 ± 0.52 |
| 12 | Hydroquinidine hydrochloride | 100 | 17.47 ± 0.52 | 15.09 ± 1.9 | 15.03 ± 1.19 | 9.23 ± 1.65 | 24.29 ± 1.25 | 22.44 ± 0.93 |
| 13 | Cinchonine | 100 | 0 ± 0 | 8.77 ± 0.79 | 6.45 ± 0.82 | 10.84 ± 1.01 | 22.83 ± 0.31 | 21.69 ± 0.18 |
| 14 | Cinchonidine | 100 | 5.25 ± 1.39 | 0 ± 0 | 10.93 ± 1.82 | 0 ± 0 | 21.5 ± 0.33 | 0 ± 0 |
| 15 | Quinidine | 100 | 0 ± 0 | 30.52 ± 0.94 | 25.7 ± 1.18 | 20.59 ± 1.08 | 36.44 ± 1.85 | 20.12 ± 0.19 |
| 16 | Quinine | 100 | 47.17 ± 0.04 | 22.98 ± 1.37 | 17.18 ± 1.52 | 0 ± 0 | 17.81 ± 1.59 | 18.46 ± 0.34 |
| 17 | Quininne hydrochloride | 100 | 0 ± 0 | 14.32 ± 2.69 | 21.95 ± 1.82 | 8.75 ± 2.29 | 11.19 ± 0.31 | 13.03 ± 0.01 |
| 18 | (9 *S*) − 10,11-Dihydro-cinchonan-6',9-diol | 100 | 16.57 ± 1.03 | 0 ± 0 | 48.42 ± 0.92 | 30.04 ± 0.01 | 7.36 ± 0.78 | 16.26 ± 1.46 |
| 19 | Plaquenil | 100 | 0 ± 0 | 0 ± 0 | 23.73 ± 0.85 | 38.83 ± 0.17 | 12.78 ± 2.26 | 20.79 ± 1.08 |
| 20 | Mefloquine hydrochloride | 100 | 73.2 ± 2.53 | 0 ± 0 | 100 ± 0 | 60.71 ± 1.47 | 66.92 ± 0.30 | 71.23 ± 1.43 |
| 21 | Bedaquiline (fumarate) | 100 | 38.76 ± 1.73 | 86.4 ± 0.9 | 89.72 ± 0.7 | 30.38 ± 1.26 | 49.23 ± 0.05 | 55.99 ± 1.05 |
| 22 | Dequalinium chloride | 100 | 47.29 ± 0.44 | 100 ± 0 | 100 ± 0 | 37.83 ± 0.29 | 68.18 ± 0.82 | 97.11 ± 0.01 |
| 23 | Lenvatinib | 100 | 66.06 ± 0.39 | 37.28 ± 1.56 | 11.86 ± 0.11 | 21.69 ± 1.02 | 22 ± 0.76 | 0 ± 0 |
| 24 | Cabozantinib | 100 | 100 ± 0 | 14.81 ± 1.01 | 58.71 ± 2.27 | 18.32 ± 0.14 | 18.28 ± 1.23 | 23.91 ± 1.95 |
| 25 | Primaquine diphosphate | 100 | 8.91 ± 0.44 | 48.57 ± 1.02 | 35.52 ± 2.75 | 0 ± 0 | 15.75 ± 0.51 | 0 ± 0 |
| 26 | Quinoxyfen | 100 | 92.45 ± 0.09 | 59.4 ± 1.16 | 29.25 ± 1.51 | 61.41 ± 1.22 | 34.02 ± 0.02 | 43.08 ± 0.13 |
| 27 | Pitavastatin calcium | 100 | 55.22 ± 1.2 | 68.0 ± 1.24 | 100 ± 0 | 74.07 ± 0.87 | 95.94 ± 0.28 | 97.4 ± 0.08 |
| 28 | Decoquinate | 100 | 16.51 ± 0.24 | 0 ± 0 | 25.69 ± 0.17 | 0 ± 0 | 0 ± 0 | 0 ± 0 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

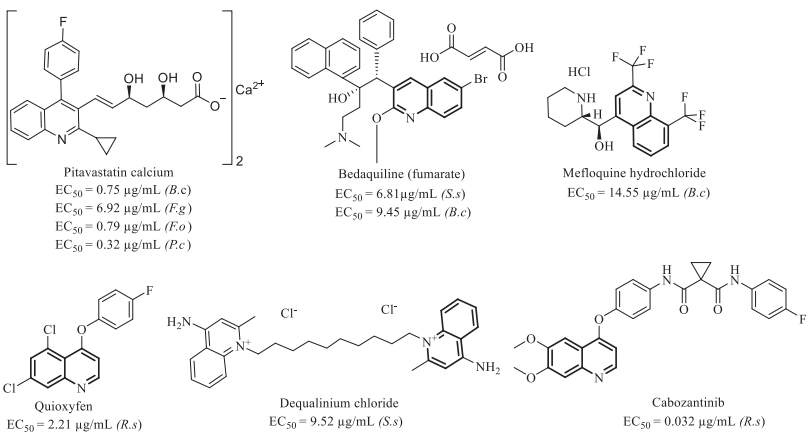



**Fig. 3** The $EC_{50}$ of quinoline alkaloids against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

**Table 4** In vitro antifungal activities (inhibition rate/%) of the benzimidazole/carbamate drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Omeprazole | 100 | 0 ± 0 | 7.07 ± 1.45 | 30.42 ± 1.88 | 11.72 ± 0.07 | 20.91 ± 0.63 | 28.2 ± 0.19 |
| 2 | Esomeprazole magnesium | 100 | 7.53 ± 1.11 | 0 ± 0 | 21.85 ± 1.25 | 14.72 ± 2.61 | 22.89 ± 0.36 | 24.33 ± 1.42 |
| 3 | Ufiprazole | 100 | 51.42 ± 1.75 | 27.93 ± 0.7 | 27.72 ± 0.25 | 36.05 ± 1.75 | 52.05 ± 0.5 | 63.33 ± 0.52 |
| 4 | Lansoprazole | 100 | 36.07 ± 1.36 | 32.07 ± 1.59 | 24.4 ± 2.55 | 23.01 ± 2.23 | 36.26 ± 1.07 | 49.72 ± 0.73 |
| 5 | Lansoprazole sulphide | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 10.23 ± 1.83 |
| 6 | R-(+)-lansoprazole | 100 | 40.35 ± 0.72 | 0 ± 0 | 22.89 ± 0.9 | 5.69 ± 0.49 | 39.58 ± 1.56 | 51.81 ± 1.09 |
| 7 | Ilaprazole (IY 81149) | 100 | 43.74 ± 1.99 | 22.9 ± 1.09 | 59.26 ± 0.78 | 12.95 ± 0.83 | 43 ± 0.32 | 49.98 ± 0.91 |
| 8 | Pantoprazole sodium | 100 | 7.46 ± 1.34 | 5.90 ± 1.11 | 18.55 ± 1.81 | 0 ± 0 | 24.34 ± 0.44 | 27.55 ± 1.53 |
| 9 | Pantoprazole thioether | 100 | 67.27 ± 0.31 | 11.75 ± 1.86 | 35.38 ± 0.25 | 32.94 ± 1.03 | 53.25 ± 0.68 | 60.46 ± 1.38 |
| 10 | Rabeprazole sulphide | 100 | 33.15 ± 1.16 | 0 ± 0 | 23.75 ± 1.1 | 63.97 ± 1.39 | 54.88 ± 1.81 | 56.38 ± 1.41 |
| 11 | Azilsartan | 100 | 0 ± 0 | 31.25 ± 1.32 | 19.15 ± 1.58 | 13.50 ± 2.16 | 5.33 ± 1.40 | 35.35 ± 1.16 |
| 12 | Telmisartan | 100 | 70.28 ± 0.97 | 82.22 ± 1.08 | 86.19 ± 0.81 | 51.44 ± 0.45 | 80.08 ± 1.94 | 80.95 ± 1.41 |
| 13 | Candesartan cilexetil | 100 | 0 ± 0 | 9.73 ± 0.21 | 0 ± 0 | 22.37 ± 0.8 | 8.77 ± 1.55 | 6.1 ± 1.14 |
| 14 | Dabigatran etexilate | 100 | 26.37 ± 1.92 | 72.09 ± 0.16 | 76.94 ± 1.16 | 0 ± 0 | 13.68 ± 0.7 | 36.76 ± 1.2 |
| 15 | Pimobendan | 100 | 0 ± 0 | 19.52 ± 2.91 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 11.42 ± 1.41 |
| 16 | Parbendazole | 100 | 97.34 ± 0.58 | 97.98 ± 0.38 | 0 ± 0 | 31.76 ± 0.7 | 35.58 ± 0.28 | 28.5 ± 0.14 |
| 17 | Oxfendazole | 100 | 100 ± 0 | 99.02 ± 0.29 | 54.09 ± 1.77 | 49.68 ± 1.72 | 40.01 ± 0.41 | 42.43 ± 5.07 |
| 18 | Fenbendazole | 100 | 100 ± 0 | 98.08 ± 0.33 | 0 ± 0 | 0 ± 0 | 38.82 ± 1.07 | 17.15 ± 1.13 |
| 19 | Albendazole | 100 | 100 ± 0 | 100 ± 0 | 0 ± 0 | 54.52 ± 0.06 | 80.64 ± 0.61 | 75.77 ± 0.69 |
| 20 | Mebendazole | 100 | 100 ± 0 | 100 ± 0 | 0 ± 0 | 47.42 ± 0.23 | 68.64 ± 1.8 | 55.36 ± 0.27 |
| 21 | Oxibendazole | 100 | 91.69 ± 0.8 | 100 ± 0 | 16.97 ± 2.54 | 33.15 ± 1.36 | 68.78 ± 0.57 | 57.89 ± 0.52 |
| 22 | Flubendazole | 100 | 30.49 ± 0.34 | 92.34 ± 1.09 | 8.35 ± 0.66 | 26.69 ± 1.43 | 39.62 ± 0.45 | 21.51 ± 0.87 |
| 23 | Albendazole S-oxide | 100 | 96.03 ± 0.47 | 100 ± 0 | 14.9 ± 1.51 | 47.13 ± 1.55 | 18.35 ± 0.72 | 19.11 ± 1.45 |
| 24 | Triclabendazole | 100 | 79.69 ± 0.03 | 74.19 ± 0.48 | 92.65 ± 1.17 | 72.23 ± 0.53 | 67.35 ± 0.58 | 67.48 ± 1.91 |
| 25 | Bilastin | 100 | 0 ± 0 | 0 ± 0 | 7.95 ± 0.61 | 11.95 ± 0.33 | 0 ± 0 | 8.15 ± 1.63 |
| 26 | Selumetinib | 100 | 6.49 ± 0.46 | 23.33 ± 1.96 | 39.24 ± 0.67 | 29.58 ± 0.60 | 7.38 ± 0.16 | 10.98 ± 0.47 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

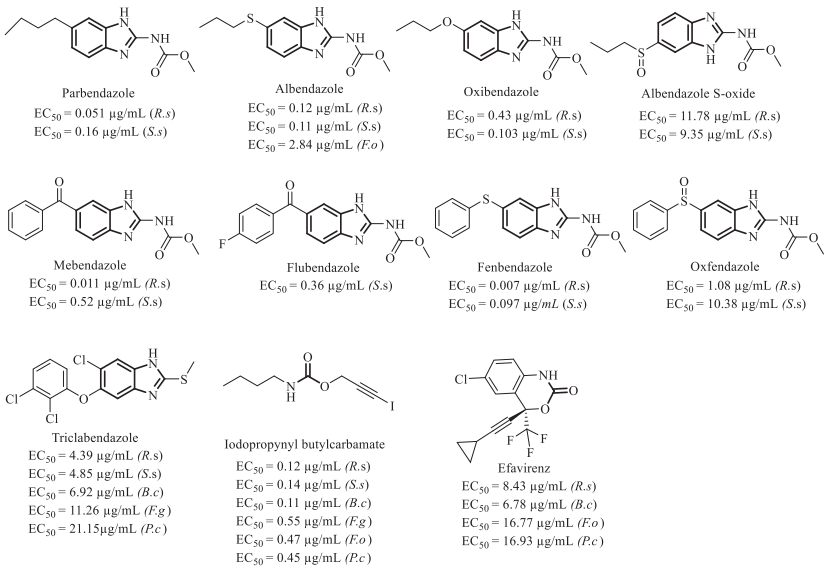



**Fig. 4** The $EC_{50}$ of benzoimidazole/carbamate drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

**Table 5** In vitro antifungal activities (inhibition rate/%) of the azole drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Ronidazole | 100 | 8.24 ± 1.98 | 12.57 ± 2.29 | 0 ± 0 | 14.20 ± 2.25 | 12.55 ± 1.30 | 9.98 ± 0.39 |
| 2 | Benzoylmetronildazole | 100 | 43.63 ± 0.32 | 21.18 ± 0.45 | 36.45 ± 1.33 | 27.64 ± 3.77 | 0 ± 0 | 13.05 ± 1.21 |
| 3 | Daclatasvir | 100 | 0 ± 0 | 33.05 ± 2.09 | 26.45 ± 0.25 | 0 ± 0 | 0 ± 0 | 6.01 ± 0.72 |
| 4 | Econazole | 100 | 89.76 ± 0.81 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 5 | Itraconazole | 100 | 25.09 ± 2.31 | 92.16 ± 0.79 | 96.0 ± 0.64 | 17.29 ± 3.32 | 87.4 ± 0.86 | 75.9 ± 1.17 |
| 6 | Posaconazol | 100 | 11.99 ± 0.35 | 100 ± 0 | 100 ± 0 | 66.44 ± 1.41 | 95.98 ± 0.32 | 100 ± 0 |
| 7 | Letrozole | 100 | 14.94 ± 1.23 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 13.15 ± 0.01 | 0 ± 0 |
| 8 | Anastrozole | 100 | 7.62 ± 0.5 | 47.48 ± 1.96 | 0 ± 0 | 0 ± 0 | 10.03 ± 0.78 | 0 ± 0 |
| 9 | Ketoconazole | 100 | 66.19 ± 2.1 | 100 ± 0 | 100 ± 0 | 94.01 ± 0.29 | 100 ± 0 | 100 ± 0 |
| 10 | Bifonazole | 100 | 89.17 ± 0.25 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 11 | KP 103 | 100 | 88.68 ± 0.93 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 12 | Isoconazole nitrate | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 97.83 ± 0.26 | 96 ± 0.75 | 100 ± 0 |
| 13 | Fenticonazole nitrate | 100 | 89.38 ± 0.04 | 97.18 ± 2.01 | 96.71 ± 0.46 | 76.8 ± 0.28 | 88.36 ± 0.41 | 94.72 ± 0.21 |
| 14 | Isavuconazole | 100 | 68.78 ± 0.49 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 15 | Atipamezole hydrochloride | 100 | 0 ± 0 | 22.85 ± 0.25 | 0 ± 0 | 13.28 ± 0.16 | 7.84 ± 1.13 | 35.77 ± 0.75 |
| 16 | Valsartan | 100 | 0.91 ± 0.21 | 0.70 ± 0.1 | 1.30 ± 0.3 | 3.09 ± 0.72 | 1.01 ± 0.02 | 0.98 ± 0.2 |
| 17 | Deferasirox | 100 | 94.51 ± 0 | 72.91 ± 0.62 | 89.16 ± 0.93 | 38.23 ± 0.44 | 80.91 ± 0.33 | 81.06 ± 0.67 |
| 18 | Topiroxostat | 100 | 10.82 ± 1.87 | 36.38 ± 1.65 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 19 | Ribavirin | 100 | 40.83 ± 0.48 | 20.75 ± 1.49 | 0 ± 0 | 0 ± 0 | 7.23 ± 0.24 | 10.86 ± 1.54 |
| 20 | Levamisole hydrochloride | 100 | 13.37 ± 1.48 | - | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 21 | Temozolomideacid | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 5.05 ± 0.71 | 0 ± 0 | 0 ± 0 |
| 22 | Imiquimod | 100 | 16.28 ± 0.81 | 13.87 ± 1.43 | 52.68 ± 0.77 | 30.09 ± 3 | 17.03 ± 2.04 | 23.49 ± 1.41 |
| 23 | Miconazole | 100 | 23.60 ± 1.48 | 13.03 ± 1.52 | 8.60 ± 0.71 | 25.13 ± 1.49 | 17.79 ± 1.96 | 11.85 ± 1.02 |
| 24 | Atipamezole hydrochloride | 100 | 0 ± 0 | 22.85 ± 0.25 | 0 ± 0 | 13.28 ± 0.16 | 7.84 ± 1.13 | 35.77 ± 0.75 |
| 25 | Levamisole hydrochloride | 100 | 13.37 ± 1.48 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 26 | Temozolomide | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 8.21 ± 1.86 | 0 ± 0 |
| 27 | (+)-Pilocarpine hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 3.03 ± 1.05 |
| 28 | Metronidazole | 100 | 4.66 ± 1.79 | 12.02 ± 2.01 | 0 ± 0 | 13.67 ± 1.97 | 7.90 ± 0.59 | 11.08 ± 0.91 |
| 29 | Ornidazole | 100 | 2.87 ± 0.38 | 5.37 ± 1.47 | 0 ± 0 | 7.14 ± 3.41 | 0.00 ± 0.00 | 11.87 ± 0.6 |
| 30 | Tinidazole | 100 | 7.04 ± 0.98 | 28.46 ± 1.86 | 0 ± 0 | 17.15 ± 2.81 | 19.13 ± 0.89 | 0 ± 0 |
| 31 | Clotrimazole | 100 | 91.15 ± 1.05 | 100 ± 0 | 100 ± 0 | 99.65 ± 0.09 | 100 ± 0 | 100 ± 0 |
| 32 | Fluconazole | 100 | 59.15 ± 0.13 | 92.03 ± 0.01 | 94.14 ± 0.29 | 0 ± 0 | 67.88 ± 0 | 100 ± 0 |
| 33 | Voriconazole | 100 | 87.55 ± 0.84 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 34 | Sulconazle nitrate | 100 | 85.21 ± 2.1 | 100 ± 0 | 100 ± 0 | 85.69 ± 0.73 | 93.27 ± 0.53 | 100 ± 0 |
| 35 | Vagistat | 100 | 88.03 ± 1.71 | 100 ± 0 | 100 ± 0 | 97.06 ± 0.54 | 100 ± 0 | 100 ± 0 |
| 36 | Butoconazole nitrate | 100 | 95.27 ± 0.02 | 100 ± 0 | 100 ± 0 | 82.53 ± 0.1 | 87.75 ± 0.17 | 100 ± 0 |
| 37 | Terconazole | 100 | 51.4 ± 1.55 | 98.69 ± 0.01 | 82.17 ± 1.29 | 39.07 ± 0.08 | 72.57 ± 0 | 96.08 ± 0.29 |
| 38 | Elubiol | 100 | 74.86 ± 1.21 | 100 ± 0 | 100 ± 0 | 75.93 ± 0.75 | 100 ± 0 | 100 ± 0 |
| 39 | Luliconazole | 100 | 95.48 ± 0.27 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 40 | Deracoxib | 100 | 39.23 ± 1.39 | 48.42 ± 1.72 | 60.7 ± 1.71 | 55.03 ± 1.32 | 20.31 ± 1.27 | 48.38 ± 0.23 |
| 41 | Cilostazol | 100 | 17.94 ± 0.54 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 27.18 ± 2.23 | 16.35 ± 1.76 |
| 42 | Ruxolitinib | 100 | 79.21 ± 1.87 | 42.33 ± 0.47 | 79.79 ± 0.01 | 53.7 ± 0.69 | 70.78 ± 0.97 | 72.32 ± 0.45 |
| 43 | Baricitinib | 100 | 18.12 ± 2.51 | 24.48 ± 1.49 | 14.74 ± 2.84 | 54.43 ± 0.99 | 48.29 ± 1.21 | 33 ± 0.61 |
| 44 | Cimetidine | 100 | 11.20 ± 0.92 | 8.73 ± 2.54 | 10.76 ± 1.73 | 3.70 ± 0.33 | 7.47 ± 0.79 | 6.24 ± 0.68 |
| 45 | Pemirolast potassium | 100 | 8.78 ± 0.63 | 15.20 ± 1.22 | 25.73 ± 1.46 | 18.05 ± 2.53 | 14.51 ± 0.32 | 9.01 ± 0.17 |
| 46 | Aprepitant | 100 | 60.09 ± 3.08 | 26.51 ± 1.65 | 62.67 ± 1.75 | 30.45 ± 1.11 | 0 ± 0 | 6.16 ± 1.27 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

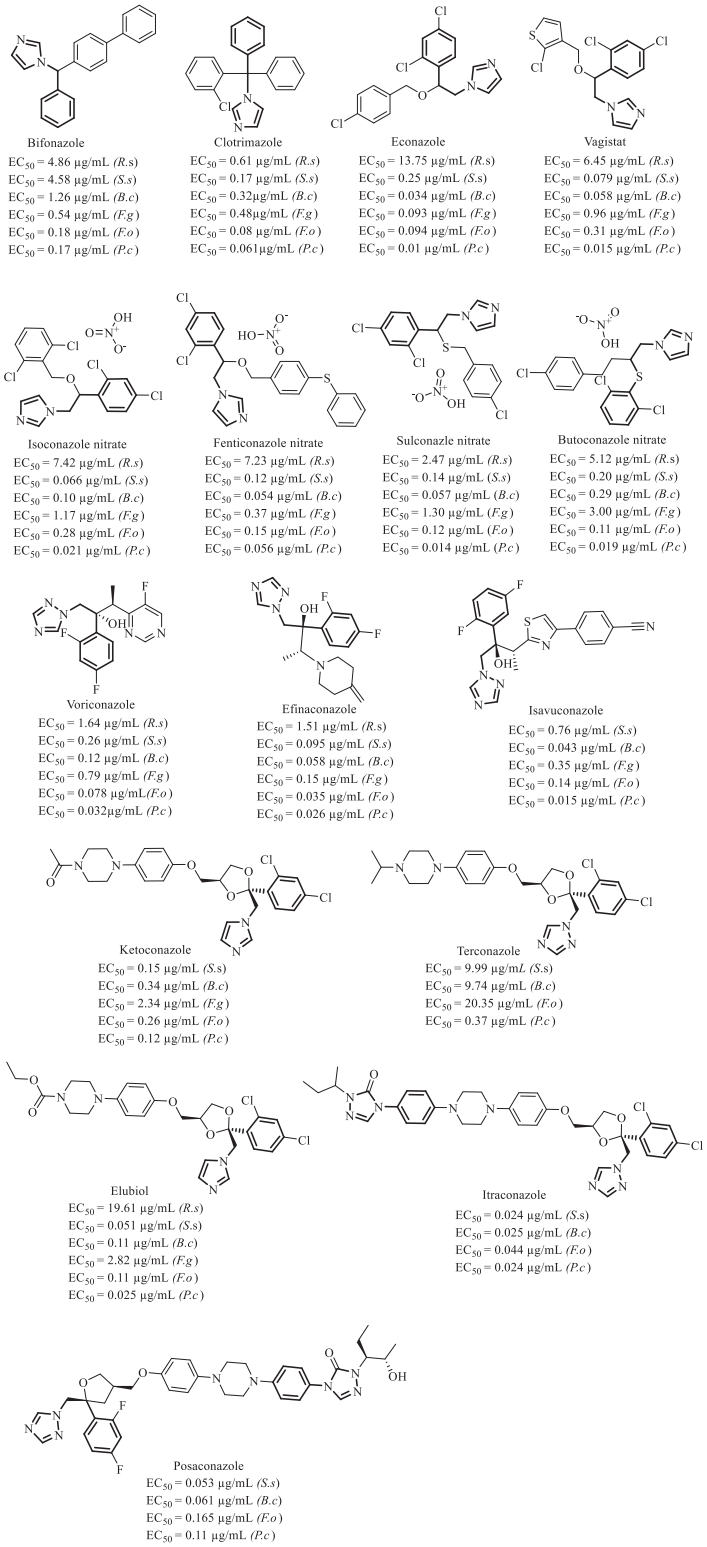



**Fig. 5** The $EC_{50}$ of azole drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

Taking 5-fluorouracil as a backbone, a molecule ((2R,3S,4R,5S)−2-(hydroxymethyl)-tetrahydrofuran-3,4-diol) was introduced to become 5-fluorouridine, which significantly enhanced its activity against plant pathogenic fungi. Compared with 5-fluorouridine, the structure of floxuridine was one less OH group, but it was slightly less active against *S. sclerotiorum* and *B. cinerea*. It showed that the introduction of this moiety directly affected the anti-pathogenic fungal activity of the compound. Compared to ganciclovir, 2'-deoxyguanosine was less active against *S. sclerotiorum*. The pyrimidine-4-amine-

**Table 6** In vitro antifungal activities (inhibition rate/%) of the isothiazolinone drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Methazolamide | 100 | 69.21 ± 0.02 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 2 | Acetazolamide | 100 | 0 ± 0 | 0 ± 0 | 63.74 ± 2.25 | 0 ± 0 | 0 ± 0 | 4.45 ± 0.34 |
| 3 | Nizatidine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 4 | Famotidine | 100 | 0 ± 0 | 0.45 ± 0.64 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 5 | 2-Mercaptobenzothiazolyl | 100 | 65.82 ± 0.96 | 83.59 ± 1.46 | 65.24 ± 1.22 | 62.11 ± 0.01 | 69.98 ± 0.31 | 74.35 ± 0.08 |
| 6 | Ethyl 2-(2-aminothiazol-4-yl)glyoxylate | 100 | 16.99 ± 2.38 | 0 ± 0 | 16.1 ± 1.63 | 6.67 ± 2.95 | 0 ± 0 | 0 ± 0 |
| 7 | Ceftazidime intermediate | 100 | 7.08 ± 0.34 | 0 ± 0 | 41.25 ± 0.11 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 8 | 6-Aminopenicillanic acid | 100 | 0 ± 0 | 11.02 ± 2.58 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 11.12 ± 0.13 |
| 9 | Aztreonam | 100 | 0 ± 0 | 16.04 ± 1.4 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 11.11 ± 0.15 |
| 10 | 4,5-Dichloro-2-octyl-isothiazolone | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 11 | 2-Octyl-2*H*-isothiazol-3-one | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 12 | Isothiazolinone chloride | 100 | 79.46 ± 1.97 | 93.27 ± 0.27 | 38.58 ± 1.98 | 41.23 ± 1.33 | 51.44 ± 1.12 | - |
| 13 | 2-Methyl-4-isothiazolin-3-one | 100 | 72.09 ± 1.30 | 72.63 ± 1.77 | 54.44 ± 1.20 | 44.23 ± 1.92 | 42.64 ± 2.00 | - |
| 14 | 1,2-Benzisothiazol-3(2*H*)-one | 100 | 83.43 ± 0.73 | 90.98 ± 0.55 | 84.89 ± 2.28 | 86.18 ± 1.50 | 75.43 ± 0.40 | 100 ± 0 |
| 15 | 2-Methyl-1,2-benzothiazol-3(2*H*)-one | 100 | 92.23 ± 0.28 | 98.84 ± 0.11 | 66.18 ± 0.18 | 58.19 ± 0.86 | 75.3 ± 0.08 | 54.07 ± 0.53 |
| 16 | 6-Fluoro-1,2-benzoisothiazol-3(2*H*)-one | 100 | 85.62 ± 0.66 | 99.33 ± 0.26 | 85.92 ± 2.97 | 66.57 ± 1.78 | 60.23 ± 0.93 | 42.70 ± 0.22 |
| 17 | Benzo[D]isoxazol-3-ol | 100 | 23.85 ± 1.65 | 87.8 ± 0.47 | 48.81 ± 0.32 | 53.79 ± 1.68 | 87.5 ± 0.24 | - |
| 18 | 6-Chlorobenzo[D]isoxazol-3-ol | 100 | 42.85 ± 1.56 | 37.05 ± 1.08 | 22.18 ± 1.18 | 37.61 ± 0.23 | 43.75 ± 0.47 | - |
| 19 | 3-Indazolinone | 100 | 17.2 ± 1.1 | 0 ± 0 | 3.60 ± 0.57 | 0 ± 0 | 15.27 ± 1.12 | - |
| 20 | 6-Bromo-1*H*-indazol-3-ol | 100 | 24.83 ± 1.41 | 26.94 ± 1.12 | 8.63 ± 1.21 | 0 ± 0 | 11.06 ± 0.43 | - |
| 21 | Saccharin | 100 | 6.45 ± 1.19 | 19.07 ± 1.80 | 0 ± 0 | 0 ± 0 | 0 ± 0 | - |
| 22 | 6-Nitro-1,2-benzisothiazolin-3-one 1,1-dioxide | 100 | 9.43 ± 1.17 | 27.63 ± 1.90 | 0 ± 0 | 0 ± 0 | 0 ± 0 | - |
| 23 | 3-(1-Piperazinyl)-1,2-benzisothiazole | 100 | 12.18 ± 1.49 | 39.65 ± 1.57 | 7.89 ± 0.77 | 18.18 ± 1.92 | 13.91 ± 1.33 | 31.8 ± 0.2 |
| 24 | Isothiazol-3-one | 100 | 95.80 ± 0.05 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 85.07 ± 0.64 | 100 ± 0 |
| 25 | 5-Chloro-3-hydroxyisothiazole | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 26 | Febuxostat | 100 | 79.65 ± 1.17 | 75.35 ± 0.05 | 63.28 ± 1.73 | 44.01 ± 1.5 | 73.85 ± 0.22 | 60.55 ± 1.12 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

based compounds showed inhibitory activity against *B. cinerea* with an $EC_{50}$ range of 2.29–13.52 μg $ml^{-1}$. Both dabrafenib and sulfatinib contain *N*-methylmethanesulfonamide, which were active against *S. sclerotiorum* and *B. cinerea*, and had superior antifungal activity to sulfamitinib. Thus, the activity of pyrimidine analogues against phytopathogenic fungi are based on the pyrimidine structure with other moieties, which are beneficial to improve the activity and can be used as candidate lead compounds against plant pathogenic fungi.

## Pyridine drugs

In agriculture, pyridines are used as insecticides, herbicides and plant growth regulators. In particular, in herbicides, a number of highly effective and low-toxicity varieties have been developed, such as pyrimethanesulfuron, pirimicarb and acetamiprid [54]. In this study, 31 drugs that have not yet been applied against plant pathogenic fungi were screened, as shown in Table 8, and 12 drugs with application potential were finally screened out, as shown in Table 1. We aim to obtain lead structures or drugs with triple action of insecticide, herbicide, and disease control.

As shown in Fig. 8, nilvadipine, nimodipine, amlodipine and amlodipine maleate belonged to the dihydropyridine group and showed activity against *B. cinerea*, among which nilvadipine had the strongest activity with an $EC_{50}$ of 5.74 μg $ml^{-1}$. This may be related to the electron-absorbing groups attached to the pyridine ring. Amlodipine maleate was a salt form of amlodipine with a slightly increased activity against *B. cinerea*. Liranaftate and pyributicarb had broad-spectrum and excellent activity against plant phytopathogens. Compared with liranaftate and pyributicarb, the activity of benzene ring-linked the cyclohexane ring with benzene ring-linked tert-butyl ring was one order of magnitude higher against five pathogenic fungi except *F. oxysporum*, among which the activity against *B. cinerea* was

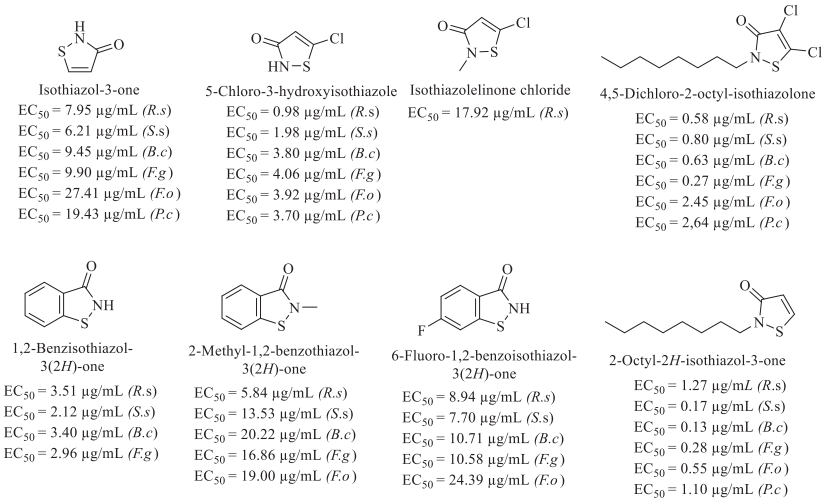



**Fig. 6** The $EC_{50}$ of isothiazolinone drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

the best, with $EC_{50}$ of 0.004 μg $ml^{-1}$. The results suggest that pyridines, especially liranaftate and pyributicarb are promising for repositioning as fungicides for the control of plant pathogens.

## Piperidine/Piperazine drugs

Piperidine ring and piperazine group are often introduced into many drug molecules to improve the pharmacokinetic properties by effectively adjusting the ratio of lipid-water distribution and acid-base balance of drugs, which improves the bioavailability of drug molecules and drug efficacy [55–58]. In this study, mainly 65 antipsychotics were used to screen agricultural fungi, as shown in Table 9, and 18 drugs with relatively good activity were obtained as shown in Table 1.

As shown in Fig. 9, the drugs with piperazine and piperidine structures include two forms of *N*-methyl group on the outside and inside, and the two forms of piperazine drugs have little difference against antifungal activity. But loratadine and penfluridol had excellent activity with $EC_{50}$ of 6.19 μg $ml^{-1}$ and 6.59 μg $ml^{-1}$ against *R. solani* and *S. sclerotiorum*, respectively. Compared with the piperazine structure with the *N*-methyl position on the outside, the piperidine structure had better anti-phytopathogenic activity. Among them, trifluoperazine not only had significant antifungal activity but also expanded the antifungal spectrum. In addition, ponatinib had the best activity against *R. solani*. The $EC_{50}$ was 0.017 μg $ml^{-1}$. Therefore, piperazine and piperidine compounds have the potential to develop drugs against agricultural pathogenic fungi.

## Ionic liquids

Ionic liquids are considered a friendly solvent and commonly used in the extraction of natural products. They are mainly classified as quaternary ammonium ionic liquids, pyridine ionic liquids, quaternary phosphate ionic liquids and imidazole ionic liquids [59, 60]. This study used 37 ionic liquids to inhibit plant pathogens as shown in Table 10. According to Table 1 and Fig. 10, 15 potential drugs were briefly analyzed in order to apply them to agriculture.

In all ionic liquids, we found that the longer the carbon chain of the drug, the better the activity against *S. sclerotiorum*. 1-Dodecyl-3-methylimidazolium chloride products better active with $EC_{50}$ of 6.12 μg $ml^{-1}$ against *S. sclerotiorum*. Compared to 1-dodecylpyridinium bromide, 1-tetradecylpyridinium chloride was less active against phytopathogenic fungi despite the carbon-chain length, so the effect on antifungal activity may be ion-related. 1-Dodecylpyridinium with the bromine ion increased the activity against *S. sclerotiorum*, *B. cinerea* and *F. oxysporum*. Compared to myristalkonium chloride, the carbon chain increased and the activity was enhanced against *S. sclerotiorum* with cetalkonium chloride $EC_{50}$ of 8.36 μg $ml^{-1}$, but significantly decreased activity against *B. cinerea*. Compared with benzyldodecyldimethylammonium bromide, chloride ion replaced by bromine ion dodecyl dimethyl benzyl ammonium bromide increased the activity of *S. sclerotiorum* and *B. cinerea*. The $EC_{50}$ values were 5.80 μg $ml^{-1}$ and 8.85 μg $ml^{-1}$, respectively. In summary, the carbon chain length of the ionic liquid drugs had a significant effect on the resistance to phytopathogenic fungi. Compared to chlorohexidine diacetate, enebicyanog had a narrower spectrum of activity against phytopathogenic fungi, but it had better activity against *S. sclerotiorum* and *B. cinerea*, with $EC_{50}$ of 0.91 μg $ml^{-1}$ and 0.62 μg $ml^{-1}$ respectively. Therefore, ionic liquids are expected to be used in the control of plant resistant pathogenic fungi.

## Miscellaneous group drugs

Miscellaneous group drugs against plant pathogenic fungi are shown in Table 11 and Table 1. Some drugs with

**Table 7** In vitro antifungal activities (inhibition rate/%) of the pyrimidine drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | 5-Fluorouridine | 100 | 93.47 ± 0.92 | 100 ± 0 | 100 ± 0 | 81.11 ± 1.22 | 88.73 ± 0.23 | 89.6 ± 0.18 |
| 2 | Doxifluridine | 100 | 92.06 ± 0.44 | 91.33 ± 0.41 | 100 ± 0 | 77.2 ± 1.56 | 79.73 ± 0.39 | 74.97 ± 0.5 |
| 3 | Avanafil | 100 | 29.26 ± 0.52 | 18.75 ± 1.42 | 36.75 ± 1.65 | 56.86 ± 0.47 | 15.27 ± 1.6 | 22.08 ± 0.85 |
| 4 | Uridine | 100 | 83.38 ± 0.81 | 92.21 ± 1.97 | 89.26 ± 1.19 | 51.65 ± 1.02 | 58.24 ± 1.48 | 57.18 ± 0.08 |
| 5 | 2'-Fluoro-2'-deoxyuridine | 100 | 0 ± 0 | 13.48 ± 2.85 | 0.94 ± 0.05 | 25.39 ± 1.21 | 0.73 ± 0.26 | 3.8 ± 2.69 |
| 6 | 1-(2-Deoxy-2-fluoro-beta-D-arabinofuranosyl)uracil | 100 | 15.47 ± 0.58 | 70.6 ± 0.39 | 6.4 ± 0.44 | 30.52 ± 2 | 5.9 ± 0.83 | 6.2 ± 0.41 |
| 7 | 1-Beta-D-Arabinofuranosyluracil | 100 | 17.04 ± 0.14 | 100 ± 0 | 100 ± 0 | 38.05 ± 1.65 | 79.19 ± 0.01 | 88.56 ± 0.01 |
| 8 | Trifluorothymine | 100 | 66.42 ± 0.95 | 100 ± 0 | 100 ± 0 | 62.18 ± 0.57 | 90.12 ± 0.68 | 90.62 ± 0.74 |
| 9 | Broxuridine | 100 | 69.6 ± 0.57 | 91.57 ± 0.84 | 90.95 ± 0.23 | 62.53 ± 0.8 | 72.06 ± 0.17 | 63.3 ± 0.83 |
| 10 | 5-Bromouridine | 100 | 19.95 ± 0.62 | 8.89 ± 1.23 | 9.49 ± 2.54 | 2.09 ± 0.3 | 0.19 ± 0.03 | 4.81 ± 1.02 |
| 11 | 5-Iodouridine | 100 | 9.38 ± 0.99 | 17.47 ± 0.01 | 6.46 ± 2.59 | 6.35 ± 0.48 | 2.3 ± 0.17 | 6.53 ± 0.66 |
| 12 | Carmofur | 100 | 2.48 ± 0.11 | 9.85 ± 1.38 | 9.95 ± 0.57 | 2.04 ± 0.23 | 1.03 ± 0.04 | 3.16 ± 2.23 |
| 13 | Tegafur | 100 | 1.93 ± 0.73 | 14.48 ± 0.98 | 9.22 ± 1.58 | 1.73 ± 0.15 | 3.91 ± 0.02 | 6.04 ± 0.83 |
| 14 | Cytidine | 100 | 1.94 ± 0.71 | 1.03 ± 1.01 | 2.00 ± 0.06 | 6.96 ± 1.26 | 2.08 ± 0.02 | 1.03 ± 0.05 |
| 15 | 5-Fluorocytidine | 100 | 1.94 ± 0.38 | 2.40 ± 0.03 | 35.9 ± 1.12 | 3.47 ± 0.17 | 1.04 ± 0.04 | 1.06 ± 0.02 |
| 16 | 5-Azacytidine | 100 | 1.97 ± 0.82 | 51.98 ± 1.21 | 1.79 ± 0.29 | 5.74 ± 0.49 | 2.73 ± 0.22 | 1.55 ± 0.36 |
| 17 | Lamivudine | 100 | 74.77 ± 0.31 | 69.04 ± 0.21 | 69.78 ± 0 | 88.88 ± 2.4 | 84.74 ± 0 | 39.57 ± 2.3 |
| 18 | Trifluridine | 100 | 44.17 ± 1.98 | 25.52 ± 0.78 | 33.36 ± 0.21 | 18.62 ± 1.79 | 19.55 ± 0 | 8.09 ± 0.69 |
| 19 | Guanosine | 100 | 2.08 ± 0.02 | 2.71 ± 0.02 | 2.01 ± 0.10 | 14.12 ± 1.44 | 1.39 ± 0.03 | 5.77 ± 0.42 |
| 20 | 2'-Deoxyguanosine | 100 | 64.42 ± 0.14 | 72.56 ± 0.12 | 100 ± 0 | 95.08 ± 0.00 | 94.05 ± 0.89 | 75.7 ± 0.02 |
| 21 | Dideoxyinosine | 100 | 1.80 ± 0 | 9.53 ± 0.79 | 1.92 ± 0.01 | 10.19 ± 0.75 | 1.35 ± 0.63 | 6.16 ± 1.11 |
| 22 | Stavudine | 100 | 0.83 ± 0.09 | 2.74 ± 0.03 | 7.95 ± 0.85 | 1.03 ± 0.04 | 3.71 ± 0.7 | 4.09 ± 0.16 |
| 23 | Abacavir | 100 | 1.88 ± 0.63 | 2.47 ± 0.92 | 0.03 ± 0.01 | 0.21 ± 0.01 | 0.21 ± 0.04 | 7.04 ± 1.12 |
| 24 | Acyclovir | 100 | 2.81 ± 0.17 | 2.93 ± 0.06 | 0.30 ± 0.01 | 2.30 ± 2.1 | 3.89 ± 0.1 | 1.00 ± 0.4 |
| 25 | Famciclovir | 100 | 0 ± 0 | 18.31 ± 2.66 | 4.01 ± 0.01 | 2.71 ± 0.03 | 5.01 ± 0.71 | 2.5 ± 1.84 |
| 26 | Penciclovir | 100 | 1.92 ± 0.81 | 4.90 ± 0.01 | 2.28 ± 0.02 | 4.08 ± 0.92 | 2.01 ± 0.08 | 3.51 ± 0.73 |
| 27 | Ganciclovir | 100 | 97.92 ± 0.11 | 96.2 ± 0.52 | 97.48 ± 0 | 75.04 ± 0.81 | 87.89 ± 1.33 | 91.68 ± 0.25 |
| 28 | Brivudine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 29 | Cytarabine | 100 | 3.81 ± 0.47 | 0 ± 0 | 11.74 ± 0.41 | 14.15 ± 1.46 | 7.10 ± 1.02 | 5.59 ± 0.49 |
| 30 | Vidarabine monophosphate | 100 | 21.73 ± 0.98 | 15.67 ± 1.03 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 31 | Idoxuridine | 100 | 7.95 ± 0.66 | 11.8 ± 0.04 | 14.95 ± 1.39 | 15.71 ± 0.24 | 20.73 ± 0.15 | 15.60 ± 0.98 |
| 32 | Thymidine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 33 | Floxuridine | 100 | 51.75 ± 2.84 | 83.70 ± 2.28 | 96.42 ± 0.38 | 81.14 ± 0.78 | 38.48 ± 0.01 | 31.11 ± 2.37 |
| 34 | 5-Fluorouracil | 100 | 74.98 ± 1.98 | 48.82 ± 1.16 | 82.15 ± 0 | 81.39 ± 1.49 | 54.46 ± 0.92 | 34.62 ± 0.12 |
| 35 | Fluorocytosine | 100 | 0 ± 0 | 56.34 ± 1.69 | 75.94 ± 0.73 | 7.78 ± 0.95 | 3.55 ± 0.66 | 0 ± 0 |
| 36 | Emtricitabine | 100 | 0 ± 0 | 13.02 ± 1.05 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 37 | 6-Thioguanine | 100 | 5.09 ± 2.48 | 0 ± 0 | 8.77 ± 1.51 | 0 ± 0 | 5.48 ± 0.19 | 5.54 ± 0.04 |
| 38 | Zidovudine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 9.16 ± 1.74 | 5.76 ± 1.02 |
| 39 | Capecitabine | 100 | 12.26 ± 1.51 | 24.62 ± 1.09 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 40 | Dasatinib | 100 | 38.91 ± 0.29 | 74.83 ± 1.62 | 89.72 ± 0.3 | 63.88 ± 1.94 | 76.26 ± 0.28 | 55.91 ± 0.22 |
| 41 | Lapatinib | 100 | 28.91 ± 1.96 | 69.92 ± 1.2 | 80.1 ± 0.69 | 48.92 ± 0.49 | 45.96 ± 0.22 | 42.33 ± 0.69 |
| 42 | Nilotinib | 100 | 0 ± 0 | 0 ± 0 | 10.93 ± 1.78 | 7.78 ± 0.78 | 0 ± 0 | 8.74 ± 0.7 |
| 43 | Pazopanib hydrochloride | 100 | 12.43 ± 0.79 | 28.21 ± 0.65 | 43.95 ± 1.46 | 34.76 ± 1.97 | 30.28 ± 0.05 | 20.39 ± 0.46 |
| 44 | Sulfatinib | 100 | 66.17 ± 7.04 | 77.12 ± 0.29 | 76.75 ± 1.92 | 62.24 ± 1.62 | 49.76 ± 0.13 | 32.5 ± 0.99 |
| 45 | CAL-101 | 100 | 48.6 ± 2.85 | 0 ± 0 | 47.66 ± 0.09 | 32.02 ± 0.07 | 20.3 ± 0.58 | 16.82 ± 1.29 |

**Table 7** (continued)

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 46 | Gefitinib | 100 | 23.29 ± 0.31 | 75.68 ± 2.59 | 92.22 ± 1 | 72.28 ± 0.63 | 67.35 ± 0.54 | 57.22 ± 0.24 |
| 47 | Erlotinib | 100 | 11.69 ± 1.62 | 0 ± 0 | 42.3 ± 0.41 | 12.17 ± 0.61 | 9.68 ± 0.96 | 15.94 ± 0.98 |
| 48 | Dabrafenib | 100 | 64.51 ± 0.9 | 83.7 ± 0.84 | 89.72 ± 1.23 | 64.2 ± 0.36 | 62.51 ± 0.47 | 65.69 ± 0.74 |
| 49 | Nilotinib hydrochloride monohydrate | 100 | 0 ± 0 | 47.15 ± 1.28 | 16.78 ± 0.46 | 10.76 ± 1.58 | 0 ± 0 | 9.46 ± 0.22 |
| 50 | Tofacitinib | 100 | 9.85 ± 1.96 | 0 ± 0 | 5.54 ± 0.36 | 11.9 ± 0.13 | 3.14 ± 0.13 | 2.62 ± 0.77 |
| 51 | Afatinib | 100 | 44.53 ± 0.76 | 78.99 ± 0.03 | 88.16 ± 0.24 | 52.59 ± 0.36 | 70.81 ± 0.21 | 45.23 ± 0.08 |
| 52 | Ibrutinib | 100 | 75.18 ± 2.12 | 93.23 ± 0.15 | 87.82 ± 0.01 | 67 ± 0.25 | 73.96 ± 1.33 | 79.25 ± 0.6 |
| 53 | Mereletinib | 100 | 56.8 ± 2.61 | 83.79 ± 0.91 | 55.15 ± 3.53 | 65.29 ± 1.14 | 81.29 ± 0.77 | 59.2 ± 0.85 |
| 54 | Gemcitabine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 55 | Pyrimethamine | 100 | 32.89 ± 0.59 | 36.34 ± 3.86 | 47.49 ± 0.16 | 43.67 ± 2.67 | 27.08 ± 0.02 | 32.67 ± 0.93 |
| 56 | Thiamine chloride | 100 | 0 ± 0 | 13.82 ± 1.32 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 2.88 ± 0.96 |
| 57 | Thiamine nitrate | 100 | 0 ± 0 | 29.26 ± 1.32 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 58 | Trimethoprim | 100 | 13.36 ± 0.90 | 58.24 ± 2.37 | 13.00 ± 0.82 | 7.12 ± 3.05 | 17.35 ± 2.67 | 12.73 ± 2.25 |
| 59 | Methotrexate | 100 | 0 ± 0 | 29.19 ± 3.11 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 60 | Triamterene | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 19.77 ± 1.85 | 0 ± 0 | 0 ± 0 |
| 61 | Revaprazan hydrochloride | 100 | 10.18 ± 3.65 | 0 ± 0 | 6.63 ± 0.35 | 16.63 ± 2.06 | 0 ± 0 | 4.93 ± 0.63 |
| 62 | Thiamine hydrochloride | 100 | 6.24 ± 2.19 | 11.51 ± 1.01 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 63 | Etravirine | 100 | 7.45 ± 1.99 | 14.73 ± 2.98 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 64 | Arprinocide | 100 | 82.28 ± 2.14 | 29.35 ± 1.6 | 23.81 ± 0.47 | 13.37 ± 1.71 | 0 ± 0 | 0 ± 0 |
| 65 | Amprolium | 100 | 6.01 ± 0.81 | 0 ± 0 | 19.1 ± 0.62 | 5.3 ± 1.8 | 0 ± 0 | 0 ± 0 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

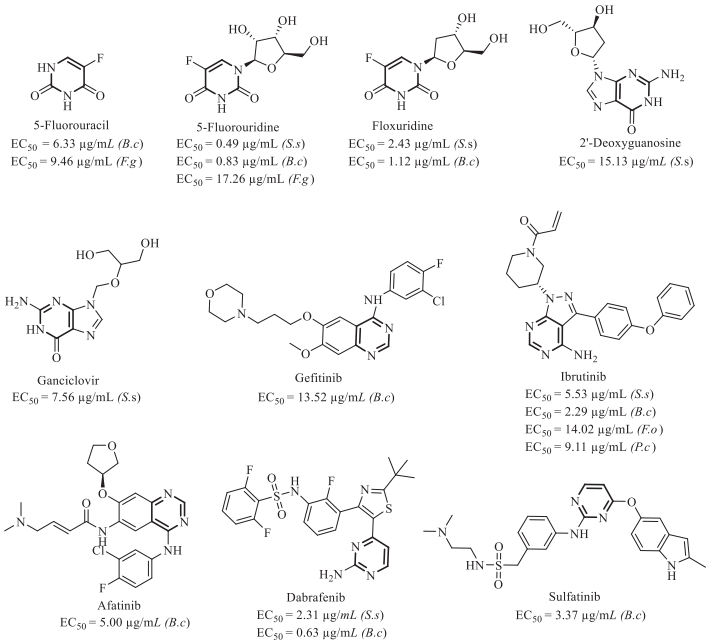



**Fig. 7** The $EC_{50}$ of pyrimidine drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

**Table 8** In vitro antifungal activities (inhibition rate/%) of the pyridines drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Nilvadipine | 100 | 47.94 ± 1.46 | 89.46 ± 0.01 | 87.47 ± 0.01 | 59.50 ± 1.98 | 77.12 ± 0.42 | 57.97 ± 0.16 |
| 2 | Roflumilast | 100 | 6.9 ± 1.92 | 19.74 ± 0.9 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 3 | Acalabrutinib | 100 | 0 ± 0 | 41.65 ± 0.9 | 11.8 ± 2.02 | 29.67 ± 2.46 | 0 ± 0 | 0 ± 0 |
| 4 | Nvp-lde225 | 100 | 71.65 ± 0.64 | 44.78 ± 1.29 | 33.58 ± 0.85 | 28.33 ± 0.21 | 0 ± 0 | 8.5 ± 1.08 |
| 5 | Sorafenib tosylate | 100 | 14.85 ± 0.95 | 25.01 ± 0.8 | 56.98 ± 0.36 | 22.5 ± 0.45 | 12.12 ± 0.47 | 22.05 ± 0.37 |
| 6 | Abemaciclib | 100 | 0 ± 0 | 54.13 ± 1.44 | 79.46 ± 0.73 | 14.97 ± 1.24 | 16.32 ± 1.71 | 13.87 ± 1.68 |
| 7 | Axitinib | 100 | 37.77 ± 0.14 | 0 ± 0 | 4.36 ± 0.82 | 11.76 ± 0.25 | 0 ± 0 | 5.02 ± 0.5 |
| 8 | Regorafenib hydrate | 100 | 27.25 ± 1.11 | 12.65 ± 0.44 | 53.24 ± 0.17 | 5.23 ± 0.07 | 5.12 ± 0.7 | 31.69 ± 0.51 |
| 9 | Pheniramine maleate | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 10 | Chlorpheniramine maleate | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 16.65 ± 1.63 |
| 11 | Amlodipine maleate | 100 | 42.06 ± 0.97 | 90.1 ± 0.33 | 93.27 ± 0.21 | 60.98 ± 1.05 | 66.89 ± 0.61 | 69.91 ± 1.11 |
| 12 | Clopidol | 100 | 9.94 ± 2.26 | 0 ± 0 | 15.9 ± 1.99 | 6.25 ± 2.75 | 0 ± 0 | 0 ± 0 |
| 13 | Liranaftate | 100 | 97.07 ± 0.34 | 100 ± 0 | 95.94 ± 0.27 | 81.72 ± 0.43 | 88.1 ± 0.10 | 81.48 ± 1.00 |
| 14 | Rosiglitazone | 100 | 23.44 ± 2.32 | 0 ± 0 | 16.17 ± 2.03 | 45.43 ± 1.26 | 61.95 ± 0.07 | 45.06 ± 0.23 |
| 15 | Pioglitazone hydrochloride | 100 | 0 ± 0 | 3.54 ± 0.06 | 5.72 ± 0.08 | 16.85 ± 0.12 | 9.75 ± 0.09 | 3.43 ± 3.41 |
| 16 | Pyributicarb | 100 | 92.93 ± 0.49 | 98.27 ± 0.11 | 92.06 ± 0.76 | 77.56 ± 0.01 | 81.45 ± 0.12 | 87.06 ± 0.09 |
| 17 | Acrivastine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 18 | Milrinone | 100 | 14.34 ± 1.36 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 10.23 ± 1.19 | 0 ± 0 |
| 19 | Tropicamide | 100 | 9.13 ± 0.69 | 11.71 ± 0.88 | 21.34 ± 0.36 | 8.92 ± 2.01 | 0 ± 0 | 0 ± 0 |
| 20 | Protionamide | 100 | 17.5 ± 1.27 | 0 ± 0 | 34.9 ± 3.34 | 10.86 ± 0.44 | 5.21 ± 1.26 | 14.43 ± 1.16 |
| 21 | Ethionamide | 100 | 36.73 ± 0.92 | 0 ± 0 | 49.06 ± 0.96 | 24.68 ± 3.44 | 0 ± 0 | 9.06 ± 0.44 |
| 22 | Amlodipine | 100 | 62.82 ± 0.83 | 92 ± 0.37 | 96.1 ± 0.07 | 53.2 ± 1.29 | 76.95 ± 1.55 | 70.47 ± 2.13 |
| 23 | Nimodipine | 100 | 53.05 ± 2.65 | 61.5 ± 0.04 | 74.06 ± 1.61 | 31.96 ± 1.26 | 75.39 ± 0.81 | 67.49 ± 0.92 |
| 24 | Isoniazid | 100 | 8.18 ± 2.55 | 0 ± 0 | 11.98 ± 0.63 | 7.4 ± 1.93 | 0 ± 0 | 9.45 ± 0.28 |
| 25 | Sodium pyrithione | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 26 | Zinc pyrithione | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 27 | Copper pyrithione | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 63.52 ± 1.33 |
| 28 | Bispyrithione | 100 | 100 ± 0 | 100 ± 0 | 82.36 ± 1.01 | 100 ± 0 | 59.39 ± 0.84 | 88.41 ± 1.99 |
| 29 | Ciclopirox ethanolamine | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 30 | Piroctone olamine | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 31 | Caprylohydroxmic acid | 100 | 91.58 ± 0.93 | 98.02 ± 0.57 | 100 ± 0 | 37.50 ± 1.31 | 58.76 ± 2.70 | 47.39 ± 1.19 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

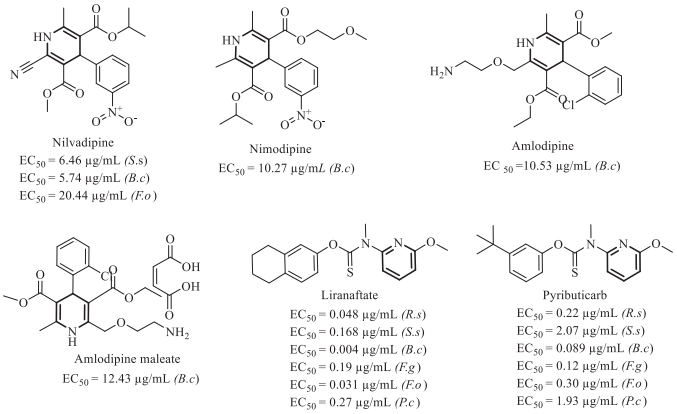



**Fig. 8** The $EC_{50}$ of pyridine drugs compounds against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

**Table 9** In vitro antifungal activities (inhibition rate/%) of the piperidine/piperazine drugs against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Piperazine | 100 | 10.13 ± 1.09 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 8.07 ± 0.4 | 0 ± 0 |
| 2 | *N*-Aminoethylpiperazine | 100 | 7.23 ± 0.89 | 26.08 ± 1.92 | 0 ± 0 | 0 ± 0 | 12.98 ± 0.87 | 0 ± 0 |
| 3 | 4-Methyl-1-piperazineethanamine | 100 | 9.38 ± 1.28 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 10.4 ± 1.09 | 0 ± 0 |
| 4 | Buclizine dihydrochloride | 100 | 33.46 ± 1.33 | 59.92 ± 0.15 | 66.63 ± 1.18 | 29.69 ± 2.47 | 23.08 ± 0.44 | 17.17 ± 1.25 |
| 5 | Flavopiridol | 100 | 89.93 ± 0.21 | 91.42 ± 0.81 | 89.23 ± 1.08 | 44.95 ± 2.38 | 56.25 ± 1.29 | 62.24 ± 1.14 |
| 6 | Terfenadine | 100 | 65.52 ± 0.22 | 100 ± 0 | 93.81 ± 0.8 | 75.97 ± 2.41 | 80.95 ± 0.9 | 69.96 ± 0.26 |
| 7 | Thioridazine hydrochloride | 100 | 91.41 ± 0.12 | 95.3 ± 0.04 | 81.65 ± 1.32 | 77.6 ± 1.14 | 87.61 ± 0.46 | 86.22 ± 0.82 |
| 8 | Pimozide | 100 | 52.60 ± 1.99 | 80.59 ± 0.77 | 87.66 ± 0.9 | 26.66 ± 2.29 | 74.42 ± 0.24 | 76.53 ± 1.29 |
| 9 | Penfluridol | 100 | 85.13 ± 0.01 | 91.7 ± 1.32 | 90.53 ± 0.58 | 87.27 ± 0.29 | 64.9 ± 0.82 | 49.98 ± 3.41 |
| 10 | Loperamide hydrochloride | 100 | 20.07 ± 2.39 | 50.38 ± 1.76 | 61.69 ± 2.72 | 54.23 ± 0.33 | 28.53 ± 0.05 | 41.3 ± 0.42 |
| 11 | Benzhexol hydrochloride | 100 | 28.46 ± 0.81 | 14.3 ± 4.44 | 33.66 ± 0.53 | 27.88 ± 1.3 | 0 ± 0 | 16.35 ± 0.77 |
| 12 | Trifluoperazine | 100 | 86.9 ± 0.43 | 94.95 ± 0.49 | 95.93 ± 0.26 | 82.95 ± 2.51 | 77.85 ± 1.61 | 84.87 ± 1.02 |
| 13 | Paroxetine hydrochloride | 100 | 66.8 ± 1.53 | 76.83 ± 0.28 | 88.59 ± 0.49 | 62.77 ± 1.72 | 64.5 ± 0.33 | 67.08 ± 1.15 |
| 14 | Ebastine | 100 | 88.1 ± 0.24 | 89.73 ± 0.12 | 90.82 ± 0.22 | 47.57 ± 2.44 | 87.09 ± 0.42 | 74.72 ± 0.56 |
| 15 | Haloperidol | 100 | 44.75 ± 1.84 | 64.38 ± 0.42 | 84.53 ± 0 | 56.68 ± 2.24 | 42.75 ± 1.23 | 42.42 ± 0.17 |
| 16 | Mizolastine | 100 | 6.85 ± 0.35 | 58.66 ± 0.77 | 86.42 ± 1.92 | 50.32 ± 2.94 | 45.1 ± 0.7 | 48.11 ± 2.81 |
| 17 | Vortioxetine | 100 | 1.50 ± 0.01 | 0.70 ± 0.20 | 3.0 ± 0.12 | 2.45 ± 0.19 | 1.82 ± 0.71 | 6.25 ± 0.54 |
| 18 | Sildenafil | 100 | 0 ± 0 | 16.68 ± 1.1 | 34.92 ± 0.01 | 22.88 ± 0 | 15.85 ± 0.04 | 25.12 ± 1.12 |
| 19 | Prochlorperazine maleate | 100 | 90.84 ± 0.07 | 85.45 ± 0.75 | 84.67 ± 1.33 | 62.29 ± 1.61 | 70.01 ± 0.34 | 84.52 ± 0.24 |
| 20 | Perphenazine | 100 | 100 ± 0 | 94.53 ± 0.9 | 85.08 ± 1.33 | 84.54 ± 2.13 | 77.46 ± 0.44 | 86.13 ± 1.34 |
| 21 | Clozapine | 100 | 44.03 ± 2.74 | 44.32 ± 0.07 | 74 ± 0.58 | 67.7 ± 1.11 | 56.56 ± 0.5 | 50.4 ± 2.67 |
| 22 | Olanzapine | 100 | 0 ± 0 | 22.77 ± 1.16 | 33.84 ± 1.37 | 33.69 ± 1.15 | 16.16 ± 1.36 | 44.43 ± 0.46 |
| 23 | Ranolazine | 100 | 9.64 ± 1.43 | 42.17 ± 0.68 | 14.1 ± 0.12 | 0 ± 0 | 7.15 ± 1.33 | 18.79 ± 0.05 |
| 24 | Amoxapine | 100 | 46.5 ± 0.34 | 78.43 ± 0.14 | 59.03 ± 0.01 | 59.22 ± 1.16 | 60.67 ± 0.01 | 60.26 ± 0.28 |
| 25 | Mirtazapine | 100 | 0 ± 0 | 47.18 ± 0.11 | 7.87 ± 0.27 | 0 ± 0 | 11.43 ± 0.44 | 26.08 ± 0.45 |
| 26 | Sitagliptin | 100 | 0 ± 0 | 43.52 ± 2.16 | 9.92 ± 0.04 | 0 ± 0 | 1.01 ± 0.06 | 9.55 ± 0.1 |
| 27 | Brexpiprazole | 100 | 23.77 ± 0.18 | 59.61 ± 1.75 | 43.04 ± 2.47 | 52.28 ± 1.98 | 65.19 ± 0.27 | 29.94 ± 0.98 |
| 28 | Aripiprazole | 100 | 84.8 ± 2.57 | 97.46 ± 0.57 | 96.66 ± 0.32 | 86.81 ± 0.74 | 82.19 ± 0.46 | 74.18 ± 0.17 |
| 29 | Ziprasidone hydrochloride | 100 | 27.61 ± 0.91 | 86.92 ± 1.14 | 22.6 ± 1.05 | 21.25 ± 2.1 | 37.33 ± 1 | 31.94 ± 0.33 |
| 30 | Cinnarizine | 100 | 5.28 ± 0.36 | 34.77 ± 1.43 | 32.62 ± 0.38 | 16.65 ± 1.34 | 10.8 ± 0.79 | 20.15 ± 1.89 |
| 31 | Cetirizine | 100 | 0 ± 0 | 0 ± 0 | 11.88 ± 1.63 | 0 ± 0 | 0 ± 0 | 12.93 ± 0.15 |
| 32 | Domperidone | 100 | 0 ± 0 | 0 ± 0 | 53.03 ± 0.43 | 16.05 ± 1.27 | 32.58 ± 0.62 | 33.23 ± 2.01 |
| 33 | Bilastin | 100 | 0 ± 0 | 0 ± 0 | 7.95 ± 0.61 | 11.95 ± 0.33 | 0 ± 0 | 8.15 ± 1.63 |
| 34 | Risperidone | 100 | 0 ± 0 | 0 ± 0 | 17.48 ± 1.01 | 21.52 ± 1.87 | 14.93 ± 2.33 | 16.71 ± 1.8 |
| 35 | Terazosin hydrochloride | 100 | 9.93 ± 1.09 | 0 ± 0 | 46.52 ± 1.49 | 22.21 ± 2.14 | 21.79 ± 1.37 | 21.64 ± 1.13 |
| 36 | Donepezil | 100 | 15.4 ± 0.43 | 43.31 ± 2.81 | 48.97 ± 2.58 | 31.26 ± 1.11 | 7.94 ± 2.31 | 19.61 ± 1.56 |
| 37 | Droperidol | 100 | 0 ± 0 | 0 ± 0 | 7.88 ± 1.62 | 5.53 ± 0.50 | 22.79 ± 1.34 | 25.66 ± 1.47 |
| 38 | Flibaserin | 100 | 39.16 ± 0.42 | 51.1 ± 0.82 | 38.81 ± 0.56 | 58.49 ± 1.53 | 61.42 ± 0.01 | 49.12 ± 1.83 |
| 39 | Piperaquinoline | 100 | 0 ± 0 | 0 ± 0 | 12.59 ± 0.85 | 34.6 ± 0.07 | 34.55 ± 0.01 | 34.86 ± 0.01 |
| 40 | Desloratadine | 100 | 25.73 ± 1.98 | 75.43 ± 0.08 | 87.24 ± 0.14 | 36.5 ± 0.64 | 67.43 ± 2.63 | 62.52 ± 0.41 |
| 41 | Loratadine | 100 | 91.93 ± 0.01 | 80.7 ± 1.62 | 86.37 ± 1.3 | 62.28 ± 1.28 | 74.13 ± 0.66 | 79.88 ± 1.34 |
| 42 | Fexofenadine | 100 | 0 ± 0 | 7.72 ± 1.26 | 0 ± 0 | 0 ± 0 | 0.6 ± 0.89 | 2.65 ± 1.61 |
| 43 | Vardenafil hydrochloride | 100 | 0 ± 0 | 69.92 ± 1.2 | 28.12 ± 2.91 | 14.7 ± 0.36 | 18.83 ± 0.71 | 21.06 ± 1.17 |
| 44 | Quetiapine fumarate | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 10.78 ± 1.1 | 35.58 ± 2.3 | 24.12 ± 0.35 |
| 45 | Imatinib | 100 | 21.94 ± 2.34 | 37.25 ± 1.04 | 55.81 ± 0.26 | 40.84 ± 0.26 | 23.07 ± 1.14 | 24.15 ± 0.72 |
| 46 | Alectinib | 100 | 19.82 ± 1.35 | 11.63 ± 0.29 | 50.06 ± 0.67 | 17.83 ± 1 | 8.67 ± 1.14 | 8.07 ± 0.21 |

**Table 9** (continued)

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 47 | Venclexta | 100 | 13.15 ± 1.06 | 0 ± 0 | 22.31 ± 0.32 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 48 | Ponatinib | 100 | 100 ± 0 | 69.58 ± 0.4 | 85.41 ± 0.3 | 67.65 ± 2.46 | 51.95 ± 0.4 | 35.42 ± 0.27 |
| 49 | Bosutinib | 100 | 35.3 ± 1.3 | 86.18 ± 0.01 | 83.58 ± 0.68 | 67.06 ± 0.22 | 56.99 ± 0.31 | 42.85 ± 0.62 |
| 50 | Vandetanib | 100 | 78.56 ± 0.44 | 84.25 ± 2.61 | 91.72 ± 0.09 | 90.26 ± 0.22 | 79.7 ± 1.49 | 67.36 ± 0.72 |
| 51 | Avitinib | 100 | 37.78 ± 1.3 | 92 ± 0.42 | 75.26 ± 1.09 | 73.36 ± 0.49 | 66.97 ± 0.14 | 35.2 ± 1.02 |
| 52 | Tandutinib | 100 | 16.89 ± 0.19 | 53.1 ± 0.95 | 60.7 ± 0.45 | 47.66 ± 0.37 | 44.74 ± 0.16 | 34.73 ± 0.82 |
| 53 | Palbociclib | 100 | 0 ± 0 | 78.56 ± 0.67 | 78.39 ± 1.01 | 35.62 ± 2.13 | 63.32 ± 0.97 | 29.8 ± 1.09 |
| 54 | Ribociclib | 100 | 11.36 ± 2.6 | 76.33 ± 0.24 | 56.63 ± 1.19 | 38.34 ± 2.14 | 54.85 ± 0.11 | 28.86 ± 0.97 |
| 55 | Brigatinib | 100 | 24.11 ± 1.03 | 68.01 ± 0.95 | 42.23 ± 2.91 | 68.85 ± 1.18 | 37.45 ± 0.38 | 27.48 ± 0.62 |
| 56 | Olaparib | 100 | 0 ± 0 | 26.69 ± 1.16 | 54.44 ± 0.96 | 10.87 ± 1.9 | 7.7 ± 0.79 | 13.04 ± 2.02 |
| 57 | Crizotinib | 100 | 48.83 ± 1.08 | 100 ± 0 | 96.02 ± 0.02 | 85.98 ± 0.21 | 86.35 ± 0.54 | 63.94 ± 0.59 |
| 58 | Niraparib | 100 | 11.13 ± 0.11 | 84.17 ± 0.63 | 81.11 ± 0.48 | 40.9 ± 2.55 | 53.85 ± 0.75 | 31.13 ± 0.8 |
| 59 | Nintedanib | 100 | 7.51 ± 0.89 | 47.64 ± 0.62 | 45.98 ± 0.93 | 13.23 ± 0.18 | 9.94 ± 0.56 | 17.71 ± 1.78 |
| 60 | Ceritinib | 100 | 83.03 ± 0.22 | 52.37 ± 0.19 | 82.9 ± 1.21 | 33.97 ± 0.03 | 41.12 ± 1.53 | 31.26 ± 0.93 |
| 61 | Cetirizine hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 14.1 ± 1.99 | 8.6 ± 0.04 | 2.88 ± 0.4 | 6.03 ± 1.4 |
| 62 | Trazodone hydrochloride | 100 | 20.46 ± 1.71 | 43.6 ± 0.62 | 17.85 ± 1.56 | 14.73 ± 0.01 | 26.78 ± 0.02 | 37.01 ± 1.7 |
| 63 | Alogliptin | 100 | 5.61 ± 2.05 | 31.87 ± 3.26 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 64 | Ticlopidine | 100 | 24.3 ± 2.74 | 44.33 ± 2.2 | 0 ± 0 | 56.11 ± 3.26 | 20.28 ± 1.53 | 16.77 ± 3.05 |
| 65 | Celecoxib | 100 | 31.09 ± 1.44 | 0 ± 0 | 39.62 ± 1.54 | 21.03 ± 0.01 | 23.32 ± 0.54 | 33.99 ± 0.89 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

relatively broad anti-pathogenic activity were selected for a brief analysis as shown in Fig. 11.

Monensin, natamycin and griseofulvin are antibiotics, but they have different effects, which monensin inhibits the growth of coccidia, gram-positive bacteria, algae and protozoa [61]. Natamycin is commonly used as a preservative to prevent mould contamination in food [62, 63]. Griseofulvin is widely used in clinical medicine to treat skin and stratum corneum fungal infections, and also in the prevention and treatment of fungal diseases in agriculture [64]. Monensin sodium salt, natamycin and griseofulvin had broad-spectrum activity against plant pathogenic fungi, with $EC_{50}$ ranging from 0.076 to 13.20 μg $ml^{-1}$. Butenafine hydrochloride, terbinafine hydrochloride and tolnaftate are a group of antifungal drugs, which are applied to the treatment of tinea capitis and other tinea diseases [65, 66]. In this screening, butenafine hydrochloride, terbinafine hydrochloride and tolnaftate were also found to have excellent activity against pathogenic fungi, with $EC_{50}$ in the range of 0.07–18.05 μg $ml^{-1}$. It was worth noting that they had significant activity in *B. cinerea*, with $EC_{50}$ of 0.07, 0.11 and 0.07 μg $ml^{-1}$, respectively. Oxyclozanide is the drug of choice for clinical anti-helminth infections, which has the characteristics of broad spectrum, low toxicity and low residue [67]. Through drug repositioning strategy, we found that oxyclozanide also had excellent activity against phytopathogenic fungi with $EC_{50}$ in the range of 0.09–0.71 μg $ml^{-1}$. Carbonyl cyanide 3-chlorophenylhydrazone (CCCP) is an inhibitor of oxidative phosphorylation that disrupts the mitochondrial membrane potential [68]. The evaluation of the in vitro activity of CCCP against pathogenic fungi revealed a broad antifungal spectrum and potent activity with $EC_{50}$ in the range of 0.38–6.07 μg $ml^{-1}$. Although this group of drugs was not analyzed by activity and structure, these results provided a structure-based screening approach to repurpose commercially available drugs with the expectation of discovering broad-spectrum, effective drugs against plant pathogens.

## Discussion and conclusion

In an era of emerging drug resistance, there is an increasing need to optimise old drugs or develop new ones to alleviate the problem. In this worrying situation, drug repurposing is a promising approach as a way to obtain effective drugs or lead structures to solve the problem. In the field of medicine, studies have been carried out with drug repurposing strategies to re-screen approved library for potential anti-tumour, anti-inflammatory, antituberculous, antimicrobial drugs [23, 69–74]. Similarly, in the agricultural field, the potential of halofuginone, kaempferol, honokiol and tavaborole against agricultural

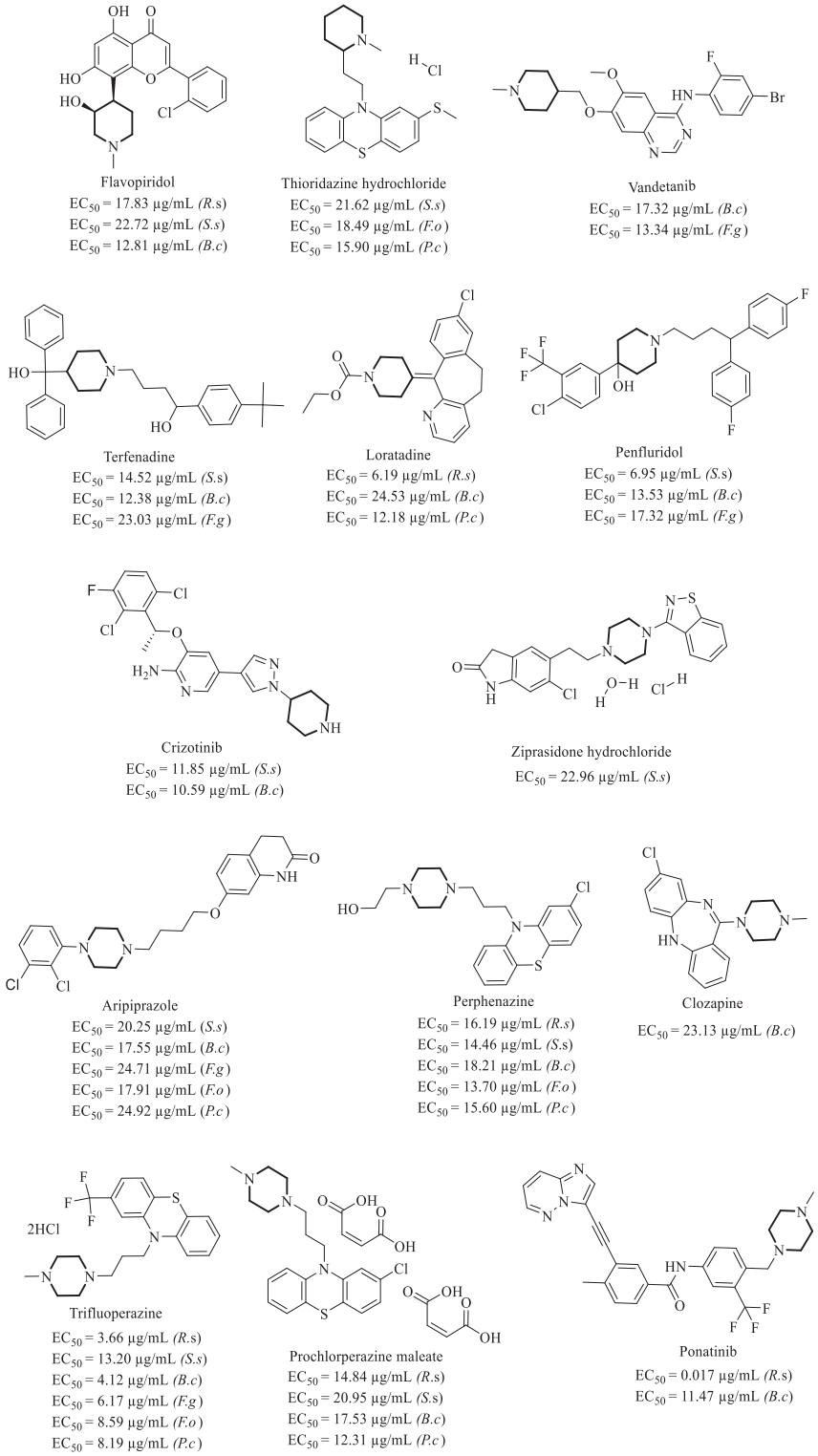



**Fig. 9** The $EC_{50}$ of piperidine/piperazine drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

pathogens has also been identified [75–78]. In addition, novel lead structures can also be found through drug repurposing. Antibacterial conversion of neamine aminoglycosides through alkyl modification could turn old drugs into agricultural fungicides [79]. In this paper, we can obtain some potential drugs or lead structures against agricultural pathogenic fungi by screening. However, studies have found that for some repurposed drugs, the original mechanism of action may become a negative side effect of the new indication. Thus, maintaining the positive effects of the new indication while eliminating the original mechanism of the drug is a more attractive study. Conversely, the study show that several AHAS inhibitors

**Table 10** In vitro antifungal activities (inhibition rate/%) of the ionic liquids against phytopathogenic fungi[a]

| No. | Compounds | Concentration (μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | 3-Methyl-1-octylimidazolium chloride | 100 | 8.69 ± 2.59 | 69.77 ± 1.81 | 32.53 ± 2.77 | 51.93 ± 1.64 | 9.88 ± 0.39 | 19.73 ± 0.21 |
| 2 | 1-Hexyl-3-methylimidazolium chloride | 100 | 0 ± 0 | 24.87 ± 2.52 | 11.14 ± 1.41 | 21.89 ± 1.42 | 0 ± 0 | 13.17 ± 0.37 |
| 3 | 1-Decyl-3-methylimidazolium chloride | 100 | 21.81 ± 1.06 | 72.67 ± 1.16 | 55.45 ± 1.28 | 88.51 ± 0.49 | 46.57 ± 0.71 | 55.45 ± 0.04 |
| 4 | 1-Dodecyl-3-methylimidazolium chloride | 100 | 47.13 ± 0.72 | 100 ± 0 | 97.77 ± 0.02 | 77.56 ± 0.68 | 63.94 ± 2.95 | 45.16 ± 1.33 |
| 5 | 1-Hexyl-3-methylimidazolium chloride | 100 | 69.61 ± 0.95 | 55.87 ± 2.85 | 95.05 ± 0.02 | 54.85 ± 1.87 | 36.67 ± 0.96 | 21.65 ± 0.02 |
| 6 | 1-Decyl-3-methylimidazolium bromide | 100 | 15.73 ± 0.87 | 58.88 ± 0.72 | 61.76 ± 0.13 | 85.96 ± 1.82 | 50.68 ± 1.86 | 42.96 ± 1.24 |
| 7 | Dodecyl dimethyl benzyl ammonium bromide | 100 | 73.33 ± 0.43 | 100 ± 0 | 95.11 ± 0.01 | 60.63 ± 0.39 | 55.92 ± 1.14 | 61.1 ± 0.55 |
| 8 | Benzyldimethylhexadecylammonium chloride | 100 | 58.29 ± 1.08 | 100 ± 0 | 92.78 ± 0.76 | 44.26 ± 2.12 | 29.23 ± 2.75 | 39.2 ± 1.61 |
| 9 | Myristalkonium chloride | 100 | 68.55 ± 0.76 | 100 ± 0 | 95.23 ± 0.01 | 62.15 ± 1.21 | 33.25 ± 0.52 | 38.36 ± 2.01 |
| 10 | Benzyldimethylstearylammonium Chloride | 100 | 31.81 ± 2.36 | 84.1 ± 1.35 | 92.45 ± 0.01 | 27.37 ± 0.94 | 28.19 ± 0.35 | 15.53 ± 1.22 |
| 11 | Benzododecinium chloride | 100 | 80.22 ± 0.65 | 6.1 ± 0.55 | 95.2 ± 0.22 | 60.48 ± 0.39 | 50.79 ± 2.96 | 34.15 ± 1.15 |
| 12 | 1-Butylpyridinium bromide | 100 | 0 ± 0 | 0 ± 0 | 5.38 ± 0.62 | 5.64 ± 0.35 | 0 ± 0 | 0 ± 0 |
| 13 | *N*-butyl-4-methylpyridinium chloride | 100 | 0 ± 0 | 5.13 ± 0.47 | 0 ± 0 | 10.65 ± 0.55 | 7.4 ± 0.62 | 0 ± 0 |
| 14 | 1-Hexadecylpyridinium bromide | 100 | 79.49 ± 1.56 | 76.72 ± 1.19 | 91.56 ± 0.21 | 56.61 ± 1.49 | 27.58 ± 2.46 | 11.43 ± 0.53 |
| 15 | 1-Dodecylpyridinium bromide | 100 | 76.02 ± 0.42 | 100 ± 0 | 100 ± 0 | 78.72 ± 1.21 | 79.39 ± 0.29 | 41.32 ± 0.84 |
| 16 | 3-Methyl-1-octylimidazolium chloride | 100 | 4.77 ± 0.84 | 19.9 ± 2.25 | 4.14 ± 0.61 | 24.56 ± 1.21 | 14.11 ± 3.02 | 13.49 ± 0.83 |
| 17 | 1,1'-Di-n-heptyl-4,4'-bipyridinium dibromide | 100 | 25.87 ± 0.88 | 97.12 ± 0.42 | 86.62 ± 0.35 | 85.75 ± 0.27 | 81.14 ± 1.29 | 52.12 ± 0.59 |
| 18 | 1-Tetradecylpyridinium chloride | 100 | 74.55 ± 0.59 | 96.45 ± 0.87 | 96.88 ± 0.72 | 73.76 ± 0.54 | 56.25 ± 1.16 | 21.25 ± 2.06 |
| 19 | 1-Hexadecyl-3-methylimidazolium chloride monohydrate | 100 | 4.13 ± 0.67 | 4.64 ± 0.18 | 0 ± 0 | 23.73 ± 3.16 | 0 ± 0 | 0 ± 0 |
| 20 | 1-Butyl-3-methylimidazolium chloride | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 8.21 ± 0.74 | 0 ± 0 | 0 ± 0 |
| 21 | 1-Propyl-3-methyl imidazolium | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 6.68 ± 0.02 | 7.55 ± 0.82 | 3.55 ± 0.74 |
| 22 | Octenidine dihydrochloride | 100 | 87.13 ± 0.62 | 89.21 ± 1.56 | 93.45 ± 0.06 | 86.47 ± 0.64 | 81.53 ± 0.48 | 79.33 ± 0.61 |
| 23 | Miltefosine | 100 | 75.63 ± 1.35 | 52.49 ± 0.85 | 92.30 ± 0.12 | 25.08 ± 5.06 | 22.27 ± 1.87 | 35.73 ± 1.94 |
| 24 | Chlorhexidine diacetate | 100 | 94.33 ± 0.18 | 100 ± 0 | 93.72 ± 0.46 | 97.84 ± 0.17 | 76.48 ± 1.18 | 71.91 ± 0.31 |
| 25 | Hexadecyl trimethyl ammonium bromide | 100 | 74.22 ± 2.27 | 67.42 ± 0.66 | 93.73 ± 1.62 | 54.38 ± 1.27 | 46.29 ± 0.35 | 15.02 ± 1.14 |
| 26 | Cetalkonium chloride | 100 | 70.43 ± 1.91 | 80.75 ± 1.56 | 94.66 ± 0.55 | 56.15 ± 1.12 | 39.23 ± 0.85 | 12.8 ± 1.31 |
| 27 | Domiphen bromide | 100 | 86.76 ± 0.49 | 100 ± 0 | 94.47 ± 0.7 | 83.74 ± 0.86 | 71.25 ± 0.04 | 46.21 ± 0.82 |
| 28 | Cetylpyridinium chloride | 100 | 70.53 ± 0.25 | 81.05 ± 0.9 | 91.4 ± 0.82 | 47.44 ± 1.05 | 32.82 ± 1.26 | 12.63 ± 0.37 |
| 29 | Diminazene aceturate | 100 | 8.23 ± 0.21 | 100 ± 0 | 96.23 ± 0.39 | 100 ± 0 | 59.38 ± 1.65 | 24.99 ± 0.25 |
| 30 | Pentamidine | 100 | 10.48 ± 1.00 | 100 ± 0 | 100 ± 0 | - | 57.11 ± 2.45 | 28.65 ± 0.37 |
| 31 | *N*-Octadecyl-4-stilbazole bromide | 100 | 0 ± 0 | 12.4 ± 1.85 | 20.02 ± 1.31 | 0 ± 0 | 0 ± 0 | 7.59 ± 1.16 |
| 32 | Enebicyanog | 100 | 80.68 ± 1.90 | 98.06 ± 0.36 | 100 ± 0 | 87.43 ± 1.86 | 46.73 ± 0.39 | 39.45 ± 1.93 |
| 33 | Perifosine | 100 | 51.28 ± 1.23 | 60.74 ± 1.92 | 93.29 ± 0.32 | 14.42 ± 2.95 | 32.64 ± 0.69 | 22.24 ± 2.74 |
| 34 | Pralidoxime chloride | 100 | 6.95 ± 1.65 | 29.13 ± 1.98 | 0 ± 0 | 34.52 ± 1.29 | 0 ± 0 | 0 ± 0 |
| 35 | Bephenium hydroxynaphthoate | 100 | 24.28 ± 1.36 | 67.72 ± 0.09 | 53.65 ± 1.35 | 5.88 ± 2.12 | 0 ± 0 | 7.74 ± 1.11 |
| 36 | Benzethonium chloride | 100 | 1.00 ± 0.02 | 2.09 ± 0.20 | 1.20 ± 0.65 | 2.91 ± 0.56 | 1.92 ± 0.07 | 10.33 ± 0.64 |
| 37 | Potassium sorbate | 100 | 16.4 ± 0.19 | 26.29 ± 1.55 | 0 ± 0 | 0 ± 0 | 8.23 ± 0.57 | - |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

developed as commercial herbicides are powerful accumulative inhibitors of *C. albicans* AHAS [80]. This provides two different directions for our subsequent research.

We have obtained 150 drug candidates through activity screening and many of the compounds had low acute toxicity. Surprisingly, we found that benzoimidazole/carbamate drugs (parbendazole, fenbendazole, mebendazole) (Fig. 4) and azole drugs (econazole, isoconazole nitrate, clotrimazole) (Fig. 5) showed excellent activity against plant pathogenic fungi and low toxicity. In this article benzoimidazole/carbamate drugs (parbendazole, fenbendazole, mebendazole) are mainly used as anthelmintics. The original use of halofuginone was found to be an anticoccidial. Through a drug repurposing strategy, it was found to have excellent activity against *Phytophthora* [78]. Therefore, we hope to obtain potential drugs or lead structures against plant pathogenic fungi through this strategy, which will provide the possibility for the development of agricultural fungicides.

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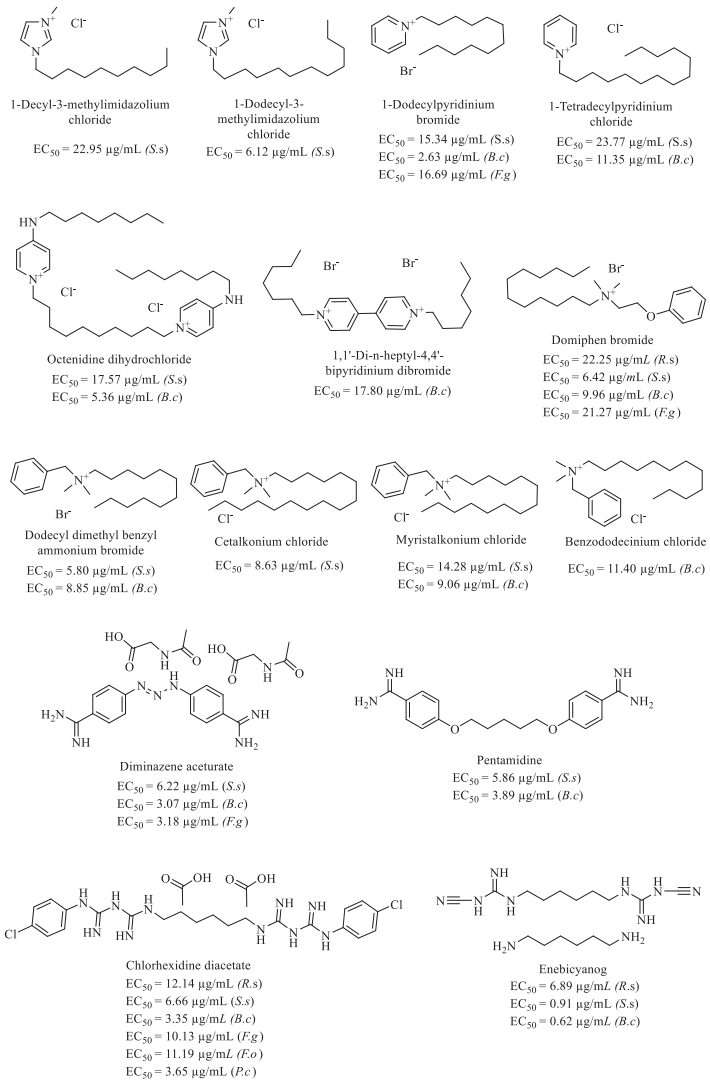


**Fig. 10** The $EC_{50}$ of ionic liquids against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

**Table 11** In vitro antifungal activities (inhibition rate/%) of the miscellaneous group against phytopathogenic fungi[a]

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 1 | Chloramphenicol | 100 | 12.82 ± 2.10 | 34.51 ± 0.63 | 11.54 ± 0.57 | 10.69 ± 1.73 | 16.80 ± 1.63 | 9.15 ± 1.03 |
| 2 | Thiamphenicol | 100 | 15.15 ± 0.43 | 40.83 ± 1.71 | 13.35 ± 2.69 | 3.09 ± 0.12 | 14.31 ± 1.26 | 5.12 ± 0.88 |
| 3 | Monensin sodium salt | 100 | 73.63 ± 2.79 | 92.9 ± 1.24 | 100 ± 0 | 47.12 ± 1.5 | 88.0 ± 0.42 | 91.3 ± 1.03 |
| 4 | Novobicin sodium salt | 100 | 40.85 ± 0.43 | 58.64 ± 3.27 | 83.95 ± 1.81 | 29.3 ± 2.92 | 17.05 ± 0.91 | 45.99 ± 2.39 |
| 5 | Rifapentine | 100 | 25.83 ± 2.61 | 0 ± 0 | 53.84 ± 0.65 | 20.36 ± 2.19 | 20.77 ± 1.95 | 46.25 ± 1.82 |
| 6 | Rifaximin | 100 | 9.78 ± 0.65 | 0 ± 0 | 65.32 ± 1.46 | 14.03 ± 0.67 | 0 ± 0 | 21.41 ± 1.24 |
| 7 | Rifamycin sodium | 100 | 78.25 ± 1.61 | 79 ± 2.85 | 83.72 ± 0.27 | 52.35 ± 2.81 | 40 ± 4.66 | 43.76 ± 1.27 |
| 8 | Rifampicin | 100 | 9.23 ± 0.28 | 0 ± 0 | 49.54 ± 0.03 | 29.38 ± 0.82 | 0 ± 0 | 31.73 ± 1.29 |
| 9 | (+)-Griseofulvin | 100 | 89.85 ± 0.82 | 84.15 ± 1.19 | 100 ± 0 | 87.69 ± 0.81 | 80.26 ± 0.86 | 85.98 ± 0.79 |
| 10 | Natamycin | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 11 | Tiamulin | 100 | 4.77 ± 0.69 | 65.13 ± 0.2 | 36.58 ± 0.67 | 37.56 ± 0.17 | 12.3 ± 0.14 | 79.63 ± 0.23 |
| 12 | Retapamulin | 100 | 17.21 ± 0.83 | 72.23 ± 0.42 | 58.09 ± 0.74 | 25.97 ± 0.39 | 41.9 ± 0.27 | 48.57 ± 1.51 |
| 13 | Naftifine hydrochloride | 100 | 56.59 ± 1.34 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 96.30 ± 0.08 | 100 ± 0 |
| 14 | Terbinafine hydrochloride | 100 | 68.44 ± 2.20 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 15 | Butenafine hydrochloride | 100 | 91.83 ± 0.65 | 100 ± 0 | 100 ± 0 | 98.27 ± 0.20 | 100 ± 0 | 100 ± 0 |
| 16 | *N*-(2-Hydroxynaphthoyl)-2,4-dimethoxy-5-chloroanilide | 100 | 53.35 ± 0.84 | 28.33 ± 1.01 | 42.56 ± 0.44 | 32.48 ± 1.75 | 17.19 ± 1.31 | 36.23 ± 2.45 |
| 17 | Tolnaftate | 100 | 84.8 ± 0.12 | 98.27 ± 0.32 | 91.63 ± 0.54 | 64.33 ± 1.02 | 79.2 ± 0.41 | 66.81 ± 0.33 |

**Table 11** (continued)

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 18 | Pyrantel pamoate | 100 | 16.05 ± 1.72 | 50.15 ± 2.7 | 62.71 ± 1.24 | 25.75 ± 1.1 | 0 ± 0 | 13.6 ± 1.42 |
| 19 | Propranolol hydrochloride | 100 | 0 ± 0 | 8.18 ± 1.5 | 48.94 ± 2.03 | 23.36 ± 0.24 | 17.44 ± 1.45 | 25.23 ± 1.36 |
| 20 | Cinacalcet | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 89.51 ± 1.09 | 93.07 ± 0.92 | 95.54 ± 1.12 |
| 21 | 1,7-Dlaminoheptane | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 11.92 ± 1.28 | 14.85 ± 0.66 |
| 22 | Tris(2-aminoethyl)amine | 100 | 0 ± 0 | 0 ± 0 | 16.88 ± 0.69 | 2.04 ± 1.57 | 0 ± 0 | 4.49 ± 0.36 |
| 23 | *N*,N'-bis(3-aminopropyl)ethylenediamine | 100 | 0 ± 0 | 0 ± 0 | 47.34 ± 1.69 | 0 ± 0 | 0 ± 0 | 6.53 ± 0.54 |
| 24 | Tetraethyenepentamine | 100 | 0 ± 0 | 0 ± 0 | 12.92 ± 1.84 | 0 ± 0 | 0 ± 0 | 8.25 ± 0.51 |
| 25 | Diethylenetriamine | 100 | 0 ± 0 | 0 ± 0 | 13.12 ± 1.48 | 3.21 ± 0.97 | 0 ± 0 | 3.27 ± 0.38 |
| 26 | N1,N1'-(butane-1,4-diyl)bis(ethane-1,2-diamine) | 100 | 0 ± 0 | 12.27 ± 2.69 | 98.53 ± 0.45 | 27.21 ± 2.51 | 3.97 ± 0.55 | 3.56 ± 2.23 |
| 27 | N- (3-Dimethylaminopropyl)-1,3-propanediamine | 100 | 0 ± 0 | 0 ± 0 | 11.05 ± 1.19 | 12.87 ± 3.58 | 0 ± 0 | 4.98 ± 1.09 |
| 28 | Cyclen | 100 | 26.59 ± 1.61 | 18.36 ± 1.15 | 0 ± 0 | 0 ± 0 | 12.93 ± 0.18 | 0 ± 0 |
| 29 | 1,4,7,10,13,16-hexazacyclooctadecane | 100 | 12.98 ± 3.11 | 12.94 ± 0.37 | 0 ± 0 | 0 ± 0 | 8.34 ± 0.39 | 0 ± 0 |
| 30 | Triethylenetetramine | 100 | 4.94 ± 0.66 | 16.65 ± 1.53 | 0 ± 0 | 0 ± 0 | 12.17 ± 0.94 | 6.41 ± 0.84 |
| 31 | Ethylenediamine | 100 | 9.07 ± 0.01 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 6.37 ± 0.78 | 0 ± 0 |
| 32 | 2-Aminoethyl(ethyl)amine | 100 | 6.53 ± 0.15 | 18.35 ± 1.92 | 14.56 ± 2.77 | 11.04 ± 0.98 | 0 ± 0 | 0 ± 0 |
| 33 | 1,3-Diaminopropane | 100 | 6.01 ± 0.65 | 13.88 ± 1.21 | 18.3 ± 0.87 | 9.53 ± 2.16 | 0 ± 0 | 0 ± 0 |
| 34 | 1,4-Butylenediamine | 100 | 10.73 ± 0.63 | 12.73 ± 0.53 | 22.97 ± 2.95 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 35 | 1,6-Diaminohexane | 100 | 11.16 ± 0.24 | 19.06 ± 0.43 | 18.05 ± 2.41 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 36 | 1,5-Diaminopentane | 100 | 7.85 ± 0.11 | 17.55 ± 4.31 | 17.09 ± 1.72 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 37 | *N*-octyl-N'-[2-(octylamino)ethyl]ethylenediamine | 100 | 63.46 ± 0.96 | 86.94 ± 0.67 | 87.71 ± 0.38 | 55.59 ± 1.31 | 68.6 ± 0.47 | 38.35 ± 0.98 |
| 38 | Ethambutol | 100 | 17.45 ± 1.19 | 11.25 ± 1.80 | 6.37 ± 0.24 | 15.67 ± 0.56 | 5.43 ± 1.76 | 9.27 ± 0.29 |
| 39 | Diethylenetriaminepentaacetic acid | 100 | 1.92 ± 0.01 | 6.25 ± 1.25 | 1.03 ± 0.04 | 5.66 ± 0.81 | 1.91 ± 0.18 | 8.24 ± 1.92 |
| 40 | Eflornithine hydrochloride hydrate | 100 | 0 ± 0 | 37 ± 0.23 | 28.45 ± 1.5 | 0 ± 0 | 81.45 ± 2.72 | 0 ± 0 |
| 41 | *N*-(3-aminopropyl)-N-dodecylpropane-1,3-diamine | 100 | 62.30 ± 0.56 | 30.58 ± 1.39 | 86.93 ± 0.96 | 64.83 ± 0.39 | 62.70 ± 0.49 | 48.66 ± 0.31 |
| 42 | Rimantadine hydrochloride | 100 | 0 ± 0 | 19.9 ± 1.83 | 0 ± 0 | 14.44 ± 0.07 | 0 ± 0 | 20.45 ± 0.54 |
| 43 | Amantadine | 100 | 0 ± 0 | 20.42 ± 2.1 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 44 | Vildagliptin | 100 | 0 ± 0 | 13.51 ± 0.27 | 11.64 ± 2.8 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 45 | Strontium ranelate | 100 | 0 ± 0 | 23.47 ± 1.01 | 7.96 ± 1.07 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 46 | 1-Adamantanamine hydrochloride | 100 | 0 ± 0 | 8.66 ± 1.49 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 5.87 ± 0.88 |
| 47 | Taurolidine | 100 | 18.3 ± 0.96 | 14.65 ± 0.82 | 34.09 ± 3.32 | 16.69 ± 1.54 | 0 ± 0 | 0 ± 0 |
| 48 | (*5 R*)-3-(4-Bromo-3-fluorophenyl)-5-hydroxy methyloxazolidin-2-one | 100 | 57.19 ± 0.05 | 0 ± 0 | 22.9 ± 0.03 | 68.54 ± 0.04 | 36.49 ± 2.42 | 23.43 ± 0.21 |
| 49 | Intermediate of linezolid | 100 | 0 ± 0 | 0 ± 0 | 6.98 ± 0.06 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 50 | Linezolid related compound | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 14.74 ± 1.73 | 19.97 ± 0.97 | 16.68 ± 0.79 |
| 51 | Rivaroxaban intermediate | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 52 | Rivaroxaban | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 7.65 ± 1.14 | 6.41 ± 2.67 |
| 53 | Linezolid | 100 | 24.9 ± 1.41 | 35.76 ± 2.54 | 0 ± 0 | 61.78 ± 0.91 | 31.44 ± 0.37 | 29.94 ± 0.77 |
| 54 | Furaltadone hydrochloride | 100 | 37.07 ± 3.77 | 18.53 ± 1.23 | 36.08 ± 1.17 | 17.28 ± 2.55 | 24.66 ± 0.01 | 36.83 ± 1.97 |
| 55 | Furazolidone | 100 | 63.35 ± 0.67 | 73.99 ± 1.6 | 54.45 ± 2.2 | 61.51 ± 1.51 | 43.28 ± 1.08 | 39.72 ± 0.92 |
| 56 | Nifuratel | 100 | 9.96 ± 2.01 | 50.16 ± 0.01 | 13.9 ± 1.03 | 48.52 ± 0.94 | 63.98 ± 1.18 | 55.51 ± 0.45 |
| 57 | L-Cycloserine | 100 | 16.64 ± 0.97 | 0 ± 0 | 51.98 ± 0.61 | 26.34 ± 2.06 | 0 ± 0 | 0 ± 0 |
| 58 | Acetylsalicylic acid | 100 | 4.17 ± 0.92 | 18.14 ± 0.16 | 7.68 ± 1.09 | 0 ± 0 | 8.35 ± 0.03 | 23.98 ± 1.32 |
| 59 | 2-Hydroxy-N-(4-hydroxyphenyl)-benzamide | 100 | 62.28 ± 0.56 | 23.18 ± 0.91 | 30.14 ± 0.59 | 41.74 ± 0.97 | 34.35 ± 1.04 | 46.4 ± 0.26 |
| 60 | 2,4-Dihydroxybenzoic acid | 100 | 0 ± 0 | 9.48 ± 0.13 | 12.68 ± 0.59 | 0 ± 0 | 8.25 ± 0.01 | 29.26 ± 1.29 |
| 61 | 4-Methoxysalicylic acid | 100 | 48.36 ± 0.72 | 34.95 ± 0.48 | 39.6 ± 1.69 | 12.81 ± 1.01 | 29.36 ± 0.31 | 38.01 ± 1.82 |
| 62 | Salicylanilide | 100 | 100 ± 0 | 66.6 ± 1.14 | 100 ± 0 | 100 ± 0 | 95.21 ± 0.58 | 100 ± 0 |
| 63 | 4-Aminosalicylic acid | 100 | 0 ± 0 | 14.92 ± 0.01 | 9.45 ± 0.88 | 8.7 ± 0.06 | 14.03 ± 0.03 | 32.08 ± 1.77 |
| 64 | 4-Fluoro-2-hydrxybenzoic acid | 100 | 5.35 ± 0.81 | 21.45 ± 0.93 | 15.89 ± 0.27 | 15.99 ± 0.69 | 23.85 ± 0.05 | 30.04 ± 0.12 |
| 65 | Ethyl 2-hydroxybenzoate | 100 | 0 ± 0 | 11.1 ± 1.13 | 0 ± 0 | 6.11 ± 0.2 | 5.86 ± 1.46 | 7.47 ± 0.89 |
| 66 | Sasapyrine | 100 | 28.57 ± 1.5 | 51.14 ± 0.77 | 53.73 ± 1.66 | 5.98 ± 0.51 | 14.88 ± 1.72 | 26.91 ± 2.02 |
| 67 | Benorilate | 100 | 20.38 ± 0.03 | 50.08 ± 0.67 | 11.13 ± 0.99 | 22.93 ± 2.54 | 9.6 ± 0.14 | 8.39 ± 1.02 |
| 68 | Thiazolidine | 100 | 0 ± 0 | 24.43 ± 0.29 | 33.64 ± 2.24 | 8.03 ± 0.53 | 1.48 ± 0.01 | 10.96 ± 0.44 |
| 69 | Salicylhydroxamic acid | 100 | 5.91 ± 0.18 | 42.9 ± 0.01 | 7.25 ± 0.44 | 34.34 ± 0.93 | 32.18 ± 0.4 | 25.48 ± 0.01 |
| 70 | Labetalol hydrochloride | 100 | 0 ± 0 | 15.73 ± 1.24 | 10.6 ± 0.27 | 10.43 ± 0.21 | 9.52 ± 0.48 | 18.26 ± 0.88 |
| 71 | Mosapride | 100 | 18.56 ± 1.34 | 34.73 ± 0.16 | 9.61 ± 0.15 | 49.02 ± 1.14 | 40.9 ± 0.56 | 39.17 ± 0.72 |
| 72 | Xipamide | 100 | 69.76 ± 1.08 | 52.3 ± 1.79 | 39.06 ± 0.55 | 14.88 ± 3.04 | 0.59 ± 0.06 | 0.87 ± 0.09 |
| 73 | Salicylamide | 100 | 27.33 ± 0.71 | 10.73 ± 1.26 | 0 ± 0 | 20.75 ± 0.54 | 22.76 ± 1.03 | 26.25 ± 1.74 |
| 74 | Niclosamide | 100 | 35.9 ± 0.82 | 49.39 ± 0.42 | - | 19.26 ± 0.8 | 8.95 ± 1.5 | 30.62 ± 0.07 |
| 75 | Salicylic acid | 100 | 15.05 ± 2.25 | 57.11 ± 2.27 | 31.44 ± 0.98 | 0 ± 0 | 10.49 ± 0.78 | 30.08 ± 0.04 |
| 76 | Oxyclozanide | 100 | 92.41 ± 1.06 | 99.21 ± 0.53 | 83.85 ± 0.4 | 55.87 ± 0.74 | 62.78 ± 1.03 | 64.47 ± 1.97 |
| 77 | Closantel | 100 | 8.75 ± 0.65 | 10.71 ± 1.16 | 0 ± 0 | 19.77 ± 0.65 | 5.23 ± 1.87 | 0 ± 0 |

**Table 11** (continued)

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 78 | Closantel sodium | 100 | 17.2 ± 0.6 | 10.46 ± 2.37 | 26.32 ± 0.97 | 42.18 ± 3.89 | 0 ± 0 | 0 ± 0 |
| 79 | Rafoxanide | 100 | 8.75 ± 0.65 | 10.71 ± 1.16 | 0 ± 0 | 19.77 ± 0.65 | 5.23 ± 1.87 | 0 ± 0 |
| 80 | Nitazoxanide | 100 | 73.03 ± 1.51 | 100 ± 0 | 100 ± 0 | 34.04 ± 0.16 | 18.41 ± 0.08 | 38.06 ± 0.26 |
| 81 | Otilonium bromide | 100 | 2.82 ± 0.37 | 0.23 ± 0.04 | 2.94 ± 0.27 | 7.23 ± 2.79 | 2.28 ± 0.31 | 7.69 ± 0.02 |
| 82 | Diflunisal | 100 | 1.57 ± 0.32 | 3.0 ± 0.18 | 2.21.±0.03 | 7.59 ± 1.38 | 5.35 ± 3.97 | 6.73 ± 1.54 |
| 83 | Sulfasalazine | 100 | 0 ± 0 | 5.13 ± 0.35 | 0 ± 0 | 15.58 ± 1.47 | 9.55 ± 0.01 | 24.04 ± 3.33 |
| 84 | Enzalutamide | 100 | 58.87 ± 0.98 | 52.21 ± 0.83 | 54.04 ± 1.95 | 11.39 ± 1.82 | 25.17 ± 0.95 | 29.94 ± 1.28 |
| 85 | Olsalazine sodium | 100 | 11.38 ± 0.4 | 25.42 ± 0.13 | 15.17 ± 0.71 | - | - | - |
| 86 | Tranilast | 100 | 13.82 ± 1.5 | 63.23 ± 1.41 | 66.9 ± 1.81 | 0 ± 0 | 19.58 ± 0.58 | 43.75 ± 1.03 |
| 87 | Metoclopramide hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 88 | Sulfasalazine | 100 | 0 ± 0 | 5.13 ± 0.35 | 0 ± 0 | 15.58 ± 1.47 | 9.55 ± 0.01 | 24.04 ± 3.33 |
| 89 | Sulfaquinoxaline sodium | 100 | 50.37 ± 0.89 | 39.96 ± 2.97 | 69.26 ± 1.06 | 89.19 ± 0.84 | 86.95 ± 0.31 | 83.33 ± 1.59 |
| 90 | Sodium N-(6-chloropyrazinyl)sulphanilamidate | 100 | 21.53 ± 0.89 | 13.04 ± 1.27 | 64.72 ± 1.17 | 38.93 ± 0.74 | 76.13 ± 0.57 | 11.4 ± 1.07 |
| 91 | Sulfamethazine | 100 | 7.78 ± 1.08 | 0 ± 0 | 44.55 ± 0.64 | 6.05 ± 1.35 | 0 ± 0 | 0 ± 0 |
| 92 | Sulfamonomethoxine | 100 | 26.8 ± 4.44 | 0 ± 0 | 55.82 ± 1.52 | 52.15 ± 1.51 | 68.05 ± 1.65 | 10.19 ± 3.72 |
| 93 | Sulfachloropyridazine | 100 | 11.93 ± 0.92 | 0 ± 0 | 59.16 ± 0.5 | 28.5 ± 2.09 | 7.23 ± 0.61 | 0 ± 0 |
| 94 | Sodium N-(5-methylisoxazol-3-yl)sulphanilamidate | 100 | 30.78 ± 1.37 | 25.33 ± 0.65 | 90.8 ± 1.05 | 84.63 ± 0.09 | 86.75 ± 0.01 | 62.85 ± 0.02 |
| 95 | Sulfamethoxypyridazine | 100 | 5.98 ± 1.61 | 0 ± 0 | 5.13 ± 0.98 | 13.44 ± 0.44 | 11.16 ± 2.24 | 2.39 ± 0.41 |
| 96 | Sulfisoxazole | 100 | 0 ± 0 | 54.52 ± 1.29 | 59.39 ± 3.07 | 51.54 ± 3.01 | 0 ± 0 | 76.85 ± 0.66 |
| 97 | Bensulfuron-methyl | 100 | 50.42 ± 1.71 | 96.7 ± 0.78 | 89.04 ± 0.64 | 75.41 ± 1.32 | 44.46 ± 0.37 | 47.11 ± 0.55 |
| 98 | Chlorimuron-ethyl | 100 | 73.12 ± 1.23 | 91.36 ± 0.51 | 92.16 ± 0.17 | 76.78 ± 0.62 | 64.46 ± 2.29 | 61.42 ± 1.2 |
| 99 | Fasudil hydrochloride | 100 | 0 ± 0 | 23.79 ± 3.65 | 8.44 ± 3.47 | 38.43 ± 1.29 | 5.79 ± 1.90 | 5.18 ± 0.92 |
| 100 | Vemurafenib | 100 | 93.29 ± 0 | 15.48 ± 2.71 | 3.82 ± 0.08 | 10.74 ± 0.14 | 0 ± 0 | 4.58 ± 0.47 |
| 101 | Brinzolamide | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 9.18 ± 2.75 | 0 ± 0 |
| 102 | Dexamethasone | 100 | 1.73 ± 0.07 | 69.93 ± 1.36 | 14.13 ± 0.72 | 8.15 ± 0.63 | 3.92 ± 0.99 | 6.77 ± 1.11 |
| 103 | Spironolactone | 100 | 33.88 ± 1.58 | 48.54 ± 0.37 | 52.52 ± 1.23 | 42.73 ± 1.89 | 24.83 ± 1.41 | 38.08 ± 0.66 |
| 104 | Triamcinolone acetonide | 100 | 0 ± 0 | 0 ± 0 | 5.8 ± 2.03 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 105 | Betamethasone | 100 | 0 ± 0 | 7.65 ± 0.94 | 0 ± 0 | 0 ± 0 | 35.41 ± 1.12 | 0 ± 0 |
| 106 | Hydrocortisone | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 10.42 ± 2.34 | 0 ± 0 | 0 ± 0 |
| 107 | Prednisolone | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 108 | Fluticasone propionate | 100 | 0 ± 0 | 0 ± 0 | 31.48 ± 1.52 | 0 ± 0 | 0.79 ± 0.56 | 1.95 ± 1.54 |
| 109 | Bardoxolone methyl | 100 | 75.15 ± 1.32 | 36.5 ± 2.81 | 88.74 ± 0.82 | 61.27 ± 0.54 | 57.32 ± 0.39 | 26.27 ± 1.17 |
| 110 | Megestrol | 100 | 0 ± 0 | 16 ± 2.63 | 0 ± 0 | 10.4 ± 1.73 | 6.98 ± 0.13 | 13.07 ± 0.89 |
| 111 | Trilostane | 100 | 7.98 ± 1.23 | 36.02 ± 1.96 | 22.35 ± 2.87 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 112 | Stanozolol | 100 | 2.92 ± 1.03 | 19.45 ± 2.16 | 20.18 ± 0.36 | 33.94 ± 1.22 | 48.6 ± 0.35 | 45.57 ± 1.96 |
| 113 | Megestrol acetate | 100 | 1.94 ± 0.5 | 2.1 ± 0.1 | 1.28 ± 0.29 | 5.98 ± 0.76 | 3.00 ± 0.1 | 1.81 ± 0.04 |
| 114 | Thiacetazone | 100 | 9.13 ± 0.55 | 0 ± 0 | 21.38 ± 0.23 | 13.33 ± 1.25 | 12.33 ± 0.36 | 18.86 ± 0.47 |
| 115 | Imidurea | 100 | 17.07 ± 0.74 | 18.11 ± 2.84 | 18.56 ± 1.04 | 6.63 ± 2.15 | 0 ± 0 | 0 ± 0 |
| 116 | Imidocarb dipropionate | 100 | 19.28 ± 0.94 | 41.27 ± 1.37 | 63.31 ± 1.08 | 73.21 ± 1.01 | 55.28 ± 2.53 | 22.58 ± 0.93 |
| 117 | Glimepiride | 100 | 15.73 ± 0.2 | 32.37 ± 2.33 | 43.39 ± 1.11 | 0 ± 0 | 16.34 ± 0.98 | 0 ± 0 |
| 118 | Triclocarban | 100 | 31.08 ± 1.2 | 39.37 ± 0.83 | 0 ± 0 | 7.22 ± 0.75 | 9.79 ± 0.54 | 27.36 ± 0.62 |
| 119 | Ripretinib | 100 | 0 ± 0 | 27.57 ± 1.15 | 13.33 ± 0.72 | 17.56 ± 1.24 | 16.8 ± 1.43 | 0 ± 0 |
| 120 | Allantoin | 100 | 0 ± 0 | 63.06 ± 0.03 | 0 ± 0 | 22.05 ± 0.31 | 11.7 ± 1.76 | 30.96 ± 0.42 |
| 121 | Dichloroisocyanyric acid | 100 | 0 ± 0 | 31.03 ± 1.27 | 7.31 ± 2.97 | 17.73 ± 0.32 | 10.65 ± 0.03 | 25.63 ± 0.59 |
| 122 | 1,3-Dichloro-5,5-dimethylhydantoin | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | - |
| 123 | Thalidomide | 100 | 12.18 ± 3.2 | 5.74 ± 0.33 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 23.83 ± 1.43 |
| 124 | Apremilast | 100 | 0 ± 0 | 59.24 ± 1.36 | 16.61 ± 1.79 | 0 ± 0 | 16.81 ± 0.44 | 0 ± 0 |
| 125 | Primidone | 100 | 0 ± 0 | 21.07 ± 1.99 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 126 | 4,4,4-Trifluoro-1-(4-fluorophenyl)butane-1,3-dione | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 85.48 ± 0.31 | 94.74 ± 0.71 |
| 127 | Sodium dehydroacetate | 500 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 128 | 1-(4-Chlorophenyl)-4,4,4-trifluoro-1,3-butanedione | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 97.11 ± 0.66 | 100 ± 0 |
| 129 | 2*H*-1,3-Benzoxazine-2,4(3*H*)-dione | 100 | 33.45 ± 1.7 | 0 ± 0 | 3.63 ± 0.93 | 24.83 ± 1.28 | 29.28 ± 0.55 | 21.69 ± 0.29 |
| 130 | Diclazuril | 100 | 25.02 ± 0.39 | 0 ± 0 | 68.33 ± 0.98 | 7.78 ± 1.78 | 30.48 ± 2.34 | 50.68 ± 1.09 |
| 131 | Avobenzone | 100 | 24.84 ± 0.09 | 0 ± 0 | 10.03 ± 0.62 | 12.19 ± 2.2 | 0 ± 0 | 0 ± 0 |
| 132 | *N*,N-methylenebis N'-1-(hydroxymethyl)-2,5-dioxo-4-imidazolidinyl urea | 100 | 17.07 ± 0.74 | 18.11 ± 2.84 | 18.56 ± 1.04 | 6.63 ± 2.15 | 0 ± 0 | 0 ± 0 |
| 133 | Theophylline | 100 | 15.4 ± 1.68 | 0 ± 0 | 22.36 ± 0.99 | 4.87 ± 0.39 | 0 ± 0 | 18.21 ± 1.55 |
| 134 | Bumetanide | 100 | 0 ± 0 | 33.73 ± 0.56 | 5.51 ± 0.28 | 23.32 ± 0.57 | 8.78 ± 0.97 | 76.71 ± 2.02 |
| 135 | Triclosan | 100 | 88.87 ± 0.57 | 92.01 ± 0.17 | 100 ± 0 | 100 ± 0 | 93.26 ± 0.17 | 89.18 ± 0.46 |
| 136 | Tamoxifen | 100 | 53.7 ± 2.67 | 100 ± 0 | 100 ± 0 | 41.21 ± 0.97 | 69.21 ± 0.33 | 62.77 ± 0.01 |
| 137 | Fluoxetine hydrochloride | 100 | 49.9 ± 1.4 | 67.16 ± 3.81 | 80.15 ± 0.53 | 65.05 ± 1.54 | 56.21 ± 1.27 | 60.84 ± 0.06 |

**Table 11** (continued)

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 138 | Benztropine mesylate | 100 | 28.64 ± 1.36 | 48.56 ± 2.36 | 80.4 ± 0.3 | 33.24 ± 1.44 | 23.88 ± 0.75 | 41.18 ± 0.67 |
| 139 | Dronedarone hydrochloride | 100 | 86.92 ± 0.01 | 78.44 ± 0.53 | 98.97 ± 0.22 | 68.88 ± 0.01 | 79.75 ± 0.42 | 76.4 ± 0.78 |
| 140 | Bazedoxifene acetate | 100 | 0 ± 0 | 64.9 ± 1.86 | 60.5 ± 2.82 | 17.93 ± 2.12 | 29.53 ± 3.07 | 36.82 ± 0.43 |
| 141 | Rolipram | 100 | 17.01 ± 0.25 | 21.2 ± 1.04 | 0 ± 0 | 0 ± 0 | 17.75 ± 0.56 | 13.61 ± 0.65 |
| 142 | Ranitidine hydrochloride | 100 | 17.86 ± 2.59 | 10.71 ± 2.08 | 16.61 ± 1.09 | 0 ± 0 | 14.67 ± 0.36 | 7.65 ± 0.19 |
| 143 | Nimesulide | 100 | 67.47 ± 0.55 | 66.11 ± 0.73 | 97.2 ± 0.87 | 55.85 ± 2.09 | 34.62 ± 2.45 | 40.55 ± 0.92 |
| 144 | Orphenadrine citrate | 100 | 28.84 ± 2.05 | 12.99 ± 2.93 | 45.9 ± 1.41 | 23.88 ± 1.29 | 0 ± 0 | 13.14 ± 1.59 |
| 145 | Diphenhydramine hydrochloride | 100 | 27.53 ± 0.3 | 11.56 ± 1.05 | 31.72 ± 0.56 | 21.66 ± 2.1 | 0 ± 0 | 12.29 ± 0.95 |
| 146 | Diphenhydramine | 100 | 0 ± 0 | 0 ± 0 | 12.22 ± 3.82 | 22.11 ± 3.99 | 0 ± 0 | 10.46 ± 1.16 |
| 147 | 5,5′-Dithiobis(2-nitrobenzoic acid) | 100 | 17.1 ± 7.15 | 12.02 ± 0.65 | 28.88 ± 2.52 | 6.63 ± 1.22 | 0 ± 0 | 6.14 ± 0.28 |
| 148 | Toltrazuril | 100 | 20.55 ± 0.6 | 0 ± 0 | 44.98 ± 1.48 | 9.36 ± 0.8 | 0 ± 0 | 14.5 ± 0.74 |
| 149 | Arbidol hydrochloride | 100 | 66.22 ± 0.13 | 84.81 ± 0.34 | 65.49 ± 0.53 | 57.95 ± 1.44 | 66.27 ± 0.49 | 59.6 ± 0.5 |
| 150 | Disulfiram | 100 | 91.86 ± 0.79 | 100 ± 0 | 58.48 ± 1.12 | 71.27 ± 1.45 | 71.51 ± 0.88 | 66.57 ± 0.01 |
| 151 | Probucol | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 152 | Benzydamine hydrochloride | 100 | 40.63 ± 2.31 | 33.35 ± 0.71 | 64.5 ± 0.91 | 35.25 ± 1.39 | 17.95 ± 1.12 | 31.62 ± 1.49 |
| 153 | Bithionol | 100 | 71.66 ± 2.32 | 70.57 ± 0.41 | 57.32 ± 0.76 | 60.02 ± 0.78 | 65.85 ± 0.7 | 75.17 ± 0.51 |
| 154 | Fluoxetine | 100 | 48.91 ± 1.22 | 63.73 ± 0.15 | 80.02 ± 3.45 | 63.55 ± 2.95 | 37.25 ± 1.93 | - |
| 155 | Carvedilol | 100 | 22.17 ± 1.27 | 65.81 ± 2.18 | 79.24 ± 0.96 | 63.44 ± 1.94 | 28.83 ± 1.10 | - |
| 156 | JX06 | 100 | 89.95 ± 0.73 | 12.35 ± 0.26 | 39.71 ± 0.84 | 59.5 ± 0.65 | 52.79 ± 0.14 | 56.32 ± 0.06 |
| 157 | Iodopropynyl butylcarbamate | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 92.05 ± 0.14 | 100 ± 0 |
| 158 | 2- Cyano-3-hydroxy-*N*-(4'-trifluoromethylphenyl)-crotone amide | 100 | 35.29 ± 1.18 | 79.74 ± 1.91 | 83.26 ± 1.46 | 6.87 ± 1.24 | 8.86 ± 1.31 | 21.17 ± 0.6 |
| 159 | Vorinostat | 100 | 0 ± 0 | 0 ± 0 | 43.4 ± 1.34 | 10.04 ± 0.38 | 8.23 ± 1.84 | 19.21 ± 0.4 |
| 160 | Florfenicol | 100 | 14.31 ± 1.95 | | 16.61 ± 0.96 | 11.95 ± 0.63 | 22.82 ± 0.68 | 6.37 ± 0.78 |
| 161 | Bicalutamide | 100 | 37.05 ± 0.7 | 53.43 ± 0.43 | 64.66 ± 1.02 | 32.35 ± 2.56 | 30.94 ± 1.68 | 28.01 ± 2.13 |
| 162 | Leflunomide | 100 | 96.77 ± 0.25 | 90.45 ± 0.46 | 86.69 ± 0.34 | 50.27 ± 2.01 | 78.5 ± 0.28 | 70.53 ± 1.6 |
| 163 | Itopride hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 2.39 ± 0.99 | 0 ± 0 | 0 ± 0 | 5 ± 1.8 |
| 164 | Entacapone | 100 | 9.8 ± 1.5 | 69.31 ± 2.32 | 7.98 ± 0.05 | 0 ± 0 | 21.8 ± 1.28 | 0 ± 0 |
| 165 | Favipiravir | 100 | 12.44 ± 1.83 | 68.29 ± 0.27 | 61.55 ± 1.07 | 0 ± 0 | 9.43 ± 1.63 | - |
| 166 | 1,2,4-Triazolo[4,3-a]pyridin-3(2*H*)-one | 100 | 0 ± 0 | 49.48 ± 1.81 | 0 ± 0 | 0 ± 0 | 7.72 ± 0.73 | 11.88 ± 0.57 |
| 167 | Tadalafil | 100 | 23.09 ± 1.73 | 0 ± 0 | 9.15 ± 0.77 | 0 ± 0 | 12.71 ± 0.87 | 12.46 ± 1.17 |
| 168 | Efavirenz | 100 | 94.85 ± 0.01 | 96.37 ± 0.04 | 62.6 ± 2.31 | 73.4 ± 1.52 | 78.25 ± 0.41 | 82.11 ± 1.37 |
| 169 | Levosimendan | 100 | 27.63 ± 1.15 | 58.5 ± 0.68 | 58.59 ± 0.62 | 16.13 ± 1.38 | 13.98 ± 0.34 | 13.91 ± 0.59 |
| 170 | Azelastine hydrochloride | 100 | 43.78 ± 1.45 | 75.59 ± 1.13 | 78 ± 0.93 | 45.1 ± 1.29 | 58.94 ± 0.39 | 51.33 ± 0.6 |
| 171 | Sunitinib | 100 | 59.79 ± 0.86 | 75.71 ± 0.81 | 87.45 ± 0.5 | 55.94 ± 2.6 | 64.79 ± 0.87 | 46.12 ± 0.36 |
| 172 | Upadacitinib | 100 | 0 ± 0 | 26.86 ± 1.92 | 12.32 ± 2.05 | 28.42 ± 3.65 | 17.41 ± 0.49 | 0 ± 0 |
| 173 | PF01367338 phosphate | 100 | 86.26 ± 0.73 | 90.65 ± 0.37 | 73.85 ± 1.23 | 38.88 ± 1.45 | 53.65 ± 1.66 | 43.16 ± 0.37 |
| 174 | Trametinib | 100 | 18.3 ± 2.6 | 0 ± 0 | 9.95 ± 0.49 | 10.79 ± 0.27 | 3.34 ± 0.61 | 0 ± 0 |
| 175 | Valnemulin hydrochloride | 100 | 0 ± 0 | 63.1 ± 0.45 | 70.73 ± 2.11 | 12.03 ± 0.31 | 25.23 ± 1.03 | 57.88 ± 1.74 |
| 176 | Nifuroxazide | 100 | 14.82 ± 1.61 | 14.05 ± 1.28 | 15.81 ± 0.55 | 16.29 ± 0.64 | 0 ± 0 | 0 ± 0 |
| 177 | Iproniazid | 100 | 0 ± 0 | 4.44 ± 0.75 | 8.06 ± 1.4 | 0 ± 0 | 0 ± 0 | 5.27 ± 0.06 |
| 178 | Cyanoacetohydrazide | 100 | 12.49 ± 1.81 | 24.16 ± 3.75 | 17.81 ± 0.84 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 179 | Praziquantel | 100 | 61.69 ± 1.82 | 22.65 ± 1.10 | 38.58 ± 2.56 | 31.59 ± 0.37 | 28.65 ± 1.06 | 24.92 ± 0.64 |
| 180 | Pyrazinamide | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 181 | Ebselen | 100 | 75.99 ± 0.93 | 24.38 ± 0.92 | 65.36 ± 0.91 | - | 30.09 ± 0.80 | 49.65 ± 0.18 |
| 182 | Temozolomideacid | 100 | 4.82 ± 0.78 | 0 ± 0 | 16.2 ± 1.03 | 11.03 ± 1.79 | 0 ± 0 | 12.02 ± 2.68 |
| 183 | Atorvastatin | 100 | 7.1 ± 1.11 | 16.44 ± 0.68 | 1.67 ± 0.38 | 28.2 ± 0.03 | 10.14 ± 2.01 | 8.06 ± 0.42 |
| 184 | Indometacin | 100 | 90.33 ± 0.45 | 65.23 ± 0.83 | 81.24 ± 1.09 | 57.2 ± 0.61 | 78.02 ± 0.41 | 59.86 ± 2.63 |
| 185 | Trimethobenzamide hydrochloride | 100 | 11.39 ± 2.65 | 27.93 ± 1.18 | 20.55 ± 1.55 | 18.71 ± 1.94 | 0 ± 0 | 0 ± 0 |
| 186 | Levetiracetam | 100 | 10.95 ± 1 | 0 ± 0 | 11.9 ± 1.01 | 18.2 ± 1.85 | 0 ± 0 | 0 ± 0 |
| 187 | 7-Aminodesacetoxycephalosporanic acid | 100 | 5.55 ± 0.58 | 17.58 ± 1.13 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 9.94 ± 0.64 |
| 188 | (2S-trans)-3-Amino-2-methyl-4-oxoazetidine-1-sulphonic acid | 100 | 3.77 ± 0.42 | 17.93 ± 2.42 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 11.82 ± 0.25 |
| 189 | Dichloro-1,2-dithiacyclopentenone | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 190 | Anethole trithione | 100 | 41.44 ± 0.74 | 49.75 ± 1.18 | 0 ± 0 | 10.92 ± 0.44 | 7.34 ± 0.74 | 13.82 ± 0.2 |
| 191 | 3*H*-1,2-Benzodithiol-3-one | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 62.89 ± 1.13 | 19.59 ± 1.51 | 62.44 ± 1.47 |
| 192 | 2,3-Dimercapto-1-propanol | 100 | 10.9 ± 0.89 | 5.93 ± 0.14 | 0 ± 0 | 15.44 ± 0.46 | 0 ± 0 | 23.24 ± 0.92 |
| 193 | Oltipraz | 100 | 33.89 ± 0.43 | 41.34 ± 1.50 | 46.53 ± 2.43 | 4.49 ± 1.16 | 4.51 ± 0.69 | 12.98 ± 2.2 |
| 194 | Sertraline hydrochloride | 100 | 100 ± 0 | 100 ± 0 | 94.11 ± 0.79 | 77.6 ± 0.45 | 88.74 ± 0.66 | 88.23 ± 0.71 |
| 195 | Ethyl bromopyruvate | 100 | 18.87 ± 1.3 | 9.17 ± 0.56 | 0 ± 0 | 20.65 ± 0.43 | 16.84 ± 0.44 | 20.51 ± 0.29 |
| 196 | Atovaquone | 100 | 0 ± 0 | 10.5 ± 1.33 | 15.98 ± 0.68 | 36.04 ± 1.85 | 14.46 ± 0.92 | 29.8 ± 0.04 |

**Table 11** (continued)

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 197 | Clorprenaline hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 4.72 ± 1.73 | 0 ± 0 | 0 ± 0 | 5.78 ± 0.23 |
| 198 | Simvastatin | 100 | 83.39 ± 0.04 | 74.06 ± 0.23 | 86.2 ± 0.68 | 56.73 ± 0.01 | 73.68 ± 2.4 | 68.46 ± 0.25 |
| 199 | Clomipramine hydrochloride | 100 | 62.01 ± 1.98 | 82.57 ± 1.33 | 88.14 ± 0.83 | 63.92 ± 0.31 | 75.11 ± 1.97 | 69.94 ± 0.71 |
| 200 | Benzbromarone | 100 | 57.66 ± 0.01 | 82.36 ± 1.45 | 98.63 ± 0.15 | 82.28 ± 2.17 | 92.04 ± 0.08 | 51.79 ± 0.04 |
| 201 | Nortaiptyline hydrochloride | 100 | 0 ± 0 | 2.01 ± 0.96 | 3.1 ± 0.05 | 0.19 ± 0.93 | 2.98 ± 0.01 | 2.60 ± 0.1 |
| 202 | Fluvastatin sodium salt | 100 | 86.78 ± 1.28 | 100 ± 0 | 100 ± 0 | 54.06 ± 0.74 | 100 ± 0 | 100 ± 0 |
| 203 | Tulobuterol hydrochloride | 100 | 12.47 ± 2.49 | 0 ± 0 | 17.18 ± 0.92 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 204 | Tilorone dihydrochloride | 100 | 10.3 ± 0.64 | 0 ± 0 | 61.23 ± 2.09 | 28.14 ± 1.93 | 19.48 ± 1.07 | 16.02 ± 0.26 |
| 205 | Dichlorophen | 100 | 96.01 ± 1.31 | 100 ± 0 | 87.6 ± 0.49 | 84.2 ± 0.45 | 87.62 ± 0.49 | 83.1 ± 0.99 |
| 206 | Clofazimine | 100 | 41.89 ± 1.84 | 18.72 ± 0.89 | 55.46 ± 2.2 | 30.52 ± 0.88 | 34.86 ± 0.02 | 32.45 ± 1.97 |
| 207 | Ethopabate | 100 | 19.63 ± 1.42 | 0 ± 0 | 31.73 ± 1.15 | 6.81 ± 1.92 | 9.45 ± 1.39 | 9.24 ± 1.75 |
| 208 | (*E*,*E*)-Farnesol | 100 | 76.7 ± 0.33 | 59.79 ± 1.57 | 72.95 ± 0.32 | 52.13 ± 1.03 | 16.28 ± 0.91 | 29.52 ± 0.9 |
| 209 | Chlorphenesin | 100 | 25.04 ± 1.93 | 54.53 ± 0.06 | 29.76 ± 0.7 | 34.94 ± 2.77 | 0 ± 0 | 36.21 ± 1.34 |
| 210 | 2-Benzoxazolinone | 100 | 20.15 ± 2.33 | 9.08 ± 0.62 | 26.61 ± 3.17 | 37.21 ± 1.24 | 0 ± 0 | 8.93 ± 0.67 |
| 211 | Triacetin | 100 | 8.4 ± 1.03 | 15.82 ± 3.67 | 18 ± 2.33 | 5.69 ± 0.81 | 0 ± 0 | 0 ± 0 |
| 212 | Bronopol | 100 | 71.19 ± 1.64 | 50 ± 1.53 | 58.31 ± 0.96 | 82.6 ± 1.08 | 53.32 ± 2.05 | 39.32 ± 0.68 |
| 213 | Flufenamic acid | 100 | 94.95 ± 0.12 | 97.95 ± 0.26 | 91.7 ± 0.19 | 77.13 ± 1.49 | 84.31 ± 0.54 | 82.43 ± 0.24 |
| 214 | Pyrantel tartrate salt | 100 | 5.08 ± 0.67 | 0 ± 0 | 5.18 ± 0.2 | 21.76 ± 1.58 | 1.89 ± 0.34 | 6.26 ± 1.3 |
| 215 | Carbonyl cyanide 3-chloro-phenylhydrazone | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 |
| 216 | Atropine sulfate monohydrate | 100 | 5.52 ± 1.64 | 0 ± 0 | 7.76 ± 0.82 | 2.31 ± 0.93 | 0 ± 0 | 5.17 ± 0.26 |
| 217 | Monomyristitin | 100 | 0 ± 0 | 0 ± 0 | 5.31 ± 1.58 | 3.79 ± 0.76 | 0 ± 0 | 0.87 ± 0.5 |
| 218 | Lumefantrine | 100 | 0 ± 0 | 22.51 ± 0.38 | 24.36 ± 2.37 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 219 | 4-(2-Aminoethyl)benzenesulfonylfluoride hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 15.96 ± 0.86 |
| 220 | Bufexamac | 100 | 19.1 ± 1.94 | 92.13 ± 0.21 | 57.14 ± 0.4 | 34.26 ± 0.81 | 0 ± 0 | 42.07 ± 0.68 |
| 221 | 1-(2,6-Dichlorophenyl)-2-indolinone | 100 | 83.65 ± 0.41 | 91.79 ± 0.86 | 78.64 ± 0.04 | 39.33 ± 0.22 | 74.43 ± 0.79 | 80.63 ± 1.16 |
| 222 | 5-Phenylpenta-2,4-dienoic acid | 100 | 68.76 ± 0.35 | 100 ± 0 | 93.72 ± 0.46 | 47.14 ± 0.21 | 33.08 ± 1.56 | 47.11 ± 2.43 |
| 223 | Hydroxyurea | 100 | 50.19 ± 0.55 | 23.08 ± 1.13 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 224 | Acetylcysteine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 12.22 ± 1.17 |
| 225 | Escitalopram oxalate | 100 | 0 ± 0 | 11.52 ± 1.51 | 0 ± 0 | 17.36 ± 1.29 | 0 ± 0 | 11.25 ± 1.5 |
| 226 | Ezetimibe | 100 | 62.77 ± 1.32 | 68.85 ± 0.73 | 63.88 ± 0.52 | 48.58 ± 0.66 | 44.76 ± 0.43 | 60.89 ± 0.51 |
| 227 | Venlafaxine hydrochloride | 100 | 0 ± 0 | 12.48 ± 0.65 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 25.47 ± 1.76 |
| 228 | (+/-)-Verapamil hydrochloride | 100 | 0 ± 0 | 2.82 ± 0.65 | 31.6 ± 2.72 | 27.8 ± 2.09 | 5.03 ± 0.84 | 9.41 ± 2.1 |
| 229 | Mecarbinate | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 5.86 ± 2.28 | 7.78 ± 1.61 | 11.26 ± 1.24 |
| 230 | Ipratropium bromide | 100 | 0 ± 0 | 0 ± 0 | 4.03 ± 0 | 4.45 ± 0.62 | 0 ± 0 | 4.82 ± 1.62 |
| 231 | Ketotifen fumarate | 100 | 24.23 ± 3.25 | 21.97 ± 0.4 | 36.68 ± 1.72 | 44.51 ± 1.46 | 0 ± 0 | 11.93 ± 1.04 |
| 232 | Verapamil | 100 | 4.9 ± 2.23 | 45.33 ± 0.97 | 17.69 ± 1.7 | 18.51 ± 1.85 | 6.73 ± 0.38 | 0 ± 0 |
| 233 | RU-58841 (72) | 100 | 4 ± 0.38 | 43.44 ± 1.04 | 0 ± 0 | 12.31 ± 1.77 | 10.25 ± 1.38 | 0 ± 0 |
| 234 | Amylmetacresol | 100 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 100 ± 0 | 70.15 ± 1.79 | 54.78 ± 0.6 |
| 235 | Nisin | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 7.53 ± 0.16 |
| 236 | Silver | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | |
| 237 | Combretastatin A-4 | 100 | 69.75 ± 0.04 | 42.08 ± 0.27 | 19.06 ± 2.17 | 11.96 ± 0.11 | 29.35 ± 0.3 | 64.04 ± 0.48 |
| 238 | Procaine | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 14.13 ± 0.28 | 13.34 ± 0.87 |
| 239 | Phenformin hydrochloride | 100 | 9.35 ± 1.75 | 36.91 ± 0.71 | 28.82 ± 0.54 | 10.65 ± 1.83 | 6.75 ± 0.34 | 20.3 ± 1.02 |
| 240 | Moroxydine hydrochloride | 100 | 13.39 ± 1.09 | 0 ± 0 | 22.41 ± 0.04 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 241 | Febantel | 100 | 100 ± 0 | 38.88 ± 1.59 | 68.78 ± 0.37 | 36.27 ± 1.81 | 6.36 ± 0.12 | 13.28 ± 0.43 |
| 242 | 3,4-dihydroquinolin-2(1*H*)-one | 100 | 21.01 ± 2.51 | 52.19 ± 1.99 | 0 ± 0 | 16.05 ± 0.52 | 13.9 ± 1 | 24.9 ± 1.4 |
| 243 | 6-Bromo--3,4-dihydro-1H-Quinolin-2-one | 100 | 84.91 ± 1.44 | 62.48 ± 0.39 | 61.03 ± 1.12 | 49.67 ± 2.81 | 64.05 ± 0.39 | 46.4 ± 0.01 |
| 244 | 7-Hydroxy-3,4-dihydro-2(1*H*)-quinolinone | 100 | 12.75 ± 0.01 | 45.63 ± 0.34 | 23.65 ± 3 | 0 ± 0 | 9.58 ± 0.02 | 21.5 ± 0.45 |
| 245 | 6-Hydroxy-1,2,3,4-Tetrahydro--2-Quinolinone | 100 | 8.89 ± 0.46 | 45.68 ± 0.57 | 5.6 ± 1.32 | 0 ± 0 | 7.95 ± 1.43 | 13.99 ± 1.28 |
| 246 | 5-Hydroxy-3,4-dihydro-2(1*H*)-quinolinone | 100 | 12.4 ± 1.16 | 45.85 ± 0.02 | 0 ± 0 | 0 ± 0 | 8.75 ± 0.39 | 15.05 ± 0.41 |
| 247 | Oxolinc acid impurity B | 100 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 5.37 ± 0.47 |
| 248 | Levofloxacin hydrochloride | 100 | 0 ± 0 | 0 ± 0 | 61.22 ± 1.05 | 24.08 ± 0.50 | 0 ± 0 | 25.68 ± 0.35 |
| 249 | Norfloxacin | 100 | 0 ± 0 | 0 ± 0 | 25.55 ± 0.17 | 39.69 ± 0.28 | 0 ± 0 | 10.73 ± 0.51 |
| 250 | Gatifloxacin | 100 | 26.47 ± 0.59 | 0 ± 0 | 46.60 ± 0.36 | 10.95 ± 0.70 | 6.95 ± 0.32 | 20.50 ± 0.53 |
| 251 | Fleroxacin | 100 | 0 ± 0 | 42.88 ± 0.44 | 42.03 ± 0.57 | 22.37 ± 0.17 | 00 ± 0 | 13.50 ± 0.83 |
| 252 | Ciprofloxacin | 100 | 0 ± 0 | 4.30 ± 0.26 | 48.90 ± 0.40 | 42.93 ± 0.24 | 4.42 ± 0.34 | 16.58 ± 0.30 |
| 253 | Enrofloxacin | 100 | 0 ± 0 | 0 ± 0 | 59.99 ± 0.45 | 8.50 ± 0.31 | 33.35 ± 0.30 | 59.60 ± 0.43 |
| 254 | Moxifloxacin | 100 | 0 ± 0 | 17.78 ± 0.44 | 45.00 ± 0.63 | 8.25 ± 0.44 | 18.42 ± 0.13 | 25.91 ± 0.24 |
| 255 | Enoxacin | 100 | 0 ± 0 | 0 ± 0 | 6.90 ± 0.57 | 4.43 ± 0.50 | 4.45 ± 0.29 | 10.50 ± 0.26 |
| 256 | Nalidixic acid | 100 | 9.87 ± 0.53 | 71.98 ± 0.60 | 5.88 ± 0.46 | 15.68 ± 0.26 | 69.57 ± 0.22 | 69.95 ± 0.54 |

**Table 11** (continued)

| No. | Compounds | Concentration(μg/mL) | Inhibition rate/% | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | *R. s* | *S. s* | *B. c* | *F. g* | *F. o* | *P. c* |
| 257 | Ofloxacin | 100 | 0 ± 0 | 48.03 ± 0.55 | 58.39 ± 0.53 | 20.78 ± 0.23 | 0 ± 0 | 17.07 ± 0.63 |
| 258 | Marbofloxacin | 100 | 0 ± 0 | 30.02 ± 0.34 | 50.31 ± 0.46 | 11.5 ± 0.20 | 0 ± 0 | 18.94 ± 0.52 |
| 259 | 2-Hydroxyacetophenone | 100 | 42.43 ± 2.66 | 75.59 ± 0.79 | 26.67 ± 1.69 | 10.18 ± 0.44 | 8.51 ± 0.18 | 18.88 ± 0.96 |
| 260 | 4'-Hydroxyacetophenone | 100 | 36.62 ± 2.69 | 18.76 ± 0.43 | 27.33 ± 1.56 | 8.93 ± 0.68 | 12.22 ± 2.17 | 0 ± 0 |
| 261 | 3'-Hydroxyacetophenone | 100 | 10.08 ± 0.93 | 27.95 ± 2.21 | 41.13 ± 1.93 | 0 ± 0 | 6.58 ± 0.68 | 13.38 ± 0.54 |
| 262 | 3,4-Dihydroxyacetophenone | 100 | 0 ± 0 | 19.83 ± 0.34 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 263 | 3,4-Dimethoxyacetophenone | 100 | 14 ± 2.59 | 0 ± 0 | 45.41 ± 0.68 | 7.67 ± 0.16 | 21.64 ± 1.53 | 17.23 ± 0.1 |
| 264 | Acetovanillone | 100 | 26.54 ± 0.69 | 21.08 ± 1.63 | 12.05 ± 0.41 | 0 ± 0 | 16.78 ± 0.12 | 9.42 ± 0.01 |
| 265 | 2',6'-Dihydroxyacetophenone | 100 | 80.59 ± 0.01 | 31.46 ± 1.81 | 78.41 ± 1.25 | 65.73 ± 0.36 | 58.92 ± 0.01 | 61.48 ± 0.02 |
| 266 | 2,4-Dihydroxyacetophenone | 100 | 62.94 ± 2.1 | 23.2 ± 1.27 | 58.31 ± 0.5 | 23.23 ± 1.93 | 41.25 ± 0.32 | 34 ± 0.28 |
| 267 | 2,4-Dihydroxyacetophenone | 100 | 25.95 ± 2.93 | 34.27 ± 0.46 | 38.9 ± 0.85 | 35.35 ± 1.47 | 25.16 ± 1.14 | 25.4 ± 0.57 |
| 268 | 2',3',4'-Trihydroxyacetophenone | 100 | 27.04 ± 1.19 | 43.18 ± 0.70 | 0 ± 0 | 15.02 ± 0.78 | 14.58 ± 0.4 | 15.16 ± 1.57 |
| 269 | 2',4',6'-Trihydroxyacetophenone monohydrate | 100 | 7.81 ± 0.49 | 13.53 ± 0.8 | 0 ± 0 | 14.24 ± 1.41 | 10.79 ± 0.19 | 15.32 ± 1.91 |
| 270 | 4,6-Diacetylresorcinol | 100 | 79.69 ± 1.15 | 96.55 ± 0.87 | 50.85 ± 1.58 | 71.88 ± 3.12 | 72.74 ± 0.46 | 63.2 ± 1.03 |
| 271 | Flopropione | 100 | 45.45 ± 0.6 | 45.25 ± 4.05 | 33.04 ± 1.03 | 24.38 ± 3.29 | 25.52 ± 0.67 | 46.37 ± 0.25 |
| 272 | 2',3',4'-Trimethoxyacetophenone | 100 | 6.91 ± 1.46 | 12.44 ± 0.38 | 19.16 ± 3.27 | 8.91 ± 1.98 | 9.81 ± 0.06 | 14.19 ± 2.51 |
| 273 | Acetosyringone | 100 | 4.4 ± 0.93 | 13.4 ± 2.03 | 0 ± 0 | 0 ± 0 | 9.42 ± 0.84 | 17.29 ± 0.64 |
| 274 | 2'-Hydroxy-4',5'-dimethoxyacetophenone | 100 | 77.92 ± 1.28 | 18.52 ± 1.61 | 60.32 ± 1.61 | 24.19 ± 2.44 | 24.11 ± 1.51 | 34.6 ± 1.63 |
| 275 | 2',4'-Dihydroxypropiophenone | 100 | 87.09 ± 0.49 | 55.05 ± 2.65 | 76.33 ± 0.63 | 62.05 ± 0.42 | 71.54 ± 0.69 | 68.29 ± 2.32 |
| 276 | Abafungin | 100 | 95.31 ± 0.38 | 100 ± 0 | 93.63 ± 0.42 | 76.34 ± 1.38 | 92.71 ± 0.04 | 88.33 ± 0.92 |

[a]*R.s*, *Rhizoctonia solani*; *S.s*, *Sclerotinia sclerotiorum*; *B.c*, *Botrytis cinerea*; *F.g*, *Fusarium graminearum*; *F.o*, *Fusarium oxysporum*; *P.c*, *Phytophthora capsici*

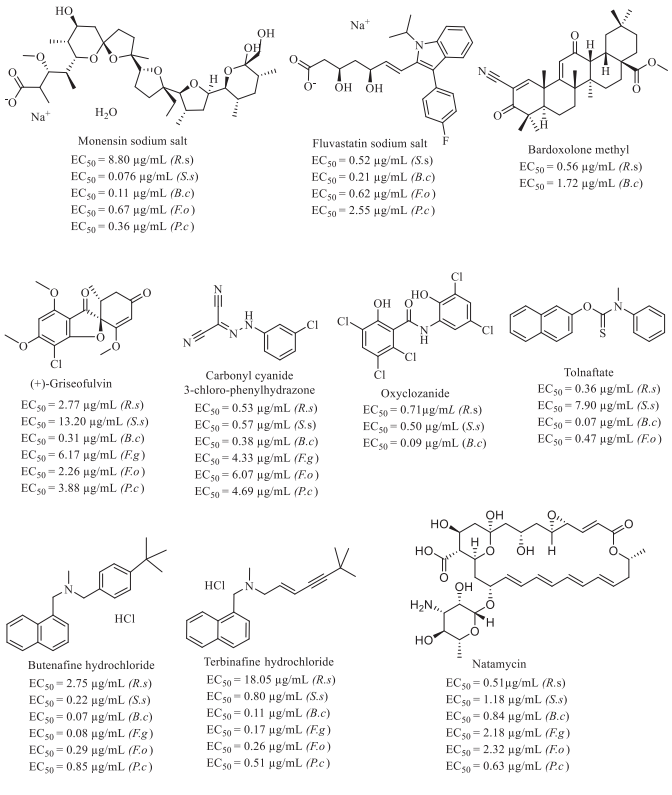


**Fig. 11** The $EC_{50}$ of miscellaneous drugs against phytopathogenic fungi[a]. [a]*R.s, Rhizoctonia solani; S.s, Sclerotinia sclerotiorum; B.c, Botrytis cinerea; F.g, Fusarium graminearum; F.o, Fusarium oxysporum; P.c, Phytophthora capsici*

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## Compliance with ethical standards

**Conflict of interest** The authors declare no competing interests.

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