# THE 1998 BRIGHTON CONFERENCE

## Pests & Diseases
## Volume 2

# SESSION 5A

# NEW COMPOUNDS, FORMULATIONS AND USES FOR DISEASE CONTROL


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| Papers | 5A-1 to 5A-8 |

# RPA 407213: A novel fungicide for the control of downy mildews, late blight and other diseases on a range of crops

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## ABSTRACT

RPA 407213 is a new fungicide exhibiting a high level of activity against a range of Oomycete diseases such as grape and vegetable downy mildews, potato and tomato late blight and *Pythium* species. It also controls a number of other pathogens comprising Ascomycetes and *Alternaria* spp. Using foliar applications, RPA 407213 demonstrates excellent protectant and curative properties at low rates. Four years of field trials have highlighted the interest of applying this fungicide in association with contact, penetrant and systemic products. Of particular merit is the combination with fosetyl-Al which is highly active against fungi including *Plasmopara viticola*, *Pseudoperonospora cubensis* and *Peronospora parasitica*. RPA 407213 can also be used as a seed treatment or soil drench to control *Pythium* spp.

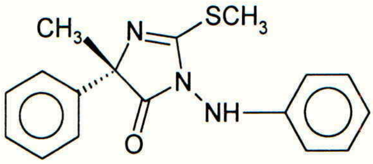
## INTRODUCTION

RPA 407213 is a novel imidazolinone fungicide discovered and patented by Rhône-Poulenc Agro. It is a pure optical isomer. RPA 407213 is the *S*-enantiomer of a racemic compound with the code number RPA 405803. Biochemical and biological tests have shown that only the *S*-enantiomer of the racemic mixture exhibits fungicidal activity. In order to reduce the quantities of chemical applied and hence the impact on the environment, Rhône-Poulenc Agro has decided to develop the pure active enantiomer. This paper summarises the biological properties of the molecule with the emphasis being placed on its potential to control Oomycete plant pathogens.

## CHEMICAL AND PHYSICAL PROPERTIES

Code number: RPA 407213
Chemical name:
IUPAC:
(*S*)-5-Methyl-2-methylthio-5-phenyl-3-phenylamino-3,5-dihydroimidazol-4-one
Chemical Abstracts:
4H-Imidazol-4-one, 3,5-dihydro-5-methyl-2-(methylthio)-5-phenyl-3-(phenylamino)-, (*S*)-

Structural formula:




| | |
|---|---|
| Molecular formula: | $C_{17}H_{17}N_3OS$ |
| Molecular weight: | 311 |
| Chemical Abstracts registry number: | 161326-34-7 |
| Physical state: | White woolly powder |
| Melting point: | 137° C |
| Density: | 1.285 |
| Water solubility: | 7.8 mg/litre at 20° C |
| Partition coefficient n-Octanol/water: | log Pow = 2.8 at 20° C |
| Vapour pressure: | $3.4 \times 10^{-7}$ Pa at 25° C |

## TOXICOLOGY

### Mammalian toxicity

| | | |
|---|---|---|
| Acute oral toxicity $LD_{50}$: | Rat | 2028 mg/kg (females)<br>> 5000 mg/kg (males) |
| Acute dermal toxicity $LD_{50}$: | Rat | > 2000 mg/kg |
| Eye irritation: | Rabbit | non irritant |
| Skin irritation: | Rabbit | non irritant |
| Skin sensitisation: | Guinea pig | negative |
| Ames test: | | negative |
| Micronucleus test: | | negative |
| Non teratogenic agent in rats and rabbits | | |

### Toxicity to wildlife

| | |
|---|---|
| Bobwhite quail (acute toxicity): | $LD_{50}$ > 2000 mg/kg b.w. |
| Bobwhite quail (dietary toxicity): | $LC_{50}$ > 5200 mg/kg |
| Mallard duck (dietary toxicity): | $LC_{50}$ > 5200 mg/kg |
| Fish (2 species): | 96-h $LC_{50}$ = 0.74 mg/litre |

## BIOLOGICAL ACTIVITY

### Mode of action

At the biochemical level, RPA 407213 inhibits mitochondrial respiration by blocking electron transport at the level of the enzyme ubihydroquinone: cytochrome *c* oxidoreductase. It is much more active than the R-enantiomer RPA 407212 (Table 1).

Table 1. Inhibition of respiration in *Agaricus campestris* mitochondria.

| Code number | Isomerism | $IC_{50}$ (µM) |
|---|---|---|
| RPA 405803 | racemic | 1.19 |
| RPA 407213 | *S*-enantiomer | 0.56 |
| RPA 407212 | R-enantiomer | > 6 |

Studies are continuing to define the precise site of action of the molecule. Due to this single site mode of action, RPA 407213 will only be developed on the major market segments in mixtures with fungicides having a different mode of action.
Against Oomycete plant pathogens RPA 407213 acts on a number of sites in the life cycles of *Plasmopara viticola* and *Phytophthora infestans* (Table 2).

Table 2. Activity of RPA 407213 in inhibiting zoospore liberation and direct cyst and sporangium germination in *P. viticola* and *P. infestans*.

| Fungicide | $LC_{90}$ mg a.i./litre | | | | |
|---|---|---|---|---|---|
| | Zoospore liberation | | Cyst germination | | Sporangium germination |
| | *P. viticola* | *P. infestans* | *P. viticola* | *P. infestans* | *P. infestans* |
| RPA 407213 | 0.2 | 0.3 | 0.3 | 0.3 | 0.5 |
| Maneb | 5.0 | - | 5 | - | 5-10 |
| Fluazinam | 0.2 | 0.2 | 150 | 150 | > 200 |

The fact that RPA 407213 is very active against zoospore liberation and direct cyst and sporangial germination ensures a consistently high level of activity in the control of vine downy mildew and late blight on potatoes and tomatoes.

RPA 407213 is active against both phenylamide sensitive and resistant strains of *P. viticola* and *P. infestans*.

### Greenhouse trials

These trials demonstrate the spectrum and type of antifungal activity (protectant, curative, systemic, antisporulant) exhibited by RPA 407213. The plants used in these experiments were grown under standard conditions and subsequently artificially infected with the test pathogens.

Table 3. Results from greenhouse trials demonstrating the spectrum, type and level of activity of RPA 407213 in controlling a range of Oomycete plant pathogens.

| Pathogen | Host plant | Type of application | $LC_{90}$ |
|---|---|---|---|
| *Plasmopara viticola* | Vine | Foliar protectant | 3-6 mg a.i./litre |
| | | 24 hour curative | 50-80 mg a.i./litre |
| | | Translaminar systemic | 15 mg a.i./litre |
| | | Foliar antisporulant | 150 mg a.i./litre |
| *Phytophthora infestans* | Potato/tomato | Foliar protectant | 25-200 mg a.i./litre |
| *Bremia lactucae* | Lettuce | Foliar protectant | 12 mg a.i./litre |
| *Peronospora tabacina* | Tobacco | Foliar protectant | 37 mg a.i./litre |
| *Pseudoperonospora cubensis* | Cucumber | Seedling drench to protect foliage | 0.2 mg/plant |
| *Plasmopara helianthi* | Sunflower | Seedling drench to protect foliage | 0.2-0.4 mg/plant |
| *Peronospora viciae* | Peas | Seedling drench to protect foliage | 0.25-0.5 mg/plant |
| *Pythium* spp. | Rice | Seed box drench (200 boxes/ha) | 20 mg/box |
| *Pythium* spp. | Maize | Seed treatment | 12-25 g/100 kg |
| *Pythium aphanidermatum* | Cotton | Seed treatment | 50-100 g/100 kg |

**Field trials**

All field trials were of a randomised block design with a minimum of 4 replicates per treatment. Trials were artificially infected by contaminating plants in the guard rows associated, where necessary, with artificial misting. Disease assessments, of both frequency and intensity, were carried out at regular intervals throughout the period of experimentation.

Grape vines

RPA 407213, both alone and in mixtures, has exhibited a high level of activity against downy mildew (*P. viticola*) on vine leaves and bunches (Tables 4, 5 and 6).

Table 4. Protectant activity of RPA 407213 against vine downy mildew on leaves and bunches (7 day spray programme), France 1994.

| Treatment | Rate g a.i./ha | % area diseased Trial 1 2 DAT 14[①] leaves | Trial 2 1 DAT 9 leaves | Trial 2 13 DAT 13 bunches | Trial 3 20 DAT 13 leaves | Trial 3 9 DAT 9 bunches |
|---|---|---|---|---|---|---|
| RPA 407213 | 75 | 28 b | 0.5 b | 0 b | 17 b | 1.7 b |
| | 100 | 19 c | 0.1 b | 0 b | 13 b | 0.8 b |
| | 125 | 13 c | 0.2 b | 0 b | 9 b | 0.7 b |
| Mancozeb | 2800 | 31 b | 0.3 b | 0.1 b | 19 b | 1.5 b |
| Untreated | - | 74 a | 11.1 a | 76 a | 84 a | 63 a |

① 2 DAT 14 = 2 days after treatment 14.
Within any given column means followed by the same letter are not significantly different at the 5% level.

Table 5. Protectant activity of RPA 407213 mixtures in controlling vine downy mildew on leaves and bunches, France 1997.

| Treatment | Rate g a.i./ha | % area diseased 7 day spray interval 9 DAT 10 Leaves | 7 day spray interval 8 DAT 11 Bunches | 12 day spray interval 12 DAT 8 Leaves | 12 day spray interval 1 DAT 6 Bunches |
|---|---|---|---|---|---|
| RPA 407213 + mancozeb | 75 + 750 | 3 b | 1 b | - | - |
| RPA 407213 + fosetyl-Al | 100 + 1500 | - | - | 5 b | 2 b |
| Mancozeb | 2800 | 7 b | 4 b | - | - |
| Fosetyl-Al + folpet | 1500 + 750 | - | - | 5 b | 4 b |
| Untreated | - | 56 a | 37 a | 38 a | 69 a |

Within any given column means followed by the same letter are not significantly different at the 5% level.

Table 6. Curative activity of an RPA 407213 + fosetyl-Al mixture against vine downy mildew, 1997.

| Treatment | Rate g a.i./ha | % leaf area diseased<br>Time between inoculation and spray treatment<br>Trial 1 - 40 h | Trial 2 - 48 h |
|---|---|---|---|
| RPA 407213 + fosetyl-Al | 100 + 1500 | 4 b | 23 b |
| Fosetyl-Al + folpet + cymoxanil | 1500 + 750 + 120 | 4 b | 13 b |
| Dimethomorph + mancozeb | 225 + 1500 | 13 b | 32 b |
| Untreated | - | 36 a | 63 a |

Within any given column means followed by the same letter are not significantly different at the 5% level.

Potatoes and tomatoes

RPA 407213, as it is active against several stages in the life-cycle of *P. infestans*, provides a high level of control of potato and tomato late blight when applied in mixtures with reduced rates of protectant fungicides on a 7 day protectant spray programme. The most striking feature of these associations is the consistency of control achieved irrespective of the environemental conditions (Table 7).

Table 7. Protectant activity of RPA 407213 mixtures in controlling late blight on potatoes (7 day spray programme), 1996-97.

| Treatment | Rate g a.i./ha | % leaf area diseased USA 4 DAT 3 | France 3 DAT 7 | Brazil 6 DAT 7 | Spain 5 DAT 5 |
|---|---|---|---|---|---|
| RPA 407213 + | 100 + 500 | 15 c | - | - | - |
| mancozeb | 125 + 625 | - | - | - | 15 cd |
| | 150 +750 | 7 c | - | - | 18 cd |
| RPA 407213 + | 100 + 500 | - | 16 c | - | - |
| chlorothalonil | 125 + 625 | - | 7 c | 8 bc | 5 e |
| | 150 + 750 | - | 7 c | 3 c | 6 e |
| Chlorothalonil | 1500 | - | 13 c | 5 c | 11 de |
| Fluazinam | 200 | 18 c | 31 b | 8 bc | 21 c |
| Mancozeb | 1600 | 43 b | 40 b | 14 b | 31 b |
| Untreated | - | 94 a | 97 a | 76 a | 81 a |

Within any given column means followed by the same letter are not significantly different at the 5% level.

In greenhouse tests, RPA 407213 has been shown to be equally effective against both $A_1$ and $A_2$ mating types of *P. infestans*.

RPA 407213 also provides a high level of protectant activity against early blight (*Alternaria solani*) on potatoes (Table 8).

Table 8. Protectant activity of RPA 407213, both alone and in mixtures, in controlling early blight on potatoes (7 day spray programme), Brazil 1997.

| Treatment | Rate g a.i./ha | % leaf area diseased Trial 1 (3 DAT 5) | Trial 2 (3 DAT 5) |
|---|---|---|---|
| RPA 407213 | 300 | 12 d | - |
| RPA 407213 + | 100 + 500 | - | 18 d |
| chlorothalonil | 125 + 625 | - | 11 e |
| Chlorothalonil | 1500 | 29 c | 29 c |
| Fluazinam | 200 | 38 b | 31 c |
| Mancozeb | 1600 | 53 a | 38 b |
| Untreated | - | 57 a | 50 a |

Within any given column means followed by the same letter are not significantly different at the 5% level.

Other crops

Field trials carried out on a range of other crops have demonstrated the excellent Oomycete control achieved with RPA 407213, when used either alone or in mixtures with fosetyl-Al. The host/pathogen complexes studied include:

| | |
|---|---|
| Brassicas | *Peronospora parasitica* |
| Cotton | *Pythium* spp. (in-furrow spray at seeding) |
| Cucurbits | *Pseudoperonospora cubensis* |
| Lettuce | *Bremia lactucae* |
| Onions | *Peronospora destructor* |
| Roses | *Peronospora sparsa* |
| Tobacco | *Peronospora tabacina* |
| Turf | *Pythium* spp. |

In addition, RPA 407213 has provided good control of a number of non-Phycomycete plant pathogens including *Alternaria* spp. on top fruit and *Mycosphaerella* spp. on bananas.

**Crop selectivity**

In all the trials carried out so far RPA 407213 has exhibited good crop safety at dose rates well above those required for practical disease control.

## CONCLUSIONS

RPA 407213 is a novel fungicide exhibiting a high level of biological activity against a range of Oomycete plant pathogens. Mixtures with protectant fungicides provide a consistent, very high level of control of early and late blight on solanaceous crops. Against the downy mildews attacking vines and vegetables, combinations with fosetyl-Al provide protectant, curative and systemic disease control based on two active ingredients with very different modes of action at the biochemical level.

## ACKNOWLEDGEMENTS

The authors would like to express their thanks for the active participation of all colleagues involved in the development of this molecule.

# Fenhexamid (KBR 2738) - A novel fungicide for control of *Botrytis cinerea* and related pathogens

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## ABSTRACT

Fenhexamid is a new foliar fungicide with protective action from the new chemical class of the hydroxyanilides. It is active against *Botrytis cinerea* and related pathogens such as *Monilinia* spp. and *Sclerotinia sclerotiorum* in grapes, berries, stone-fruit, citrus, vegetables and ornamentals with excellent plant compatibility. Use rates range from 500 to 1000 g/ha. Fenhexamid is safe for applicators, consumers and environment. It is classified by US-EPA as 'reduced risk pesticide'. It is safe for beneficials and therefore suited for IPM programmes. Especially interesting for the growers are its short pre-harvest intervals, the excellent lasting activity and the good storage protection of soft fruits. Fenhexamid has a new mode of action and shows no cross-resistance to any other known botryticide. It inhibits strongly germ tube elongation and mycelium growth. In the natural *Botrytis* population, a few isolates are found which can metabolise the active ingredient *in vitro* under certain conditions. The presence of these isolates in the field does not influence the activity of fenhexamid.

## INTRODUCTION

Fenhexamid, tested under the code name KBR 2738, is a novel foliar fungicide with preventive action and excellent activity against *Botrytis cinerea* and related pathogens in grapes, berries, citrus, stone-fruit, vegetables and ornamentals. It belongs to the newly discovered fungicidally active group of the hydroxyanilides and was synthesized and patented by Bayer AG in 1989 (Kuck *et al.*, 1997).
Besides the excellent biological activity and excellent plant compatibility, the active ingredient exhibits a very favourable toxicological and ecotoxicological profile resulting in the 'reduced risk pesticide' classification by US-EPA.
Fenhexamid will be marketed under the tradenames Teldor® and Password® (Japan). In the US, it will be marketed by Tomen Agro Inc. under the tradename Elevate®.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Common name (ISO): | fenhexamid |
| Chemical family: | hydroxyanilides |
| CAS number: | 126833-17-8 |
| Chemical name (C.A.): | N-(2,3-dichloro-4-hydroxyphenyl)-1-methyl-cyclohexanecarboxamide |
| Chemical name (IUPAC): | 1-Methyl-cyclohexanecarboxylic acid (2,3-dichloro-4-hydroxy-phenyl)-amide |

Structural formula:


| | |
|---|---|
| Molecular formula: | $C_{14}H_{17}Cl_2NO_2$ |
| Molecular weight: | 302.2 g/mol |

## PRODUCT SAFETY

### Mammalian toxicity:

| | |
|---|---|
| Acute oral $LD_{50}$, rat | > 5000 mg a.i./kg b.w. |
| Acute dermal $LD_{50}$ (24h), rat | > 5000 mg a.i./kg b.w. |
| Acute inhalation ($LC_{50}$, 4h), rat | > 5057 mg a.i./$m^3$ in air (dust) |
| Dermal irritation, rabbit | non-irritant |
| Eye irritation, rabbit | non-irritant |
| Dermal sensitisation, guinea pig | non-sensitising |
| Teratogenicity | non-teratogenic |
| Carcinogenicity | non-carcinogenic |
| Metabolism (rats) | fast absorption and elimination<br>no accumulation |

### Toxicity to wildlife:

| | |
|---|---|
| $LC_{50}$ (96h), fish (2 species) | 1.34-3.42 mg a.i./l |
| $LD_{50}$ birds | > 2000 mg a.i. /kg b.w. |
| $EC_{50}$, *Daphnia magna* (48 h) | > 18.8 mg a.i./l |
| $LC_{50}$ earthworms (*Eisenia foetida*) | > 1000 mg a.i./kg of dry weight soil |
| Predatory mites (*Typhlodromus pyri*) | non-toxic at 2 kg a.i./ha |
| $LC_{50}$ (oral), bee | non-toxic (> 97.7 µg a.i. /bee) |
| $LC_{50}$ (contact), bee | non-toxic (> 188 µg a.i. /bee) |
| Rove beetles (*Aleochara bilineata*) | non-toxic at 2 kg a.i. /ha |
| Ladybirds (*Coccinella septempunctata*) | non-toxic at 2 kg a.i. /ha |
| Parasitoids (*Aphidius rhopalosiphi*) | non-toxic at 2 kg a.i./ha |

### Environmental behaviour:

| | |
|---|---|
| Soil degradation, $DT_{50}$ | ≤ 1 day |
| Mobility in soil | non-mobile |
| Solubility in water | 20 mg/l (pH 5-7) at 20 °C |
| Partition coefficient n-octanol/water (log Pow): | 3.51 (pH 7) at 20 °C |
| Vapour pressure | 4 x $10^{-7}$ Pa at 20 °C (extrapolated) |
| Microbial mineralisation | no negative effect |

These data indicate that fenhexamid poses no relevant risk for non-target organisms and the environment, even after repeated applications. Therefore the active ingredient is very well suited for use in IPM programmes.

## FORMULATIONS

Fenhexamid will be formulated as a solo product as dust-free 50 % water dispersible granules (WG) and 50 % suspension concentrate (SC). Both formulations exhibit an excellent rain stability. For certain countries a 50 % wettable powder (WP) is also available. Combination products with different other active ingredients like tebuconazole, tolylfluanid and chlorothalonil are under development.

## BIOLOGICAL PROFILE

### Grapes

In field tests in different countries under varying local spray regimes and under different climatic conditions, fenhexamid proved its outstanding efficacy against grey mould (*B. cinerea)* in grapes with dosage rates of 500 to 750 g /ha. The efficacy level is equal to or even better than the best new standards (Table 1) combined with an excellent plant compatibility and lasting efficacy.

Table 1. Efficacy (%) of fenhexamid against grey mould (*B. cinerea)* in grapes. France, Germany, Italy 1995 - 1997.

| | g a.i./ha | France | | | Italy | Germany |
|---|---|---|---|---|---|---|
| | | 1995 | 1996 | 1997 | 1995-97 | 1995-97 |
| Untreated (% severity) | | (26) | (18) | (25) | (22) | (23) |
| Fenhexamid | 500 | - | - | - | 84 | - |
| | 750 | 82 | 86 | 75 | - | 93 |
| Vinclozolin | 750 | - | - | - | 63 | - |
| Pyrimethanil | 800 | - | - | - | 77 | 84 |
| | 1000 | 68 | - | - | - | - |
| Cyprodinil | 375 | - | 88 | 80 | - | 91 |
| + fludioxonil | + 250 | | | | | |
| No of treatments | | | 4 | | 2 | 2-4 |
| application timing | | | A-B-C-D [1] | | B-D | A-B-C-D |
| No of corresponding trials | | 5 | 8 | 5 | 6 | 12 |

- : no data [1]A: end of bloom, B: berry touch, C: veraison, D: 3 weeks before harvest

Wine fermentation tests were performed in France, Germany, Italy, Spain and the US. Compared to various standards, no difference in the alcoholic and malolactic fermentation was found nor was a negative influence detected on taste or flavour of the bottled and stored wines. Also, no delay in ripening of the berries in the field after treatment with fenhexamid was seen.

Of special interest is the outstanding lasting activity of fenhexamid against *B. cinerea* in grapes (Table 2). This gives the vine-grower some flexibility in fixing the date of harvest according to his particular situation.

Table 2. Lasting efficacy (%) of fenhexamid against *B. cinerea* in grapes. France 1996.

| | g a.i. /ha | T4 + 27 days | T4 + 41 days | T4 + 21 days | T4 + 27 days |
|---|---|---|---|---|---|
| Untreated (% severity) | | (40) | (70) | (32) | (34) |
| Fenhexamid | 750 | 99 | 96 | 98 | 97 |
| Pyrimethanil | 1000 | 89 | 74 | 98 | 82 |
| Fludioxonil | 500 | 82 | 53 | 94 | 88 |
| Cyprodinil | 375 | 94 | 79 | 100 | 97 |
| + fludioxonil | + 250 | | | | |
| Grape cultivar | | Folle Blanche | | Semillon | |
| No of applications | | 4 (A-B-C-D) | | 4 (A-B-C-D) | |

To prevent build-up of resistance of botryticides, spray programmes with alternation of chemicals against *B. cinerea* are highly recommended and becoming more and more common practice. So, another important aspect for fenhexamid in grapes is its flexibility in spray timing when used in spray programmes.
Trials in France showed that fenhexamid can be applied at each timing, end of bloom (timing A) as well as later in the season (timing C and D) exhibiting very good efficacy compared to a standard spray programme (Table 3). Therefore, it is well suited to become an integral part of any spray programme in grapes.

Table 3. Efficacy (%) of fenhexamid against *B. cinerea* in grapes in spray programmes.

| | Grape cultivar: | Pinot Meunier | Sauvignon |
|---|---|---|---|
| Timing A | Timing C | | |
| Untreated (% severity) | | (9) | (33) |
| Fludioxonil (500 g /ha) | procymidone (750 g /ha) | 71 | 48 |
| Fenhexamid (750 g /ha) | procymidone (750 g /ha) | 79 | 68 |
| Fludioxonil (500 g /ha) | fenhexamid (750 g /ha) | 91 | 57 |

It is well known that *Botrytis* infected berries undergo a dramatic change in the acid, glucidic and enzymatic profile leading to problems during the fermentation process (Pallota *et al.*, 1998). Therefore, in order to produce clean musts which are a prerequisite for producing high quality wines, an excellent control of *B. cinerea* in the field by an excellent botryticide like fenhexamid is necessary.

For the table-grape producers it is important to stress the fact that the proposed pre-harvest interval (PHI) for fenhexamid ranges from 3 - 7 days depending on the country. This short PHI helps the growers to schedule the date of harvest according to their particular working situation and market demands. It also supports sanitary measures in the packing house to control *B. cinerea* infections during storage or transport of the berries.

**Strawberries**

In strawberries, *B. cinerea* infections in the field or in storage are the most damaging threats to every strawberry grower or seller. Therefore, suitable control measures - with chemical control being an important part of it - have been common practice for a long time. In many years of field testing under different climatic conditions, fenhexamid proved its excellent efficacy against *B. cinerea* in strawberries. With dosage rates of 750 and 1000 g/ha, it equalled or even outperformed the current standards (Table 4).

Table 4. Efficacy (%) of fenhexamid against *B. cinerea* in strawberries.
France, Spain, Germany 1994 - 1997; 3 - 5 applications.

| | g a.i./ha | France | Spain | Germany |
|---|---|---|---|---|
| Untreated (% diseased fruits) | | (21) | (38) | (23) |
| Fenhexamid | 750 | 80 | 79 | - |
| | 1000 | 82 | - | 84 |
| Vinclozolin | 750 | 67 | - | - |
| Pyrimethanil | 800 | - | 62 | - |
| Tolylfluanid | 2500 | - | - | 73 |
| No of corresponding trials | | 9 | 6 | 10 |

- : no data

Besides *Botrytis* infections in the field, infections occuring during transport and storage are of considerable and direct economical impact especially for those growers who export a considerable amount of their strawberry production or those at a distance from points of sale. Efficacy tests showed that fenhexamid - when applied in the field - gives better protection of the fruits after storage than a standard product (Table 5).

Table 5. Efficacy (%) of fenhexamid against *B. cinerea* in strawberries after storage.
Spain, Belgium 1995 - 1997; 4 - 6 applications.

| | g a.i./ha | Spain | Belgium |
|---|---|---|---|
| Untreated (% diseased fruits) | | (24) | (25) |
| Fenhexamid | 750 | 88 | - |
| | 1000 | - | 87 |
| Pyrimethanil | 800 | 70 | 56 |
| Days in storage | | 7 - 8 | 6 |
| No of corresponding trials | | 4 | 2 |

- : no data

Based on the very favourable toxicological properties of fenhexamid, the proposed PHI in strawberries is short (1 - 3 days depending on the country). Applications of fenhexamid to the fruits have no negative influence on their taste or smell. Nor were adverse effects of the fenhexamid treatments detected following processing.
Consequently, with its excellent biological activity and the short PHI, fenhexamid gives the strawberry grower the efficacy and also the necessary flexibility at the same time to produce a high quality crop.
In addition to strawberries, registration of fenhexamid is targeted in other berry crops such as raspberries, blackcurrants etc.

Besides the straight product, a combination with tolylfluanid is also under development. This combination adds to the excellent *Botrytis* activity of fenhexamid the broad-spectrum activity of tolylfluanid against various other pathogens, especially leather rot caused by *Phytophthora cactorum*, and offers a built-in anti-resistance management at the same time.

**Stone-fruit**

In addition to its excellent activity against *B. cinerea* in different crops, fenhexamid offers very good activity against related pathogens, e.g. against *Monilinia* diseases which play an important role in stone-fruit production (Table 6).

Table 6. Efficacy (%) of fenhexamid against *Monilinia* spp. in stone-fruit. Italy, Belgium, France, Germany, 1994 - 1996; 2 - 4 applications.

| | g a.i./ ha | Efficacy against twig infection | | | Efficacy against fruit infection | |
|---|---|---|---|---|---|---|
| Untreated | | (86) [1] | (52) [1] | (42) [1] | (40) [2] | (19) [2] |
| Fenhexamid | 750 | 78 | 74 | 87 | 52 | 58 |
| Dicarboximide | 750 | 75 | - | - | 50 | - |
| Thiram | 2400 | - | 41 | - | - | - |
| Triforine | 428 | - | - | 81 | - | 57 |
| No of trials | | 7 | 5 | 5 | 6 | 7 |

[1] : No of infected twigs per tree    [2] : % infected fruits

Against twig infections as well as against fruit infections at the end of the season, the efficacy of fenhexamid is better or equal to commercial standards.
Recently, it was found that cracking of sweet-cherries was reduced by a considerable amount after treatments with fenhexamid. This very interesting phenomenon is currently under detailed investigation.
Also in stone-fruit, the proposed PHI is short, 1 - 3 days, offering the growers maximum flexibility in applying fenhexamid according to their specific needs.

**Vegetables**

In some vegetables, especially head-lettuce, a mixed infection caused by *B. cinerea* and the related pathogen *Sclerotinia sclerotiorum* is often found in practice. This pathogen is difficult to control because, besides an airborne infection, a soilborne infection can also take place resulting in varying control levels of the standards. With 0.075 %, fenhexamid exhibited good control against *S. sclerotiorum* in the activity range of commercial standards (Table 7).

Table 7. Efficacy of fenhexamid against *S. sclerotiorum* in lettuce. Italy, 1993 - 1997, 2 - 4 applications.

| | rate a.i. | % disease control |
|---|---|---|
| Untreated (% infected plants) | | (12) |
| Fenhexamid | 0.075 % | 62 |
| Dicarboximide | 0.075 % | 61 |
| No of trials | | 8 |

Also in vegetables, the proposed PHI is short with 1 - 3 days only which is extremely useful for greenhouse tomato production.
To fulfil the grower´s demand for a broad-spectrum compound in vegetables, besides the single active, a combination with tebuconazole is also under development.

## MODE OF ACTION

At present, the biochemical target is unknown. Detailed studies are in progress. However, there are clear indications that fenhexamid has a new mode of action (Kuck *et al.*, 1997; Suty *et al.*, 1997):

- new chemistry
- no cross-resistance with benzimidazoles, dicarboximides, triazoles, anilinopyrimidines, N-phenylcarbamate
- no effect on oxygen consumption
- no effect on mitochondrial electron transport
- no effect on excretion of pectinases

In vitro studies showed that fenhexamid is a strong inhibitor of germ tube elongation and mycelium growth (Leroux *et al.*, 1998). Spore germination is only inhibited at relatively high concentrations (Table 8).

Table 8. In vitro activity of fenhexamid against *B. cinerea.*

| | ED50 (mg a.i./litre) | | |
|---|---|---|---|
| | spore germination | germ tube elongation | mycelial growth |
| Fenhexamid | > 10 | 0.07 | 0.05 |

Microscopical studies with germ tubes demonstrated that fenhexamid damages the cell wall finally resulting in leakage of cell plasm. Also, the formation of appressoria is affected.
Fenhexamid exhibits only very limited translocation after penetration into the leaf (loco-systemic activity). Therefore, based on its protective action the active ingredient has to be applied in a preventive spray schedule.

## SENSITIVITY MONITORING

Monitoring the sensitivity of *Botrytis* isolates from different trial sites in France, Germany and Italy started already very early in the development of fenhexamid and has been continued ever since. It was found that in the wild population of *B. cinerea* a low and variable percentage (0 - 6 %) of less sensitive strains can be detected under laboratory conditions. The existence of these strains is not correlated with fenhexamid treatments (Santomauro *et al.*, 1997). Even after 5 - 6 years of consecutive applications with fenhexamid on the same site, no selection of less sensitive strains was observed in the field (Suty *et al.*, 1997). This phenomenon could be due to the fact that these strains show some reduced fitness indicated by reduced sporulation and higher frost sensitivity.
It must be stressed that the efficacy of fenhexamid was always excellent irrespective of the presence of less sensitive strains. This was also the fact in grape trials artificially inoculated with a less sensitive strain.
Studies with radioactive-labelled fenhexamid revealed the fact that these strains are capable of metabolising the active ingredient *in vitro* into inactive metabolites. However, this metabolisation can only take place when a substantial amount of mycelium is supplied with an energy source (sugars) under humid conditions for longer time intervals. Further studies are in progress.

All these data indicate that fenhexamid does not pose a risk of resistance development which is higher than that generally encountered with specific botryticides. Also, appropriate anti-resistance management strategies will be implemented.

## CONCLUSIONS

The new active ingredient fenhexamid is characterised by a new chemical group, a new mode of action and no cross-resistance to any other known botryticide. It exhibits an excellent activity against *B. cinerea* and related pathogens combined with an excellent plant compatibility. It is safe for consumers, applicators and the environment resulting in the 'reduced risk pesticide' classification by US-EPA. It is absolutely safe for beneficial insects and therefore very well suited for any IPM programme. Consequently, fenhexamid will become a very valuable tool for the growers to produce high quality crops.


## ACKNOWLEDGEMENTS

The authors would like to thank all colleagues who contributed to the worldwide development of fenhexamid.


## REFERENCES


Kuck K-H; Krüger B-W; Rosslenbroich H-J; Brandes W (1997). Nouveau fongicide de la famille des hydroxyanilides, actif sur *B. cinerea* et *Monilia* spp. *ANPP-Cinquième conférence internationale sur les maladies des plantes,* Tours, 3-5 Décembre 1997, **II**, 1055-1062.

Leroux P; Chapeland F; Arnold A; Gredt M (1998). Resistance de *B. cinerea* aux fongicides. *Phytoma* **504**, 62-67.

Pallotta U; Castellari M; Piva A; Baumes R; Bayonove C (1998). Effects of *B. cinerea* on must composition of three Italian grape varieties. *Viticultural and Enological Sciences* **53** (1), 32-36.

Santomauro A; Tauro G; Sorrenti M; Pollastro S; De Guido A; Faretra F (1997). Miglioramenti nella protezione dell'uva da tavola dalla muffa grigia (*Botryotinia fuckeliana*). *La Difesa delle Piante* **20** (1-2), 5-20.

Suty A; Pontzen R; Stenzel K (1997). KBR 2738 : Mode d'action et sensibilité de *B. cinerea*. *ANPP-Cinquième conférence internationale sur les maladies des plantes,* Tours, 3-5 Décembre 1997, **I**, 561-568.

# RH-7281: A novel fungicide for control of downy mildew and late blight

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## ABSTRACT

RH-7281 is a new, high performance fungicide currently under development by Rohm and Haas for foliar use on potatoes, vines, and vegetables. Specifically targeting Oomycete fungi, RH-7281 exhibits strong preventive activity combined with excellent rainfast and residual properties. In numerous field trials conducted worldwide, RH-7281 demonstrated excellent efficacy against *Plasmopara viticola*, *Phytophthora infestans*, and *Pseudoperonospora cubensis*. It has a different mode of action from the current Oomycete fungicides which involves the binding to tubulin and the inhibition of nuclear division. As a consequence, RH-7281 controls phenylamide-resistant strains of downy mildew and late blight. RH-7281 acts after spore germination to arrest germ tube elongation, control mycelial growth, and inhibit fungal penetration. Characterized by an extremely favorable toxicology and environmental profile, RH-7281 provides an exceptional margin of safety to consumers, applicators, and the environment.

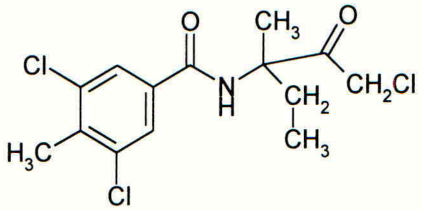
## INTRODUCTION

RH-7281 is a new foliar fungicide discovered and patented by Rohm and Haas. It is being developed alone, and in combination with other fungicide partners, in a range of formulations. In mixtures, RH-7281 complements and enhances the biological activity of many companion fungicides, while its spectrum may be expanded by an appropriate partner. This paper describes the chemical, physical, and fungicidal properties of RH-7281 as well as its mode of action, field performance, and product safety.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Code number: | RH-7281 |
| Chemical name: (IUPAC): | 3,5-Dichloro-N-(3-chloro-1-ethyl-1-methyl-2-oxopropyl)-4-methylbenzamide |
| Molecular formula: | $C_{14}H_{16}Cl_3NO_2$ |
| Molecular weight: | 336.65 |

Structural formula:




| | |
|---|---|
| Melting point: | 159.5-160.5 °C |
| Water solubility: | 0.681 mg/litre (20 °C) |
| Partition coefficient n-octanol-water: | log Pow = 3.76 (20 °C) |
| Vapour pressure at 25 °C, 35 °C, 45 °C : | $<1x10^{-7}$ torr |
| Formulation: | 2F (240 g/litre, aqueous flowable)<br>80 WP (weight %, wettable powder) |

## TOXICOLOGY

**Mammalian toxicity:**

| | |
|---|---|
| Acute oral $LD_{50}$ (rat): | >5000 mg/kg body weight |
| Acute dermal $LD_{50}$ (rat): | >2000 mg/kg body weight |
| Inhalation $LC_{50}$ (rat): | >5.3 mg/litre |
| Skin irritation (rabbit): | non-irritant |
| Eye irritation (rabbit): | non-irritant |
| Dermal irritation (guinea pig): | sensitizer |
| Mutagenicity (4 tests): | negative |
| Teratology (rabbit, rat): | no developmental toxicity |
| Reproduction (rabbit, rat): | no adverse effects |
| Chronic toxicity/oncogenicity: | no oncogenic potential |

**Toxicity to wildlife:**

| | | |
|---|---|---|
| Avian: | Mallard duck, $LC_{50}$: | >5250 mg/kg diet |
| | Bobwhite quail, $LC_{50}$: | >5250 mg/kg diet |
| Aquatic: | Trout, acute $LC_{50}$: | 160 µg/litre |
| | Bluegill, $LC_{50}$: | > solubility limit |
| | *Daphnia*, acute, $EC_{50}$: | > solubility limit |
| Beneficials: | Honeybee (contact), $LD_{50}$: | >100 µg/bee |
| | Earthworm, $LC_{50}$: | >1070 mg/kg soil |
| | *Typhlodromus pyri:* | harmless |

## ENVIRONMENTAL FATE

| | |
|---|---|
| Soil half-life: | 2-10 d in various soils |
| | ($CO_2$ is the major soil metabolite, 48% at day 120) |
| Aqueous hydrolysis: | pH 4 ~15 d, pH 7 ~15 d, pH 9 ~8 d |
| Aqueous photolysis: | 7.8 d half life |
| Soil mobility: | Koc 1166-1224, low mobility, no leaching potential |

## MATERIALS AND METHODS

### Laboratory studies

Experimental plants were produced under controlled environmental conditions in a glasshouse. Aqueous spore suspensions of the respective plant pathogens were used for inoculations. Inoculated plants were placed in dew chambers for the infection period and then incubated in controlled temperature chambers with the appropriate conditions for disease development. Disease was assessed as a percentage of the plant or leaf area infected and reported as percent control.

### Field trials

Field trials have been conducted since 1992 in several European countries according to European Plant Protection Organization (EPPO) methods. Complete randomized block designs with 4 to 6 replicates were used. Plot sizes varied from 7.5-50 $m^2$. Spray volumes ranged from 200 to 1000 litres/ha for potatoes, tomatoes, and cucurbits to 1000-1500 litres/ha for vines. Sprays were conducted on a fixed, preventive schedule either with experimental sprayers equipped with booms or with motorized backpack sprayers. Disease evaluations consisted of visual assessments of percentage area infected on both leaves and fruits, using the sample size recommended by EPPO.

## RESULTS AND DISCUSSION

### Mode of action

The mechanism of action of RH-7281 is unique among Oomycete fungicides. Nuclear division is arrested by binding to the β-subunit of tubulin and disruption of the microtubule cytoskeleton. RH-7281 does not affect zoospore motility, encystment, or germination. Germ tube elongation is arrested concomitant with the first cycle of nuclear division, preventing fungal penetration of the host plant. Attempts to generate resistant mutants in the laboratory using *Phytophthora capsici* and *P. infestans* have been unsuccessful, suggesting the risk of rapid resistance development in the field is low. Laboratory isolates which are resistant to phenylamides and dimethomorph do not show cross-resistance to RH-7281.

## In vitro fungitoxicity

RH-7281 showed high activity towards Oomycetes *in vitro*, with moderate activity towards certain other fungal pathogens (Table 1).

Table 1. Fungitoxicity *in vitro* in amended agar plates.

| Organism | $LC_{50}$ mg a.i./litre |
|---|---|
| *Pythium ultimum* | 0.006 |
| *Phytophthora infestans* | 0.009 |
| *Phytophthora capsici* | 0.35 |
| *Venturia inaequalis* | 0.44 |
| *Sclerotinia homeocarpa* | 0.58 |
| *Pseudocercosporella herpotrichoides* | 0.75 |
| *Botrytis cinerea* | 0.75 |
| *Monilinia fructicola* | 1.70 |
| *Mycosphaerella fijiensis* | 2.05 |

## Laboratory characterization

RH-7281 demonstrated exceptional activity against grape downy mildew (*Plasmopara viticola*), potato and tomato late blight (*Phytophthora infestans)*, and cucumber downy mildew (*Pseudoperonospora cubensis)* in routine glasshouse experiments. It provided protectant control at low doses of 1-5 g a.i./ha as shown in Table 2. When RH-7281 was applied curatively, 24 hours after inoculation, higher doses were required to provide the same level of efficacy against *Phytophthora infestans* and *Plasmopara viticola* (Table 3).

Table 2. Protectant control of *Plasmopara viticola, Phytophthora infestans* and *Pseudoperonospora cubensis* in glasshouse studies.

| Rate | | Percent Disease Control | |
|---|---|---|---|
| (g a.i./ha) | *P. viticola* | *P. infestans* | *P. cubensis* |
| 75 | 100 | 100 | 99 |
| 19 | 100 | 100 | 90 |
| 5 | 50 | 99 | 75 |
| 1 | 50 | 90 | 50 |
| Untreated* | (70) | (80) | (95) |

* Percent infection

Excellent residual efficacy against *Phytophthora infestans* was observed in glasshouse tests in which intermittent misting was used to simulate overnight dew cycles. Sub groups of fungicide-treated plants were inoculated 1, 3, 6, and 8 days after treatment. Under these experimental conditions, as shown in Table 4, the residual efficacy of RH-7281 equalled or surpassed that of commercial standards. Comparable results were obtained with *Plasmopara viticola* and *Pseudoperonospora cubensis.*

Table 3. Curative control of *Plasmopara viticola* and *Phytophthora infestans* in glasshouse studies.

| Rate (g a.i./ha) | Percent Disease Control *P. viticola* | *P. infestans* |
|---|---|---|
| 300 | 90 | 95 |
| 75 | 50 | 90 |
| Untreated* | (70) | (90) |

* Percent infection

Table 4. Residual control of *Phytophthora infestans* on tomatoes.

| Treatment | Rate (g a.i./ha) | Percent Disease Control* 1 d | 3 d | 6 d | 8 d |
|---|---|---|---|---|---|
| RH-7281 | 150 | 100 | 98 | 93 | 73 |
| | 38 | 92 | 98 | 80 | 77 |
| Cymoxanil | 300 | 100 | 88 | 42 | 25 |
| Dimethomorph | 150 | 100 | 100 | 95 | 75 |
| Untreated** | | (100) | (83) | (83) | (83) |

*Sub-groups of treated plants were inoculated 1, 3, 6, and 8 d after treatment. Disease control was evaluated 7 d after inoculation.
**Percent infection.

RH-7281 demonstrated superior rainfastness. The data (Table 5) illustrate the efficacy of RH-7281 following 100 mm of rain administered 24 hours after fungicide application. Microscopic and analytical examination of spray deposits on plastic petri dishes exposed to the same protocol confirmed that RH-7281, both technical and formulated, is highly resistant to wash-off.

Table 5. Rainfastness of RH-7281 on *Phytophthora infestans* on tomatoes.

| Treatment | Rate ( g a.i./ha) | Percent Disease Control no rain | 100 mm rain (24 h after spraying) |
|---|---|---|---|
| RH-7281 240 SC | 200 | 100 | 100 |
| | 100 | 100 | 96.3 |
| RH-7281 technical | 200 | 93.8 | 81.5 |
| | 100 | 100 | 98.8 |
| Fluazinam | 200 | 87.7 | 66.7 |
| Mancozeb | 600 | 98.8 | 74.1 |
| Chlorothalonil | 400 | 87.7 | 55.6 |
| Untreated* | | (83) | (98) |

*Percent infection

## Field performance

### Potatoes

RH-7281 and premixtures of RH-7281 and mancozeb have been tested extensively over several years in many trials against potato late blight. Excellent selectivity versus all cultivars of potatoes has been demonstrated in multivariety studies conducted in several European countries. Very good efficacy against leaf blight was achieved with RH-7281 at rates from 150 to 200 g a.i./ha. Rates of 125 to 150 g a.i./ha of RH-7281 combined with mancozeb provided outstanding control of leaf blight under high disease pressure, and were superior to standards. Excellent tuber blight control was also observed (Table 6). In addition, this mixture has shown superior rain persistence in comparative field studies.

Table 6. Control of *Phytophthora infestans* on potatoes (applications every 7 d).

| | | Percent Disease Control | | | |
|---|---|---|---|---|---|
| | | Leaves | | | Tubers |
| | | UK | France | Holland | France |
| Product | Rate (g a.i./ha) | 1997 (2DAT3) | 1996 (4DAT9) | 1997 (1DAT8) | 1996 (after storage) |
| RH-7281 | 125 | 89.0 | | - | - |
| RH-7281 | 150 | 90.9 | 65.9 | - | - |
| RH-7281 + mancozeb | 125 + 1000 | 98.4 | 91.3 | 95.5 | 95.9 |
| RH-7281 + mancozeb | 150 + 1200 | 97.7 | 92.9 | 97.9 | 100 |
| Mancozeb | 1275 | 92.5 | - | - | - |
| Mancozeb | 1600 | - | 69.2 | 97.8 | - |
| Fluazinam | 150 | 94.1 | 84.3 | - | 95.9 |
| Fluazinam | 200 | 95.7 | 87.3 | 97.3 | 100 |
| Untreated* | | (93.5) | (88.5) | (95) | (8) |

* Percent infection

### Grapes

On grapes, RH-7281 provided a consistently high level of control of *Plasmopara viticola* at rates of 12.5 to 15.0 g a.i./hl in trials in France, Italy, Spain, and Germany. A particular strength of the product is its activity on bunches, which is often superior to the commercial standards. Combination with mancozeb further enhanced the performance offering excellent efficacy on a 7- to 10-day application schedule (Table 7). An additional benefit of the mixture is good control of black rot (*Guignardia bidwellii*).

In official studies, no adverse effects on fermentation or wine quality was observed.

Table 7. Control of *Plasmopara viticola* on grapes (1996-1997).

| Product | Rate* (g a.i./hl) | Percent Disease Control Italy 7 d interval bunches (3DAT7) | Italy 7-10 d interval leaves (7DAT10) | Italy 7-10 d interval bunches (7DAT10) | France 10 d interval leaves (2DAT8) | France 10 d interval bunches (4DAT9) |
|---|---|---|---|---|---|---|
| RH-7281 | 12.5 | 95.9 | 86.0 | 89.0 | - | - |
| RH-7281 | 15.0 | 95.8 | 88.0 | 92.0 | 97.0 | 93.4 |
| RH-7281 | 20.0 | - | - | - | 97.5 | 95.9 |
| RH-7281 + mancozeb | 12.5 + 140 | - | - | - | 97.7 | 95.9 |
| RH-7281 + mancozeb | 12.5 + 100 | 99.3 | 92.0 | 94.0 | 97.4 | 94.3 |
| RH-7281 + mancozeb | 15.0 + 120 | 99.4 | 92.0 | 96.0 | 98.7 | 94.9 |
| Mancozeb | 160 | 91.7 | 91.0 | 95.0 | | |
| Mancozeb | 280 | - | - | - | 97.0 | 86.5 |
| Folpet | 100 | 99.3 | 92.0 | 93.0 | - | |
| Folpet | 150 | - | - | - | 97.2 | 91.4 |
| Untreated ** | | (86.0) | (57.0) | (22.0) | (65.2) | (55.7) |

*Rates based on a spray volume of 1000 l/ha.

** Percent infection

## Vegetables

Table 8. Control of *Phytophthora infestans* on tomatoes and *Pseudoperonospora cubensis* on cucumbers (1997).

| Product | Rate (g a.i./hl) | Percent Disease Control *P. infestans* on Tomato Italy 7-10 d Interval Leaves (6DAT5) | *P. infestans* on Tomato Italy 7-10 d Interval Fruits (16DAT5) | *P. cubensis* on Cucumber Spain 7 d Interval Leaves (8DAT4) |
|---|---|---|---|---|
| RH-7281 + mancozeb | 12.5 + 100 | 97.4 | 95.6 | 94.0 |
| RH-7281 + mancozeb | 15.0 + 120 | 98.6 | 96.5 | 90.0 |
| Mancozeb | 160 | - | - | 93.0 |
| Chlorothalonil | 150 | 98.5 | 97.4 | 71.0 |
| Copper oxychloride. | 250 | 77.1 | 87.4 | - |
| Cymoxanil + copper | 12.6 + 120 | 95.7 | 91.8 | - |
| Untreated* | | (78.4) | (50.5) | (60.4) |

*Percent infection

Protectant applications of RH-7281, alone and in mixture with mancozeb, have been evaluated for control of late blight and downy mildew on several vegetables, including tomato, cucumber, squash, and pepper. At rates from 12.5 + 100 to 15 + 120 g a.i./hl, excellent efficacy, equivalent or better than current standards, is obtained. In addition to the results shown in Table 8 for tomato and cucumber, RH-7281 has also been shown to provide very good control of white rust (*Albugo occidentalis*) on spinach.

### Other diseases

Other pathogens which have been controlled or suppressed by RH-7281 in glasshouse or field studies are *Botrytis cinerea, Bremia lactucae, Cercospora arachidicola, Phytophthora capsici, P. erythroseptica*, *Sphaerotheca fuliginea* and *Peronospora parasitica.*

## SUMMARY AND CONCLUSIONS

RH-7281 is a highly active, protective fungicide with good persistence and excellent rainfastness. It exhibits very good crop safety to a broad range of crops at recommended application rates. On vines, RH-7281 is particularly effective in controlling downy mildew infections on the bunches. On potato, under heavy infection pressure, good control of foliar, stem, and tuber blight is obtained. Combinations with mancozeb and other selected fungicides broaden disease spectrum and enhance activity. Other notable features of RH-7281 include its novel mode of action and lack of potential cross-resistance to other commercial downy mildew and late blight fungicides. It also has exceptionally low mammalian toxicity and is very safe to the environment. These characteristics make RH-7281 a good candidate for integrated disease control and resistance management programs.

## ACKNOWLEDGEMENTS

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# MON65500: A unique fungicide for the control of take-all in wheat

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## ABSTRACT

MON65500 (N-Allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide) is a highly-active new compound providing excellent control of take-all disease in cereals caused by the fungus *Gaeumannomyces graminis* var. *tritici*. Delivered as a seed-treatment in a flowable concentrate formulation to field trials conducted between 1994 and 1997, it has provided significant yield protection in crops attacked by *G. graminis* var. *tritici*. MON65500 has outstanding protectant activity, providing long duration of control of root infections and significant control of the characteristic white head development commonly associated with this disease later in the season.

MON65500 has excellent toxicological, environmental and eco-toxicological profiles, is compatible with other seed-treatments when co-applied and offers an excellent tool to cereal producers to maintain yield potential of crops at risk from take-all infections. This compound is specific for take-all, comes from a new family of chemistry and provides a new mode of action in fungicide chemistry.

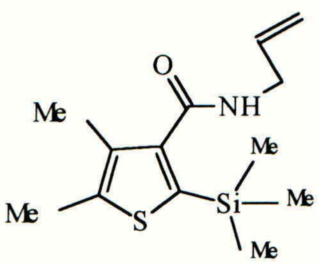
## INTRODUCTION

Take-all of wheat caused by the soil-borne fungus *Gaeumannomyces graminis* var. *tritici* (Ggt) is known world wide as a major yield-limiting factor. Whilst it is known that some members of the triazole family of chemistry have short-term efficacy, particularly triadimenol (Bockus, 1983), most means of control lie with cultural methods such as rotation, delayed drilling and increased nitrogen inputs. With wheat playing an increasingly important role in world food supply, the importance of optimising inputs and reducing yield losses becomes critical.

A synthesis programme specifically targeted at Ggt identified the activity of a new family of compounds, the hindered silyl amides (Phillion *et al.*, 1993), with specific activity towards this pathogen. Field trials were first conducted in the USA in 1989-90 and over 300 field trials have since been made, the majority in Europe. Analogue testing resulted in the selection of MON65500 in 1994, based on high unit activity and favourable environmental profile. This paper describes the characterisitcs of MON65500 and its biological performance.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Code number: | MON65500 |
| Chemical class: | Hindered silyl amide |
| Chemical name: | N-Allyl-4,5-dimethyl-2-trimethylsilylthiophene-3-carboxamide |
| Structural formula: | |




| | |
|---|---|
| Chemical formula: | $C_{13}$ $H_{21}$ O N S Si |
| Molecular weight: | 267.46 |
| Physical state: | White crystalline powder. |
| Melting point: | 86.1 - 88.3 °C |
| Water solubility: | 35.3 mg/litre at 20°C |
| Partition coefficient: | log $P_{ow}$ = 3.48 (n-octanol/water at 20°C) |

## PRODUCT SAFETY:

### Acute Toxicology

| | |
|---|---|
| Acute oral $LD_{50}$ rat: | >5000 mg/kg |
| Acute dermal $LD_{50}$ rat: | >5000 mg/kg |
| Skin irritation rabbit: | non-irritating |
| Eye irritation rabbit: | non-irritating |
| Ames test: | negative |
| CHO/HGPRT gene mutation: | negative |
| *In vitro* cytogenicity study: | negative |
| Mouse micronucleus: | negative |

### Environmental Fate:

| | |
|---|---|
| Soil degradation: | $DT_{90}$<365 days |

## MODE OF ACTION

The biochemical mode of action of MON65500 is currently under investigation. It is known that its mode of action is different from other groups of fungicide chemistry such as the strobilurines and triazoles. MON65500 has an effect on energy production in the cell, possibly on ATP. It acts very specifically and very fast (15 - 90 min.) with a rapid effect on oxygen consumption.

## MATERIALS AND METHODS

### Laboratory Studies

The efficacy of MON 65500 was tested in Petri dish studies in comparison to known triazoles. Technical material of each treatment was incorporated into minimal Czapek Dox medium and 4 mm diameter plugs of Ggt were grown on these at 20°C in the dark for 5 days. Inhibition (%) of mycelium growth was calculated by using the formula [1-(mm treatment-4)/(mm control-4)]x100.

### Growth room Studies

The spectrum of activity of MON65500 was tested in growth room tests against a range of known plant pathogens using small pots with curative and protectant sprays, soil drenches or seed treatments at a range of rates. Screening of efficacy against Ggt was conducted in 'Conetainer' tests. Replicate 'Conetainers', 25 mm diameter and 200 mm tall were filled with 20 ml vermiculite, 50 ml of Ggt-infested soil (4% by volume of oat inoculum), planted with 3 treated seeds of wheat and then covered with an additional 15 ml of infested soil and a thin layer of vermiculite. Following watering these were incubated in a growthroom at 18/15°C (light/dark) for 3 weeks before assessments of root rot and stem lesions were made.

### Field Trials

Trials were conducted between 1994 and 1997 in France, Belgium, UK, Germany, Ireland and the USA. Trials were either small-plot randomised design or large-strip trials with one or two replicates. Randomised block designs had a minimum of 4 replicates with plot size of 3.3 to 20 $m^2$, all being double plots, the left hand plot used for sampling and the right hand plot for harvest. Large strip trials were drilled and harvested with farm equipment using plots of 3000 - 6000 $m^2$. Some tests were conducted with inoculated small plots, by drilling infested oat grain inoculum with test treatments (1.5 g/m row). Assessments were made of speed of emergence (GS 1-11, on a 0-10 scale), plant stand (GS 13-20, number of plants/ $m^2$), vigour (GS 13-20, 0-10 scale, where 0 = no crop and 10 = plot with greatest biomass in block), phytotoxicity (GS 13-20, % total leaf area affected by chlorosis and necrosis), yield (GS 92, t/ha at 15% moisture) and thousand grain weights. Assessment of root infection by Ggt (GS 13-75) was made from at least 20 plants per plot, 100 plants per treatment, calculating incidence of take-all (number of plants with take-all / number of plants assessed x 100), intensity of take-all using a take-all index (TAI = (0a + 10b + 30c + 60d+100e) / T .where a, b, c, d, e represent the number of plants in each of 5 categories: 0 = healthy roots; 1= 1-10% roots infected; 2 = 11-30% roots infected; 3 = 31-60% roots infected; 4 = 61-100% roots infected; and T is the total number of plants examined (a+b+c+d+e)), and whitehead incidence (%) (GS 69-75). Choice of variety, sowing date, sowing rate, fertilisers and pesticides were as normal farm practice. All seed were treated with a basic treatment: 5 g of fludioxonil /100 kg seed or 90 g of bitertanol + 5.5 g of fuberidazole/100 kg seed in the UK, 60 g of guazatine /100 kg seed in Ireland, 5 g of fludioxonil + 1 g of tebuconazole/100 kg seed or 5 g of fludioxonil + 20 g of difenoconazole/100 kg seed in Germany, and 5 g of fludioxonil + 50 g anthraquinone / 100 kg seed in France. Some trials included 37.5 g of triadimenol + 5.5 g of fuberidazole/100 kg seed or 10 or 20 g difenoconazole + 2 g of metalaxyl/100 kg seed. MON65500 was formulated as a 125 g/litre FS and applied in addition to the basic seed treatment.. All treatments were made with a Hege 14 seed treater, a Rotogard 534 or a mini Rotostat. MON 65500 treatments were diluted with water to apply in a final volume of 600 ml/100 kg seed and all other treatments were diluted with water to apply in a final volume of 400 ml/100 kg seed.

## RESULTS AND DISCUSSION

### Laboratory and Growth room Studies

Laboratory studies showed a very high unit activity of MON65500 towards Ggt, with $LD_{50}$% inhibition of hyphal growth at 0.1 μg/litre of active material in agar. Growth room tests in sterile soil confirmed this high degree of efficacy, this being significantly greater than triazole treatments (Table 1). Spectrum analysis in laboratory and growth room tests demonstrated the specificity of MON65500, although a slight activity was found towards both *Microdochium nivale* and *Tilletia caries*. Activity against other plant pathogens or against non plant pathogens was not detected. Thus, MON65500 is unlikely to alter the balance of other fungi within the rhizosphere.

Table 1. Comparison of MON65500 with triazole seed treatments for the control of take-all in growthroom 'Conetainer' tests.

| Treatment | Control of take-all root rot (%) | Control of take-all stem lesions (%) |
|---|---|---|
| MON65500<br>12.5 g a.i./100 kg seed | 87 a | 96 a |
| Triazole | 20 b | 41 b |
| MON65500 + Triazole | 88 a | 98 a |

All figures are means from eight growth room trials. Root rot severity on nontreated plants averaged 41% and the incidence of stem lesions on nontreated plants averaged 59%. Triazole and MON65500 + Triazole figures are means from treatments with the following triazoles: difenoconazole (60 g/100 kg seed), tetraconazole (30 g/100 kg seed), triadimenol (37.5 g /100 kg seed) and triticonazole (120 g /100 kg seed). Figures not followed by the same letter differed significantly ($P$=0.05) in a Duncan's Multiple Range Test.

**Field trials**

Take-all development during the testing period varied from year to year due to changes in climatic conditions. The 1994/5 season was generally high in take-all with an average take-all index of 32.14 (mean from total of 28 trials) and a mean untreated yield of 6.55 t/ha. Treatments with MON65500 provided significant control of Ggt root rot and whiteheads (Figure 1). Significant increases in yield were also observed (Figure 2), the mean yield increase in high take-all sites (Index of ≥40, mean index of 59.6, GS 69) for the 25 g a.i./100 kg seed rate was 1.38 t/ha (8 trials). In a medium take-all situation (disease index 20-40, mean of 29.3) the mean yield increase with the 25 g rate was 0.49 t/ha (7 trials), whilst in a low take-all situation (DI <20, mean of 9) was 0.17 t/ha (11 trials).

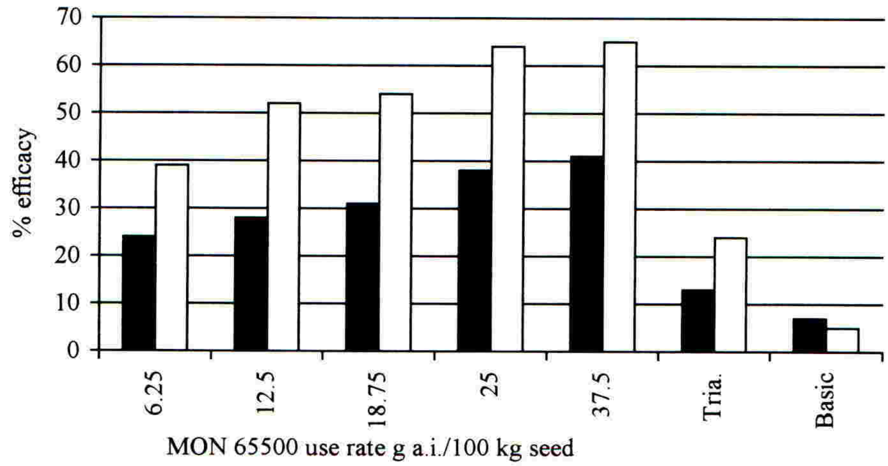



Figure 1. Efficacy of MON65500 against Ggt from European field trials in 1994/95. Tria., 37.5 g triadimenol + 4.5 g fuberidazole/100 kg seed; Basic, 5 g fludioxonil + 50 g anthraquinone/100 kg seed in France, 5 g fludioxonil + 20 g difenoconazole/100 kg seed in Germany, 5 g fludioxonil/100 kg seed in UK;

Table 2. Effect of MON65500 on take-all index and yield of winter wheat - 1995/6 season (47 large-strip trials).

| Take-all pressure | Treatment | Take-all Index | | | | White heads(%) | Yield (t/ha) |
|---|---|---|---|---|---|---|---|
| | | Tillering | Stem ext. | Heading | Grain filling | | |
| HIGH | Ctl | 5.6 | 21.6 | 48.4 | 64.8 | 50.0 | 4.62 |
| | MON | 0.8 | 5.5 | 20.0 | 30.4 | 22.5 | 7.01 |
| MID | Ctl | 7.8 | 9.5 | 25.7 | 21.6 | 13.3 | 5.63 |
| | MON | 3.0 | 5.3 | 15.0 | * | 8.9 | 6.06 |
| LOW | Ctl | 1.5 | 2.4 | 3.4 | 8.4 | 4.6 | 7.89 |
| | MON | 0.8 | 1.8 | 1.5 | 3.5 | 1.3 | 8.14 |

Ctl, control treated with basic seed treatment; MON, MON65500 @ 12.5 g a.i./100 kg seed; *, missing data.

The 1995/96 season was low in take-all with an average index of 14.21 at GS 69 (mean from 75 European trials), and an untreated yield of 7.76 t/ha. MON65500 continued to provide significant control of root rot and whiteheads and significant increases in yields. Mean yields taken from 47 large-strip trials indicated that yield advantages from large plots could be greater than those from small-plot trials (Table 2).

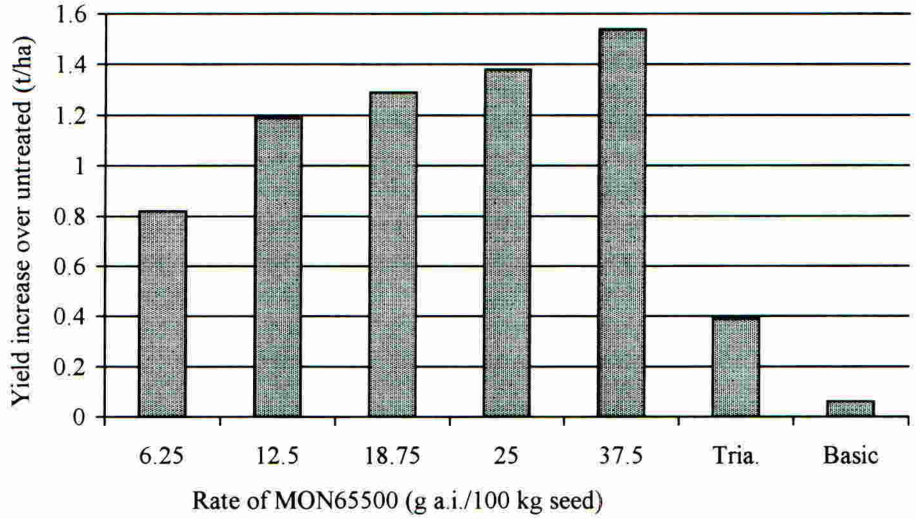



Figure 2. Yield benefit following MON65500 treatments in high take-all sites during 1994/5 (8 EU sites). Basic, 5 g fludioxonil + 50 g anthraquinone/100 kg seed in France, 5 g fludioxonil + 20 g difenoconazole/100 kg seed in Germany, 5 g fludioxonil/100 kg seed in UK; Tria., 37.5 g triadimenol + 4.5 g fuberidazole/100 kg seed.

Take-all levels in the 1996/97 season were moderately severe, with an average index of 18.71 at GS 69 and an average untreated yield of 7.31 t/ha (124 European trials). The performance of MON65500 was again significant (Table 3), in the UK for example the 50 g rate provided an average 43% control of root infections, as late as GS75, and an average yield increase of 0.64 t/ha. Trials conducted in the USA in a range of locations with second wheat crops showed significant yield benefits for spring sown as well as winter sown wheat (Table 4). Take-all control and yield increase following MON65500 seed treatment were significantly greater than those following triazole seed treatments (Table 5).

Analysis of small-plot trials across years, for a range of natural infestation levels, demonstrated the significant yield benefits of MON65500 (Table 6). Averages across years for large-strip trials demonstrated similar or greater levels of yield recovery. At the 25 g a.i./100 kg seed rate, MON65500 provided a mean yield increase of 1.54 t/ha in high take-all sites and 0.39 t/ha yield increase in moderate take-all sites. The highest level of yield recovery obtained with MON65500 in any of the test sites during the three year period was 4.5 t/ha.

Table 3. Mean crop effects, take all levels and yields following treatments with MON65500 in small-plot trials within the UK - 1996/7.

| Treatment | Vigour | Plants/m$^2$ | TA Index (GS75) | Efficacy (%) | Yield (t/ha) |
|---|---|---|---|---|---|
| Untreated | 9.59 | 234 | 20.33 | 0.00 | 6.84 |
| MON 12.5 | 9.58 | 234 | 15.61 | 23.19 | 7.20 |
| MON 25 | 9.62 | 229 | 12.58 | 38.13 | 7.36 |
| MON 50 | 9.56 | 239 | 11.51 | 43.36 | 7.48 |
| Beret Gold | 9.66 | 235 | 19.64 | 3.38 | 6.96 |
| | (13 trials) | (13 trials) | (8 trials) | (8 trials) | (8 trials) |

No significant differences were found between treatments for vigour or plants/m$^2$ whilst treatments differed significantly ($P$=0.05) for take-all index, efficacy and yield.

Table 4. Yield data from small-plot field trials with spring and winter wheat after wheat - USA 1997.

| | | Treatments and rates (g a.i./100 kg seed) | | | |
|---|---|---|---|---|---|
| Location | Description | CTL | 25M | 25M+12D/M | 12D/M |
| OR/SO9 | DL/W | 4.33 a | 4.86 b | 4.78 b | 4.92 b |
| OR/S11 | DL/S | 4.34 a | 4.52 ab | 4.76 bc | 4.88 c |
| WA/S12 | DL/S | 3.59 a | 3.86 bc | 4.01 c | 3.76 ab |
| OR/S13 | DL/S | 0.67 a | 1.00 b | 1.21 c | 0.98 b |
| WA/S14 | DL/S | 3.23 a | 3.78 bc | 4.02 c | 3.60 b |
| WA/S15 | DL/S | 3.83 a | 4.17 bc | 4.24 c | 4.09 b |
| WA/S16 | DL/S | 3.08 a | 3.56 b | 3.83 c | 3.22 a |
| WA/DF1 | DL/W | 4.16 ab | 5.49 c | 4.43 b | 3.37 a |
| WA/JG1 | I/W | 1.77 a | 1.51 ab | 1.38 b | 1.37 b |
| WA/MQ3 | I/W | 6.35 a | 7.31 ab | 8.17 b | 7.19 ab |
| Mean yield (t/ha) | | 3.54 | 4.01 | 4.08 | 3.74 |
| Yield increase (t/ha) | | | 0.47 | 0.55 | 0.20 |
| Yield increase (%) | | | 13.28 | 15.47 | 5.72 |

CTL, Untreated control; M, MON65500; D/M, 10 g difenoconazole + 2 g metalaxyl; DL, dry-land; I, irrigated; S, spring wheat; W winter wheat; Figures not followed by the same letter differed significantly ($P$=0.05) in a Duncan's Multiple Range Test.

Table 5. Results from an inoculated trial in dry-land winter wheat (Manhattan, KS, 1997).

| | Treatments (rate in g a.i./100 kg seed) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | NIC | CTL | 6.25 | 12.5 | 25 | 50 | D10 | TRI | D20 |
| Whiteheads(%) | 0.5 | 53.8 | 0.5 | 0.0 | 0.0 | 0.0 | 47.5 | 33.5 | 41.3 |
| Sig. ($P$=0.05) | d | a | d | d | d | d | ab | c | bc |
| Yield (t/ha) | 3.04 | 1.74 | 3.28 | 3.20 | 3.35 | 3.38 | 1.90 | 2.41 | 2.32 |
| Sig. ($P$=0.05) | a | d | a | a | a | a | cd | b | bc |

NIC, non inoculated control; CTL, inoculated control; D10 & D20, difenoconazole @ 10 g or 20 g/100 kg; TRI, triadimenol @ 37.5 g/100 kg.

Table 6. Summary for yield recovery with MON65500 in relation to severity of take-all.

| Rate of MON65500 (g a.i./100 kg seed) | Low take-all | | | Medium take-all | | | High take-all | | |
|---|---|---|---|---|---|---|---|---|---|
| | Yield (t/ha) | Gain (t/ha) | Gain (%) | Yield (t/ha) | Gain (t/ha) | Gain (%) | Yield (t/ha) | Gain (t/ha) | Gain (%) |
| 0 | 7.66 b | | | 7.18 b | | | 6.61 b | | |
| 12.5 | 7.84 a | 0.18 | 2.4 | 7.63 a | 0.45 | 6.3 | 7.10 a | 0.49 | 7.4 |
| 25 | 7.85 a | 0.19 | 2.5 | 7.58 a | 0.40 | 5.5 | 7.21 a | 0.60 | 9.1 |

Data are means from 129 European field trials 1995-1997 with similar protocols. Low take-all, trials with an index <20; Medium take-all, an index >=20,<40; High take-all, index >40. Means not followed by the same letter differed significantly ($P$=0.05) in an Duncan's MRT.

## CONCLUSIONS

MON65500 is a low use rate seed treatment highly specific for Ggt, and comes from a new family of fungicide chemistry. It will for the first time enable management of take-all disease, providing significant yield recovery at a range of infestation levels. It has excellent crop and environmental safety characteristics and can be co-applied with any other currently commercially available seed treatment.

## ACKNOWLEDGEMENTS

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## REFERENCES

Bockus W W (1983). Effects of fall infection by *Gaeumannomyces graminis* var. *tritici* and triadimenol seed treatment on severity of take-all in winter wheat. *Phytopathology*, **73**, 540-543.

Phillion D P; Braccolino D S; Graneto M J; Phillips W G; Van Sant K A; Walker D M; Wong S C (1993). Preparation of heterocyclic and aromatic compounds as fungicides for control of take-all disease of plants. *Europe Patent Application*, **EP538231**, 21 April 1993.

# IKF-916 - A novel systemic fungicide for the control of oomycete plant diseases

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## ABSTRACT

IKF-916 is a novel systemic cyanoimidazole fungicide discovered and currently under development by Ishihara Sangyo Kaisha Ltd. This fungicide is very active against a broad spectrum of oomycetes (such as *Phytophthora, Plasmopara, Pseudoperonospora, Pythium*), and Plasmodiophoromycetes (*Plasmodiophora brassicae*). Glasshouse studies have shown excellent preventative activity along with stable residual activity and rainfastness. In field studies, IKF-916 exhibits excellent performance for control of potato late blight, tomato late blight, grapevine downy mildew and cucumber downy mildew at 60-100 g a.i./ha. It has a good toxicological, environmental and eco-environmental profile.

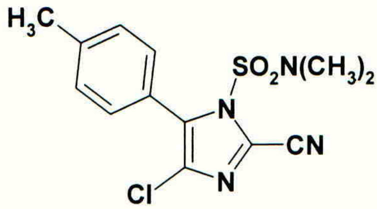
## INTRODUCTION

IKF-916 is a novel systemic fungicide from a new chemical class based on the cyanoimidazole moiety, discovered and currently under development by Ishihara Sangyo Kaisha, Ltd. The compound shows promise as a control agent for oomycete and *Plasmodiophora* plant diseases. This new fungicide is being developed for use as a foliar treatment for potato, grapevine, tomato, cucurbits, onion, lettuce, rice and Chinese cabbage. Soil treatments are also being evaluated for turf, cabbage and Chinese cabbage. This is the first report describing the properties, mode of action and field performance of IKF-916 against key target pathogens in vegetables, grapevine and rice.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Code number: | IKF-916 |
| Chemical class: | Cyanoimidazole |
| Chemical name (IUPAC): | 4-chloro-2-cyano-*N*,*N*-dimethyl-5-*p*-tolylimidazole-1-sulfonamide |
| Structure formula: | $C_{13}H_{13}ClN_4O_2S$ |

Molecular formula:




| | |
|---|---|
| Molecular weight: | 324.8 |
| Appearance: | Ivory, odourless, powder |
| Water solubility: | 0.121 ppm (pH 5, 20 °C) |
| Melting Point: | 152.7 °C |
| Vapour pressure: | $<1.33 \times 10^{-5}$ Pascal |
| Partition coefficient n-octanol/water: | Log Po/w: 3.2 (25 °C) |
| Soil adsorption: | Koc: 490-6300 |
| Soil degradation: | $DT_{50}$: 4-5 days |

**PRODUCT SAFETY**

| | |
|---|---|
| Acute oral (rat) $LD_{50}$: | >5000 mg/kg |
| Acute dermal (rat) $LD_{50}$: | >2000 mg/kg |
| Subchronic toxicity (90 day dog study): | No treatment related effects up to 1000 mg/kg/day |
| Carp $LC_{50}$ (96hr): | >70.5 mg/kg |
| Mutagenicity: | Ames negative |

**FORMULATION**

IKF-916 is currently available as a suspension concentrate (100 and 400 g a.i./litre ) and will be marketed under various trademarks including "Ranman", "Docious" and "Mildicut". A water dispersible granule formulation and mixtures of IKF-916 with other fungicides are also under evaluation.

**BIOLOGICAL ACTIVITY**

**Materials and Methods**

The antifungal activity against *Phytophthora infestans* strains was determined by measurement of mycelial development on agar medium amended with IKF-916. For pot tests (glasshouse tests), cucumber and tomato seedlings were sprayed with one of various concentrations of IKF-916 (water volume; 800 litre/ha). After drying, each seedling was inoculated with a zoospore suspension of pathogens. Fungicidal activities were determined by observing the area of lesion visually and by comparison with that of the untreated. All field trials were laid down as randomized blocks replicated 2-5 times. The water volume for fungicides applications was, potato: 300-1000 litre/ha, grapevine: 600-1000 litre/ha, tomato: 500-1500 litre/ha and cucumber: 500-1200 litre/ha. Spray timing followed the normal grower practice for the area (7-10 day intervals). Frequency or intensity of infected leaves were assessed.

## RESULTS

### Biochemical mode of action

IKF-916 specifically interferes with complex Ⅲ activity (ubiquinol-cytochrome c reductase), in the mitochondrial respiratory chain of oomycetes only. $\beta$-methoxyacrylates also inhibit complex Ⅲ, however the precise mode of action of IKF-916 is different from that of the $\beta$-methoxyacrylates. IKF-916 is an inhibitor of Qi (ubiquinone-reducing site) of cytochrome bc1 and $\beta$-methoxyacrylates are inhibitors of Qo (ubiquinol-oxidizing site) of cytochrome bc1 (Mansfield & Wiggins, 1990; Wiggins & Jager 1993).

### Biological mode of action

IKF-916 inhibits all stages in the life cycle of *P. infestans*, including germination and formation of zoosporangia, gemination of cystospores, zoospore motility and mycelial growth.

### Antifungal activity against *P. infestans* strains showing different sensitivity to phenylamides

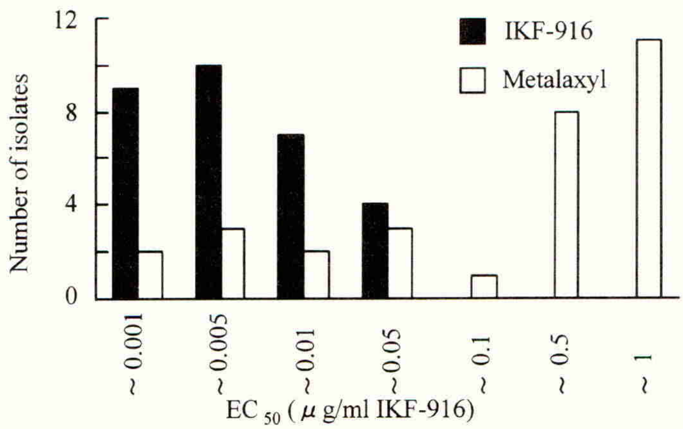



Figure 1. Cumulative EC $_{50}$ (mycelial growth) distribution values of *Phytophthora infestans* from potatoes.

IKF-916 sensitivity of 30 isolates of *P. infestans* was evaluated. All strains were isolated from Hokkaido, Japan and mycelial growth of the strains was measured. IKF-916 was equally effective against phenylamide sensitive and resistant strains. The sensitivity ($EC_{50}$) of 30 field isolates of *P. infestans* to IKF-916 ranged from 0.038 to <0.01 $\mu$ g/ml (Figure 1).

**Glasshouse tests**

Special emphasis is given to the minimum inhibitory concentration for preventive activity of IKF-916. To our knowledge, IKF-916 has the highest preventive activity against *P. infestans* on tomato and *Pseudoperonospora cubensis* on cucumber among all known fungicides. (Tables 1 and 2 are these sample experiments). IKF-916 has stable residual activity and rainfastness (Table 3). IKF-916 exhibits good control against *Pythium* sp. on rice and against *Plasmodiophora brassicae* on Chinese cabbage (Tables 4 and 5).

Table 1. Preventive activity of IKF-916 against *Phytophthora infestans* on tomato.

| Treatment | % Disease control | | | | | |
|---|---|---|---|---|---|---|
| | 50 | 13 | 3 | 0.8 | 0.2 | ($\mu$ g a.i./ml) |
| IKF-916 | - | 96 | 93 | 77 | 23 | |
| Azoxystrobin | 92 | 92 | 59 | 48 | 0 | |
| Dimethomorph | 98 | 79 | 52 | 14 | - | |
| Famoxadone | 70 | 34 | 20 | 16 | 6 | |
| Mancozeb | 78 | 54 | 53 | 30 | - | |

Disease in control (% leaf area infected) : 100

Table 2. Preventive activity of IKF-916 against *Pseudoperonospora cubensis* on cucumber.

| Treatment | % Disease control | | | | | |
|---|---|---|---|---|---|---|
| | 13 | 3 | 0.8 | 0.2 | 0.05 | ($\mu$ g a.i./ml) |
| IKF-916 | - | 98 | 99 | 89 | 23 | |
| Azoxystrobin | 90 | 70 | 40 | 0 | - | |
| Dimethomorph | 95 | 70 | 22 | - | - | |
| Famoxadone | 89 | 59 | 45 | 10 | - | |
| Mancozeb | 90 | 50 | 43 | - | - | |

Disease in control (% leaf area infected) : 100

Table 3. Rainfastness activity of IKF-916 against *Phytophthora infestans* on tomato and *Pseudoperonospora cubensis* on cucumber.

| Treatment | $\mu$ g a.i./ml | % Disease control | |
|---|---|---|---|
| | | Rainfastness on tomato (artificial rain 20 mm) | Residual on cucumber (glasshouse for 7 days) |
| IKF-916 | 13 | 94 | 100 |
| IKF-916 | 3 | 75 | 94 |
| IKF-916 | 0.8 | 41 | 80 |
| Mancozeb | 130 | 75 | 80 |
| Mancozeb | 30 | 14 | 28 |

Disease in control (% leaf area infected) : 100

Table 4. Preventive activity of IKF-916 against *Pythium* sp. on rice.

| Treatment | Rate (mg a.i./nursery box) | % Disease control |
|---|---|---|
| IKF-916 | 50 | 82 |
| IKF-916 | 25 | 50 |
| Metalaxyl + hymexazol(I) | 20+150 | 54 |

Disease in control (% leaf area infected) : 79

Table 5. Preventive activity of IKF-916 against *Plasmodiophora brassicae* on Chinese cabbage.

| Treatment | Rate (g a.i./1000m$^2$) | % Disease control |
|---|---|---|
| IKF-916 | 400 | 100 |
| IKF-916 | 300 | 79 |
| IKF-916 | 200 | 69 |
| Flusulfamide | 90 | 66 |

Disease in control (% root area infected) : 100

## Field trials

### *Potato*

IKF-916 at 60-100 g a.i./ha gave outstanding control of potato late blight (Table 6). The activity was equal to or superior to the standard fungicides. Suppression of tuber blight was also noted (data not shown).

Table 6. Control of *Phytophthora infestans* with IKF-916 on potato.

| Treatment | g a.i./ha | % Disease control | | | |
|---|---|---|---|---|---|
| | | Japan | U.K. | | Germany |
| | | 1996 | 1996 | 1997 | 1997 |
| IKF-916 | 100 | 96 | - | - | 94 |
| IKF-916 | 80 | - | 80 | 96 | 94 |
| IKF-916 | 60 | 92 | - | 95 | - |
| Fluazinum | 200 | - | - | 95 | 95 |
| Mancozeb + cymoxanil | 1360 + 90 | - | 11 | - | - |
| Mancozeb | 1320 | 53 | - | - | - |
| Disease in control (% leaf infection) | | 100* | 100 | 93 | 83* |

*% leaf area infected

### *Grapevine*

IKF-916 at 100 g a.i./ha consistently provided good control of grapevine downy mildew (Table 7). The activity was superior to the standard mancozeb + cymoxanil at 1395 + 120 g a.i./ha.

Table 7. Control of *Plasmopara viticola* with IKF-916 on grapevine in France.

| Treatment | g a.i./ha | % Disease control | | |
|---|---|---|---|---|
| | | 1995 | 1996 | 1997 |
| IKF-916 | 100 | 73 | 86 | 83 |
| Mancozeb + cymoxanil | 1395 + 120 | 58 | 75 | 81 |
| Disease in control (% leaf area infected) | | 100 | 63 | 100 |

### *Tomato*

IKF-916 at 80-100 g a.i./ha showed good activity against tomato late blight (Table 8). The activity was superior to the standard mancozeb + cymoxanil.

Table 8. Control of *Phytophthora infestans* with IKF-916 on tomato.

| Treatment | g a.i./ha | % Disease control | | |
|---|---|---|---|---|
| | | Italy | South Africa | Spain |
| | | 1996 | 1996 | 1997 |
| IKF-916 | 100 | - | 74 | - |
| IKF-916 | 80 | 75 | 43 | 57 |
| Mancozeb + cymoxanil | 1631 + 140 | - | 13 | - |
| Mancozeb + cymoxanil | 1200 + 120 | 61 | - | 35 |
| Disease in control (% leaf infection) | | 72 | 100* | 58 |

* % leaf area infected

### *Cucumber*

IKF-916 at 60-100 g a.i./ha showed good activity against cucumber downy mildew (Table 9). The activity was equal to or superior to the standard fungicides.

Table 9. Control of *Pseudoperonospora cubensis* with IKF-916 on cucumber.

| Treatment | g a.i./ha | % Disease control | | | |
|---|---|---|---|---|---|
| | | Japan | | Italy | Spain |
| | | 1996 | 1997 | 1997 | 1997 |
| IKF-916 | 100 | 70 | 82 | 73 | - |
| IKF-916 | 80 | - | - | 70 | - |
| IKF-916 | 60 | - | - | - | 77 |
| Azoxystrobin | 250 | - | 57 | - | - |
| Chlorothalonil | 1000 | - | 66 | - | - |
| Mancozeb + cymoxanil | 1200 + 120 | - | - | 68 | - |
| Mancozeb | 1875 | - | - | - | 48 |
| Mancozeb | 1250 | 60 | 44 | - | - |
| Disease in control (% leaf infection) | | 76* | 66* | 40 | 57 |

* % leaf area infected

## Crop safety

There are no phytotoxicity concerns for potatoes, grapevines, tomatoes, cucumbers and onions even at use rates of up to 400 g a.i./ha.

## CONCLUSION

IKF-916 is a new oomycete fungicide from a new chemical class. In field trials, it shows excellent control of potato and tomato late blight, grapevine and cucumber downy mildew in several year at use rate 60-100 g a.i./ha. It has a good fungicidal and environmental profile (data not shown) and can be used in integrated pest management programmes.

## REFERENCES

Mansfield R W; Wiggins T E (1990). Use of photoaffinity labelling to identify the binding site of the novel $\beta$ -methoxyacrylate agrochemical fungicides. *Brighton Crop Protection Conference-Pests and Diseases,* 867-871.

Wiggins T E; Jager, B J (1993). Mode of action of the new methoxyacrylate antifungal agent ICIA5504. *Biochemical Society Transactions* **22**, 68S.

# AC 382042 - A new rice blast fungicide

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## ABSTRACT

AC 382042 (N-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide) is a new systemic rice blast fungicide which acts through the inhibition of melanin biosynthesis in the fungal pathogen *Pyricularia oryzae*. AC 382042 has a very low mammalian and environmental toxicity. Relative to other melanin biosynthesis inhibiting rice blast fungicides, AC 382042 has excellent extended residual activity against rice blast after foliar application using dust and flowable formulations. In addition, AC 382042 is very effective for the control of panicle blast after into-water application using a granule formulation.

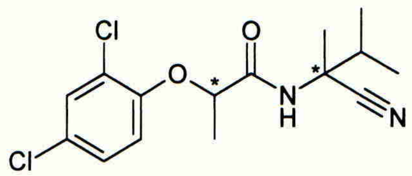
## INTRODUCTION

AC 382042 is a systemic fungicide for the control of rice blast. It was discovered at the Shell Forschung GmbH Laboratories in Schwabenheim, Germany and became property of American Cyanamid following acquisition of the Shell Agrochemical business. AC 382042 is being co-developed by American Cyanamid Company and Nihon Nohyaku Company. This paper describes the properties of AC 382042 and its basic biological profile which was defined in laboratory and greenhouse experiments and field trials carried out by American Cyanamid and Nihon Nohyaku. AC 382042 is the American Cyanamid code for this new rice blast fungicide, whereas it is coded NNF-9425 by Nihon Nohyaku for Japan Plant Protection Association (JPPA) official field trials.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Family: | Phenoxyamide |
| Chemical name: | N-(1-cyano-1,2-dimethylpropyl)-2-(2,4-dichlorophenoxy) propionamide (R,S)- and (R,R)- and (S,R) - and (S,S) |
| CAS registry no.: | 115852-48-7 |
| Other designations: | CL 382042, AC 901216, WL 378309, NNF-9425 |

Structure:



*AC 382042 has two chiral centres and, thus, is a mixture of 4 isomers. The development compound consists of a mixture of two major diastereomers (R,R and R,S) and two minor diastereomers (S,R and S,S).

| | |
|---|---|
| Molecular formula: | $C_{15}H_{18}Cl_2N_2O_2$ |
| Molecular weight: | 329.23 |
| Density: | 1.22 g/cm$^3$ at 20° C |
| Appearance/physical state: | off white, odourless solid |
| Melting point: | 69.0 - 71.5 ° C |
| Solubility: | 30.7 ± 0.3 x 10$^{-3}$ g/l in water (at 20° C), soluble in most organic solvents |
| Partition coefficient n-octanol/water: | $P_{ow}$ = 3390 ± 133 at 25° C |
| Stability: | Essentially stable within the relevant pH range |
| Vapour pressure: | 0.21 ± 0.021 x 10$^{-4}$ Pa at 25° C |

## TOXICOLOGY

AC 382042 is of very low acute mammalian toxicity. It is safe to birds, fish and water organisms.

**Mammalian toxicity:**

| | |
|---|---|
| Oral $LD_{50}$ (rat, male) | >5000 mg/kg body weight |
| Oral $LD_{50}$ (rat, female) | 4211 mg/kg body weight |
| Oral $LD_{50}$ (mouse, male and female) | >5000 mg/kg body weight |
| Dermal $LD_{50}$ (rat, male and female) | >2000 mg/kg body weight |
| Inhalation $LC_{50}$ | >5.18 mg/l (analytical) |
| Eye irritation (rabbit) | Non-irritating (EU guidelines) |
| Skin irritation (rabbit) | Non-irritating |
| Dermal sensitisation (guinea pig) | Nonsensitiser |
| Mutagenicity | Non-mutagenic in Ames test, DNA repair test, chromosome aberration assay and mouse micronucleus assay |
| Teratogenicity | Not a teratogen in rat and rabbit |

**Toxicity to wildlife:**

| | |
|---|---|
| Bird toxicity | NOEL>2000 mg/kg (quail) |
| Fish & water organism toxicity | Non-toxic to carp, killifish and Daphnia |

## MODE OF ACTION

AC 382042 has been shown to prevent rice plants from the infection of *P. oryzae* (*Magnaporthe grisea*) through the inhibition of melanin biosynthesis in the fungal pathogen. As such, AC 382042 belongs to the class of fungicides referred to as melanin biosynthesis inhibitors.

Evidence suggests that the specific mode of action of AC 382042 within the melanin biosynthesis pathway is the inhibition of dehydratase enzymes which dehydrate scytalone to trihydroxynaphthalene and vermelone to dihydroxynaphthalene. Further work on the biochemical mode of action is still on-going.

## BIOLOGICAL PROPERTIES

### Residual activity

Similar to other melanin biosynthesis inhibitors (MBI), AC 382042 is a protective fungicide for the control of *P. oryzae*. . Glasshouse data demonstrate that AC 382042 has excellent extended residual activity after foliar application. Table 1 shows the efficacy of AC 382042 for the control of rice blast in comparison to another MBI when rice plants were inoculated at 0, 3 and 7 days after application of the compounds.

Table 1. Relative blast control by AC 382042 after application to the foliage of rice seedlings grown in the greenhouse.

| | 0 DAT | 3 DAT | 7 DAT |
|---|---|---|---|
| AC 382042 (20% SC) | 9.0 | 8.3 | 6.0 |
| Tricyclazole (20% SC) | 8.7 | 6.0 | 4.7 |
| Untreated | 0 | 0 | 0 |

All compounds were applied at 100 mg a.i./litre. Plants were inoculated 0, 3 or 7 days after treatment (DAT). The evaluation scale is non-linear where 0 = no control, 5 = 60-74% control, 6 = 75-89% control, 7 = 90-95% control, 8 = 96-99% control, and 9 = 100 % control. Data are means of 4 replicates.

AC 382042 is taken up into rice plants from paddy water, and provides a high level of efficacy and long residual activity. In glasshouse experiments $\geq$90% disease control was obtained when plants were inoculated 27 to 56 days after application of AC 382042 to the paddy water (Table 2). In this trial a granule (G) formulation with 5% a.i. of AC 382042 and a commercial standard was applied. Other greenhouse experiments indicated that the optimum application timing for into-water application was 3-7 days before blast infection occurred.

Table 2. Efficacy (%) of AC 382042 (5% G) against rice leaf blast after into water application in a simulated paddy rice greenhouse experiment.

| | *27 DAT* | *35 DAT* | *42 DAT* | *49 DAT* | *56 DAT* |
|---|---|---|---|---|---|
| AC 382042 (5% G) | 87 | 90 | 93 | 91 | 88 |
| Pyroquilon (5% G) | 90 | 93 | 86 | 81 | 77 |
| Untreated (Disease incidence, %) | (100) | (100) | (100) | (100) | (100) |

Plants were inoculated with *P. oryzae* spores at different days after application of the compounds (DAT). All compounds were applied at 0.63 kg a.i./ha. Evaluations are means of 3 replicated pots.

**Systemicity**

Excellent systemic activity of AC 382042 is easily demonstrated in glasshouse trials after foliar application. Table 3 shows the results of an experiment where plants were inoculated with a *P. oryzae* spore suspension 7 days after application of the compounds. Activity of the compounds were evaluated on the leaves which received the spray deposit and on leaves which had emerged since the time of the application (and hence on which no compound was deposited). It is clear from the results that besides excellent residual activity on the sprayed leaves, the compound had protected the newly-grown leaves against rice blast.

Table 3. Rice blast control on newly-emerged leaves by systemic action of AC 382042, 7 days after application in a glasshouse experiment.

| Treatment | Dose (mg a.i./litre) | Disease control %) Sprayed leaves | Newly-emerged leaves |
|---|---|---|---|
| AC 382042 (20% SC) | 100 | 100 | 99 |
| | 50 | 100 | 83 |
| Tricyclazole (20% SC) | 100 | 80 | 65 |
| | 50 | 74 | 58 |
| Untreated (No. of lesions/leaf) | | (35.4) | (32.8) |

## FIELD EFFICACY

Field trials to compare formulations, doses and application methods of AC 382042 with commercial rice blast fungicides for the optimum control of rice leaf and panicle blast were carried out in Japan using normal paddy rice cultivation systems. Trial sites differed in climatic conditions and soil types and different rice varieties were grown at different locations. A randomised block design with 3 replicates was used at each site. The plot size varied from 6 to 50 m$^2$. SC formulations were diluted with 1200 litres/ha for sprays against leaf blast and with 1500 litres/ha for sprays against panicle blast. Dust (DL) formulations were applied with special dust applicators. Granule (G) formulations were either applied by hand or with special granule applicators to the paddy water. Visual assessments of the infected leaves and panicle heads were made in 40 hills for each plot and the percent efficacy of each treatment was calculated.

**Field activity after foliar application**

For the control of rice leaf blast, AC 382042 and commercial standards were applied twice to the foliage. Two formulations of AC 382042 were evaluated, a 20% SC and a 1% DL. The first application was made at the first appearance of disease symptoms, and the second application 7-14 days later. For the control of panicle blast, AC 382042 was twice applied to the foliage. The first application was made at the boot stage and the second at full heading.

The 20% SC formulation of AC 382042 provided excellent control of leaf blast and panicle blast at a relatively low field dose (Figure 1). At 100 mg a.i./litre of AC 382042, corresponding to 120 g a.i./ha for leaf blast control and 150 g a.i./ha for panicle blast control, the efficacy was equivalent to that of the standard applied at 200 mg a.i./litre.

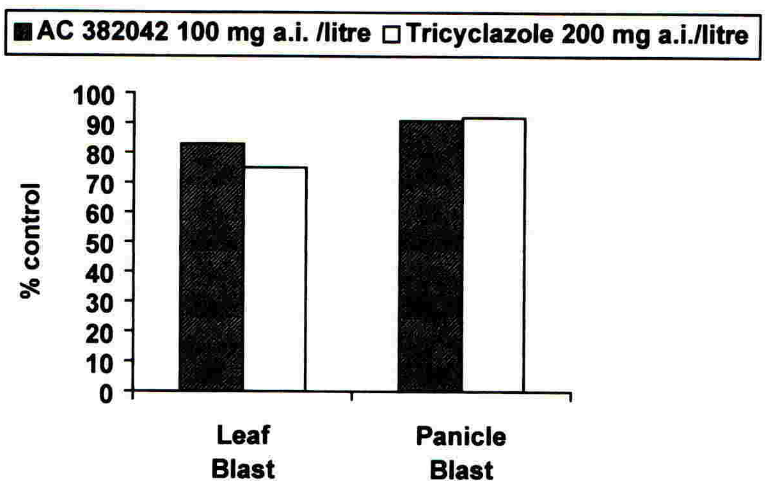



Figure 1. Efficacy (% control) of the 20% SC formulation of AC 382042 against leaf and panicle blast after foliar application in 1996 and 1997 field trials. (Means of 5 trials).

Also the dust formulation of AC 382042 was highly active. It was applied twice at 30 kg/ha for leaf blast control and twice at 40 kg/ha for panicle blast control at application timings similar to those of the 20% SC formulation. The results shown in Figure 2 indicate that the DL formulation of AC 382042 is consistently very active against both leaf and panicle blast.

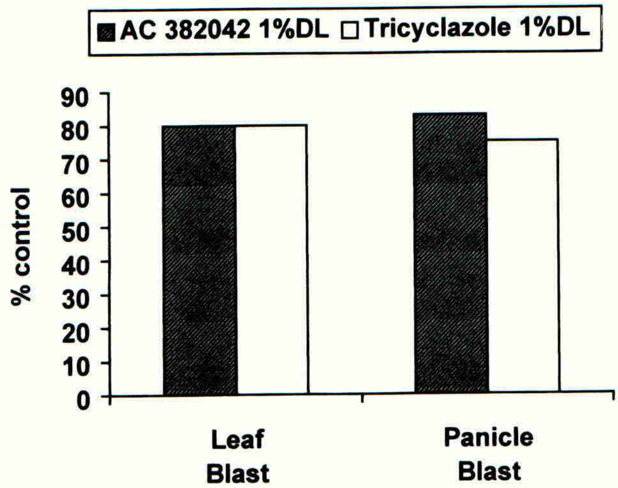



Figure 2. Efficacy (% control) of the 1% DL formulation of AC 382042 and the 1% DL of tricyclazole against leaf blast and panicle blast after foliar application in 1996 field trials. (Mean from three JPPA official field trials. Infection pressure was moderate in these trials).

The treatment of rice with AC 382042 increased yields, as exemplified by results of a trial where the 20% SC formulation was compared with the 1% DL formulation and with a standard (Table 4).

Table 4. Control of rice leaf blast and panicle blast, Aichi, Japan 1995 (JPPA field trial).

| Treatment | Dose mg a.i./ litre | Leaf blast Disease control (%) | Panicle blast Disease control (%) | Yield (kg/ha) Winnowed paddy | Milled brown rice |
|---|---|---|---|---|---|
| AC 382042 (1%DL) | - | 85 | 90 | 6847 a | 5280 a |
| Tricyclazole (1%DL) | - | 73 | 93 | 6481 a | 5104 a |
| AC 382042 (20%SC) | 133 | 87 | 85 | 6796 a | 5489 a |
| | 200 | 89 | 86 | 6874 a | 5518 a |
| Tricyclazole (20%SC) | 200 | 74 | 82 | 6534 a | 5175 a |
| Untreated | - | (9.52)* | (47.5)** | 3883 b | 2406 b |

Numbers followed by the same letter in the same column are not significantly different at P=0.05 level according to Duncan's multiple range test. * Leaf area diseased (%), ** grains diseased (%)

**Field activity after into-water application**

Granule formulations of AC 382042 at a dose of 30 kg/ha and with concentrations of 8% and 9% a.i. were tested for efficacy after into-water application to paddy fields. The application was either sequential with itself (i.e. AC 382042 was broadcast once for leaf blast control and once for panicle blast control) or a commercial compound (mainly probenazole in the 8% G formulation at 30 kg product/ha) was applied as granule for leaf blast control followed by a 30 kg/ha granule application of AC 382042 for panicle blast control.

The performance of AC 382042 against leaf blast after one granule application was similar to that of the commercial standard probenazole 8% G, comparing dose for dose and same timings (results not shown).

AC 382042 consistently provided a stable and high level of panicle blast control after granule into-water application in all the trials carried out over several years. Table 5 shows data from 6 trials carried out by JPPA at four different sites in Japan which differ in soil and climatic conditions. The mean percent panicle blast control by 2400 and 2700 g a.i./ha of AC 382042 was higher than that of the standard, 66% and 71% control by AC 382042 vs. 58% control by the standard. The efficacy of the 9% G application of AC 382042 provided a consistent performance which is also illustrated by the low variability in efficacy from 67-75% between the trial sites whereas the standards variability was from 45-76% control. These results indicate that AC 382042 is a robust compound which can successfully be used for panicle blast control, also by this application method, across diverse soil types and climates.

Table 5. Panicle blast control efficacy (%) AC 382042 applied at 30 kg/ha either as 9% G or 8% G at different trial sites, in comparison to 40 kg/ha of a pyroquilon 5% G. JPPA 1996 and 1997 field trials.

| Year and site | AC 382042 (9% G) 30 kg granules/ ha Efficacy (%) | AC 382042 (8% G) 30 kg granules/ha Efficacy (%) | Pyroquilon (5% G) 40 kg granules/ha Efficacy (%) | Disease incidence in untreated (%) |
|---|---|---|---|---|
| 96 Fukui | 75 | 72 | 45 | 20.7* |
| 96 Akita Omagari | 74 | 84 | 76 | 9.9** |
| 96 Aichi | - | 62 | 55 | 64.3** |
| 97 Akita Omagari | 69 | 57 | 50 | 60.0** |
| 97 Niigata | 67 | 60 | 51 | 35.3* |
| 97 Aichi | 68 | 59 | 72 | 12.2** |
| Mean efficacy (%) | 71 | 66 | 58 | |

*Disease severity; **grains diseased

The robustness of the performance of AC 382042 was further shown by the results of field trials where granule applications of AC 382042 or of a commercial standard were applied into water at different times before heading of the rice plants (Table 6). Compared to pyroquilon, application timings of 10-21 days before heading did not affect the excellent performance of AC 382042 against panicle blast.

Table 6. Control of rice panicle blast by a single into-water application of granule formulations, Osaka, Japan 1996 and 1997.

| Treatment | Rate (kg/ha) | Application time (days before heading) | Panicle blast % grains diseased | |
|---|---|---|---|---|
| | | | 1996 | 1997 |
| AC 382,042 (9% G) | 30 | 21 | 3.1 a | - |
| | 30 | 14 | 4.1 a | - |
| | 30 | 10 | - | 4.0 a |
| Pyroquilon (5% G) | 40 | 21 | 6.3 a | - |
| | 40 | 14 | 3.1 a | - |
| | 40 | 10 | - | 3.8 a |
| Untreated | - | - | 19.3b | 9.9 b |

Numbers followed by the same letter in the same column are not significantly different at P=0.05 level according to Duncan's multiple range test.

## CONCLUSION

AC 382042 is a systemic protective fungicide that has excellent efficacy against rice blast, the most economically important disease in rice culture. AC 382042 provides good opportunities to control both rice leaf blast and panicle blast by foliar application, due to its long-lasting preventative activity and systemic movement to newly-emerged leaves. The other unique feature of AC 382042 is its consistent and high level of systemic activity after into-water application. Granule formulations for into-water applications offer robust performance under various rice growing conditions with a consistently high level of protection against panicle blast.

## ACKNOWLEDGEMENTS

The authors would like to thank all their many colleagues in the American Cyanamid Company and Nihon Nohyaku Co., Ltd. who have contributed to the data presented in this paper.

# SZX 722: A novel systemic oomycete fungicide

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## ABSTRACT

SZX 722 (proposed common name Iprovalicarb) is a new fungicide for the control of diseases caused by Oomycetes. It belongs to the new chemical class of amino acid amide carbamates. The favourable environmental and toxicological properties of SZX 722 make it an ideal compound for use in IPM. This paper describes its chemical properties, mode of action, fungicidal spectrum of activity and performance in the field.

The compound inhibits the growth of the germ tubes of zoospores and sporangia, the growth of mycelium and the sporulation of oomycete fungi, leading to strong protective, curative and eradicative efficacy. SZX 722 has systemic properties and is distributed throughout the plant by the transpiration stream. It does not show cross resistance to specific oomycete compounds such as metalaxyl or cymoxanil, indicating a different mode of action.

SZX 722 is especially active against *Plasmopara viticola* on grape vine, with excellent activity on leaves as well as on bunches. The compound also controls *Phytophthora infestans* on potatoes and tomatoes effectively and is highly active against other oomycete pathogens on vegetables e.g. *Pseudoperonospora cubensis* on cucumber and bluemold (*Peronospora tabacina*) on tobacco. Furthermore, SZX 722 is currently under development for the control of soilborne *Phytophthora* diseases e.g. on tobacco, citrus and other crops. A number of combination products (e.g. with contact fungicides such as folpet, propineb, mancozeb, or tolylfluanid) are being developed to provide a broad spectrum of activity under the various growing conditions of the different target crops and good anti-resistance management. SZX 722 is expected to be introduced onto the European market in 2000.

## INTRODUCTION

Diseases caused by Oomycetes are of increasing importance because of their severe effects on crop quantity and quality and their ability rapidly to develop resistance against specific fungicides. SZX 722, a compound from the new chemical class of amino acid amide carbamates, was discovered in 1989 and has been developed as a systemic fungicide for the control of certain ooymcete diseases. Commercial introduction into the main European markets is scheduled for the year 2000. This paper describes its chemical properties, mode of action, fungicidal spectrum of activity and performance in the field.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Common name: | Iprovalicarb (ISO proposed) |
| Chemical class: | amino acid amide carbamates |
| Structural formula: | SZX 722 is a mixture of two diastereomers (SS, SR): |

| | |
|---|---|
| Molecular formula: | $C_{18}H_{28}N_2O_3$ |
| Molecular mass: | 320.5 g/mol |
| Chemical name (CAS): | *with specification of stereochemistry* (CA-No. 140923-25-7): Carbamic acid, [2-Methyl-1-[[[1-(4-methylphenyl)ethyl]amino] carbonyl]propyl]- 1-methylethylester, [S-(R*, S*)] *without specification of stereochemistry* (CA-No. 140923-17-7): Carbamic acid, [2-Methyl-1-[[[1-(4-methylphenyl)ethyl]amino] carbonyl]propyl]- 1-methylethylester For each diastereomer, CAS-numbers have not yet been given. |
| Chemical name (IUPAC): | [2-Methyl-1-[1-(4-methylphenyl)-ethylaminocarbonyl]-propyl]-carbamic acid isopropyl ester |
| Solubility in water (20°C) | 11 / 6.8 mg / litre (SR / SS) |
| log $P_{OW}$ | 3.2 / 3.2 (SR / SS) |

## TOXICOLOGY AND ECOTOXICOLOGY

**Mammalian toxicity:**

| | |
|---|---|
| Acute oral rat | $LD_{50}$ > 5000 mg/kg bw |
| Acute dermal rat | $LD_{50}$ > 5000 mg/kg bw |
| Acute inhalation rat | $LC_{50}$ > 4977 mg/m³ air (dust) |
| Irritation (rabbit; eye, skin) | not irritating, either to the skin or to the eye |
| Sensitization | not sensitizing |
| Neurotoxicity | no neurotoxic potential |
| Genotoxicity | no mutagenic/genotoxic potential, either *in vitro* or *in vivo* |
| Reproductive toxicity: | no embryotoxic potential; no primary reproductive toxicity |
| Chronic toxicity | no carcinogenic potential |

**Toxicity to wildlife:**

| | | |
|---|---|---|
| Bobwhite quail, acute oral | $LD_{50}$ | >2000 mg a.i./kg b.w. |
| Bobwhite quail / Mallard duck, 5 d-feeding | $LC_{50}$ | >5000 mg a.i./kg feed |
| Rainbow trout (96h) / Bluegill Sunfish (96h) | $LC_{50}$ | >22.7 / >20.7mg a.i./litre |
| Waterflea (48h) (*Daphnia magna*) | $EC_{50}$ | >19.8 mg a.i./litre |
| Green algae (72h) (*Selenastrum capricornutum)* | $E_rC_{50}$ | >10.0 mg a.i./litre |
| Earthworm (14d) (*Eisenia fetida*) | $LC_{50}$ | >1000 mg/kg dry weight soil |
| Honeybee (48h) (*Apis mellifera*) oral/contact | $LD_{50}$ | >199/200 µg a.i./bee |
| Predatory mite (*Typhlodromus pyri*) | no negative effects at 460 g a.i./ha | |
| Mobility in soil | intermediate to low mobility | |
| Degradation in soil | $DT_{50}$ | 2.0 – 29.6 d |

## MODE OF ACTION AND SYSTEMICITY

SZX 722 strongly affects the growth of the germ tubes of zoospores and sporangia, the growth of mycelium and the sporulation of oomycete fungi.

Although the biochemical mode of action of SZX 722 is not yet known, it appears to influence amino acid metabolism. The free amino acid pool in treated fungal cells is significantly reduced and its composition altered. SZX 722 does not significantly affect respiration, metabolism of lipids or nucleic acids, or the integrity of the plasma membrane in Oomycetes.

After penetration into the leaf or uptake by the roots, SZX 722 is quickly distributed throughout the plant by the transpiration stream. The compound becomes uniformly distributed in less than one day, indicating high xylem mobility. Only traces are distributed in the phloem. Penetration into the leaf is greater at higher temperatures and at high relative humidity or after re-wetting by rain or dew. Adjuvants, such as plant oils, have a significant impact on the uptake of the compound, leading to enhanced efficacy of systemic action.

## BIOLOGICAL PROPERTIES

SZX 722 is a specific fungicide exhibiting a high level of activity against various Ooymcetes from the families *Pythiaceae* and *Peronosporaceae*. There is no apparent species- or pathotype- (e.g. A1/A2 of *Phytophthora infestans*) dependent difference in the level of sensitivity towards the compound (Table 1). *Pythium* and fungal orders outside the Oomycetes are not affected by SZX 722.

Table 1. In vitro spectrum of activity of SZX 722.

| Species | | $ED_{50}$ (mg a.i./litre) mycelial growth |
|---|---|---|
| *Phytophthora* | *infestans* | 0.14 (0.03 - 0.26[1]) |
| " | *cactorum* | 0.12 |
| " | *cinnamomi* | 0.12 |
| " | *cryptogea* | 0.12 |
| " | *megasperma* | < 0.1 |
| " | *nicotianae* | 0.29 |
| " | *palmivora* | 0.11 |
| " | *syringae* | 0.11 |
| " | *spp.* (isol. from citrus) | 0.39 |

[1] various strains tested

In glasshouse tests, SZX 722 showed marked protective and curative effects on disease severity. It also affected sporulation, especially that of *Plasmopara viticola* (Table 2). After curative treatment, sporulation was inhibited drastically even if the number of oil spots could not be reduced because infection was already progressed. The curative effects demonstrate the systemic properties of the compound.

Table 2. Protective and curative efficacy of SZX 722 against *Plasmopara viticola* on grape vine seedlings in the glasshouse.

| Compound | Application rate mg a.i./litre | % Control (Abbott) of DS[1] / SI[2] after treatment at 24 h aI[3] | | 48h pI[3] | |
|---|---|---|---|---|---|
| | | DS | SI | DS | SI |
| SZX 722 | 100 | 100 | 100 | 28 | 97 |
| | 50 | 99 | 100 | 11 | 87 |
| Dimethomorph | 100 | 100 | 100 | 34 | 64 |
| | 50 | 100 | 100 | 23 | 65 |
| Cymoxanil | 100 | 97 | 96 | 21 | 95 |
| | 50 | 74 | 71 | 32 | 85 |

[1] DS = Disease Severity (% diseased leaf area)
[2] SI = Sporulation Index (% diseased leaf area with sporulation)
[3] aI = ante infectionem, pI = post infectionem

SZX 722 has been intensively tested world-wide, but with an emphasis on trials in Europe, for its activity against various oomycete pathogens. SZX 722 will be marketed as WG- or WP-formulations in combinations with other fungicides (e.g. contact fungicides) to offer mixtures with a broad spectrum of efficacy and to ensure an appropriate anti-resistance management in practice. Table 3 summarizes the findings of the field trials done with the recommended application rates (see Tables 4-10), showing the broad applicability of SZX 722 in grape vine, vegetables and other crops.

Table 3. Spectrum of activity of SZX 722 in the field.

| Pathogens | Crops | Activity[1] |
|---|---|---|
| *Plasmopara viticola* | Grape vine | ++++ |
| *Phytophthora infestans* | Potatoes, Tomatoes | +++ |
| *Peronospora* spp. | Tobacco, Vegetables | +++ |
| *Pseudoperonospora* spp. | Cucumber, Hop | +++ |
| *Bremia lactucae* | Lettuce | +++ |
| Soilborne *Phytophthora* spp. | Citrus, Avocado, Tobacco | ++ |

[1] Excellent (++++), good (+++), and sufficient (++) activity

In grape vine, SZX 722 alone and in combination with contact fungicides showed an excellent efficacy against downy mildew. The pathogen is controlled effectively on leaves as well as on bunches. When comparing with standard mixes, the lower application rates of the SZX-combinations should be considered. Tables 4-7 show the results obtained with SZX 722 alone and in combinations with folpet, mancozeb, tolylfluanide and copper oxychloride. Similar results were obtained with propineb.

Table 4. Efficacy of SZX 722 alone and in combination with folpet against downy mildew on grape vine in field trials (1994 to 1996).

| Compounds | Application rate g a.i. / ha | % Control (Abbott) on Leaves | Bunches | No of trials |
|---|---|---|---|---|
| SZX 722 | 300 | 97 | 86 | 3 |
| Dimethomorph | 300 | 89 | 87 | |
| SZX 722 + [1] folpet | 150 + 938 | 97 | 100 | 3 |
| Dimethomorph / [2] folpet | 225 / 1000 | 97 | 100 | |
| SZX 722+folpet | 120 + 750 | 83 | 94 | 15 |
| Cymoxanil+mancozeb | 120 + 1400 | 68 | 87 | |
| SZX 722+folpet | 120 + 750 | 98 | 99 | 3 |
| Cymoxanil+fosetyl-Al+folpet | 120 + 1500 + 750 | 96 | 97 | |

[1] In-can combinations used (a+b)
[2] Tank-mix (a/b)

Table 5. Efficacy of SZX 722 in combination with mancozeb against downy mildew on grape vine in field trials (average of 6 trials; 1994 to 1996).

| Compounds | Application rate g a.i. / ha | % Control (Abbott) on Leaves | Bunches |
|---|---|---|---|
| SZX 722+mancozeb | 120+1200 | 96 | 84 |
| Dimethomorph+mancozeb | 198+1320 | 96 | 86 |
| Metalaxyl+mancozeb | 200+1600 | 87 | 79 |

Table 6. Efficacy of SZX 722 in combination with tolylfluanid against downy mildew on grape vine in field trials (1994 to 1996).

| Compounds | Application rate g a.i. / ha | % Control (Abbott) on Leaves | Bunches | No of trials |
|---|---|---|---|---|
| SZX 722+tolylfluanid | 120+750 | 90 | 99 | 6 |
| Cymoxanil+dithianon | 120+300 | 78 | 99 | |
| SZX 722+tolylfluanid | 120+750 | 95 | 87 | 7 |
| Dimethomorph+mancozeb | 198+1320 | 84 | 86 | |

Table 7. Efficacy of SZX 722 in combination with copper oxychloride against downy mildew on grape vine in field trials (average of 3 trials; 1994 to 1996).

| Compounds | Application rate g a.i. / ha | % Control (Abbott) on Leaves | Bunches |
|---|---|---|---|
| SZX 722+copper oxychloride | 126+1050 | 81 | 79 |
| Cymoxanil+copper oxychloride | 126+1190 | 82 | 67 |

Incorporated into spray programmes SZX 722 combinations showed superior activity against downy mildew (Table 8). The treatment of grape vine with SZX 722 did not have any deleterious influence on the maturity of grapes, the kinetics of fermentation, or on the gustatory qualities of the wines produced. With regard to plant compatibility, SZX 722 appears safe, because plant damage was never observed in any of the trials.

Table 8. Efficacy of SZX 722 in a spray programme against downy mildew on grape vine in Germany, 1996 (average of 3 trials in commercial vineyards; cv. Chardonnay, Kerner, Spätburgunder).

| Compounds in spray programme | Application rate g a.i./ha | Applications (total of 7 applications) | % Control (Abbott)on Leaves | Bunches |
|---|---|---|---|---|
| Propineb | 1120 | 1,2 | | |
| SZX 722+tolylfluanid | 120+750 | 3, 4, 5 | | |
| SZX 722+copper-oxychloride | 120+1260 | 6, 7 | 99 | 99 |
| Propineb | 1120 | 1,2 | | |
| Cymoxanil+dithianon | 100+167 | 3, 4, 5 | | |
| SZX 722+copper-oxychloride | 120+1260 | 6, 7 | 98 | 97 |
| Propineb | 1120 | 1,2 | | |
| Cymoxanil+dithianon | 100+167 | 3-7 | 95 | 90 |

1997 was characterized by severe potato late blight epidemics in the main growing areas of Europe. Under these extreme disease conditions, the levels of control achieved by a SZX 722 combination with a contact fungicide was almost equivalent to that achieved by the commercial standard combination (Table 9). If adjuvants (Table 9) are added as a tank-mix, the uptake of SZX 722 into the plant is improved. Especially under severe conditions this is likely to increase the efficacy.

Table 9. Efficacy of SZX 722 against potato late blight in field trials in 1997 in Northern and Central Europe (average of 14 trials).

| Compounds | Application rate g a.i. / ha | % Control (Abbott)[1] | % Disease Severity[1] in untreated |
|---|---|---|---|
| SZX 722+mancozeb | 180+1200 | 76 | 71 |
| SZX 722+mancozeb/adjuvant | 180+1200/500-1000[2] | 81 | |
| Dimethomorph+mancozeb | 180+1200 | 80 | |

[1] Average over all assessments
[2] Local adjuvants (e.g. Oleo 11E, Atpolan, Hyspray, Nu-Film 17) at recommended rates

In vegetables, SZX 722 controlled various oomycete diseases very effectively (Table 10). Even with lower application rates, disease control by SZX 722 exceeded that of the standard compounds. Similar results were obtained for blue mold on tobacco (*Peronospora tabacina*). Plant compatibility was excellent for all crops tested.

Table 10. Efficacy of SZX 722 in combination with mixture-partners against *Phytophthora infestans* (PHYTIN), *Bremia lactucae* (BREMLA) and *Pseudoperonospora cubensis* (PSPECU).

| Compounds | Application rate g a.i./ha | % Control (Abbott) | | |
|---|---|---|---|---|
| | | PHYTIN tomatoes (7)[1] | BREMLA lettuce (5)[1] | PSPECU cucumber (5)[1] |
| Untreated | | (59)[2] | (21) | (47) |
| SZX 722+Propineb | 138+1530 | 94 | 90 | - |
| SZX 722+mancozeb | 120+1200 | - | - | 81 |
| Dimethomorph+mancozeb | 180+1200 | 93 | - | - |
| Metalaxyl+mancozeb | 200+1200 | - | 88 | 76 |
| Metalaxyl+mancozeb | 240+1920 | 89 | - | - |
| Fluazinam | 200 | 87 | - | - |

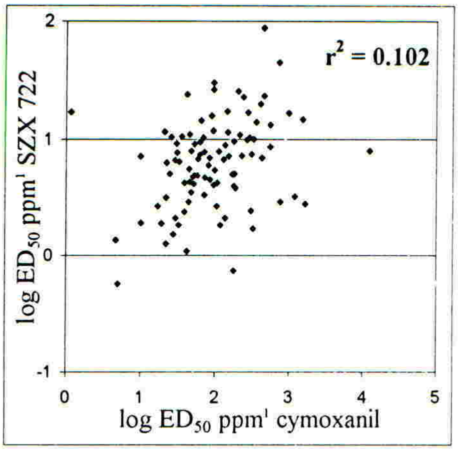
[1] Number of trials; [2] Disease severity in untreated control

## BASELINE-SENSITIVITY AND CROSS-SENSITIVITY

The baseline sensitivity of *P. viticola* and *P. infestans* was investigated in the major grape vine- and potato-growing areas in Europe over two years. The sensitivity of *Plasmopara* isolates towards SZX 722 and cymoxanil was tested on grape vine plants, while *Phytophthora*-isolates were tested against SZX 722 and metalaxyl on detached tomato leaves. There was variation in sensitivity to SZX 722 across the tested areas with an average $ED_{50}$ of ca. 2 mg a.i./litre for both *P. viticola* and *P. infestans*.

As expected from the mode of action studies, no cross-sensitivity could be detected to either standard compounds cymoxanil and metalaxyl. As shown in Figure 1, the populations tested so far produced correlation coefficients indicating no cross-sensitivity. Also with a limited number of isolates tested with different sensitivities towards dimethomorph there was no indication of a cross-sensitivity.

a)




b)

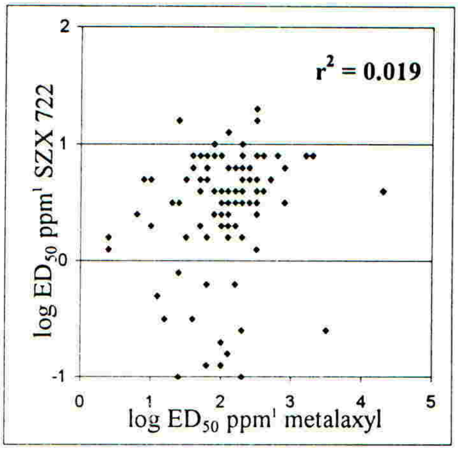



Figure 1.Cross-sensitivity studies between a) SZX 722 and cymoxanil (*Plasmopara viticola*), and b) SZX 722 and metalaxyl (*Phytophthora infestans*).
Fungal isolates originating from different locations in Europe were sampled in 1997.
[1] ppm = mg a.i./litre

## CONCLUSIONS

SZX 722 is a systemic oomycete fungicide of a new chemical class showing excellent activity, especially against downy mildew on grape vine. The systemic activity of the compound leads to a marked and durable action after protective treatment and/ or curative activity against already established infections. The use of adjuvants can further improve the systemic activity. To ensure a broad spectrum of activity and good anti-resistance management, it is recommended that SZX 722 should be used strictly protective in combination with other fungicides e.g. contact fungicides.

Because of its favourable toxicological and ecotoxicological properties, SZX 722 represents the ideal fungicide for use in IPM. As there is no cross resistance to existing fungicides, SZX 722 will certainly offer a much-needed new option for resistance management in the high-value crops grape vine, vegetables and potatoes.

## ACKNOWLEDGEMENTS

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# CGA 279202: A new broad-spectrum strobilurin fungicide

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## ABSTRACT

CGA 279202 is a new strobilurin fungicide developed by Novartis with protective, curative, penetrative and novel redistribution properties. It has a very broad and balanced spectrum of activity as a foliar fungicide against diseases of temperate, sub-tropical and tropical crops. The compound has a very favourable toxicological profile, dissipates rapidly from soils and surface water and is unlikely to cause any undue hazard to non-target organisms.

On cereals, it controls the major leaf and ear diseases. At rates of 125-187.5 g a.i./ha in combination with DMI fungicides, it provides long-lasting protection with timing flexibility. Treated crops stay greener longer giving higher yields. On grapes, excellent control of powdery mildew is achieved at 6.25-7.5 g a.i./hl. A mixture with cymoxanil at 12.5 + 12 g a.i./hl provides optimised control of downy mildew. The apple diseases, scab and powdery mildew, are controlled at relatively low use rates; scab at 3.75-5.0 g a.i./hl in protective or curative schedules and powdery mildew at 5-7.5 g a.i./hl. Control of powdery mildew of cucurbits is obtained at 6.25-12.5 g a.i./hl. The foliar diseases of peanuts, early and late leaf spots as well as rust, are controlled at 70-105 g a.i./ha or in combination with propiconazole at 62.5 + 62.5 g a.i./ha. On bananas, outstanding control of black Sigatoka is achieved at 70-90 g a.i./ha.

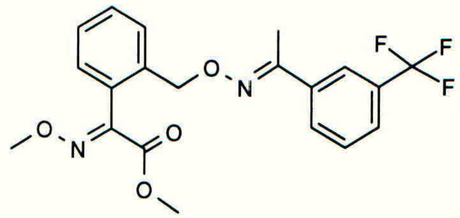
## INTRODUCTION

CGA 279202 is a new strobilurin fungicide developed by Novartis. It is active against Ascomycetes, Fungi Imperfecti, Oomycetes and Basidiomycetes. Since its discovery in 1989, it has undergone extensive international evaluation in small plot field trials. Data are presented which demonstrate the chemical and biological properties and its field performance in cereals, grapes, apples, cucurbits, peanuts and bananas.

## CHEMICAL AND PHYSICAL PROPERTIES

| | |
|---|---|
| Trademark of active ingredient: | FLINT® |
| Chemical class: | oximinoacetate |
| Chemical Name (IUPAC): | (E,E)-methoxyimino-{2-[1-(3-trifluoromethyl-phenyl)-ethylideneaminooxymethyl]-phenyl}-acetic acid methyl ester |

Structural Formula:




| | |
|---|---|
| Molecular Formula: | $C_{20}H_{19}F_3N_2O_4$ |
| Molecular weight: | 408.4 |
| Physical state: | odourless white powder |
| Melting Point: | 72.9°C |
| Boiling point: | approx. 312°C (decomposition starts at 285°C) |
| Vapour pressure: | $3.4 \times 10^{-6}$ Pa at 25°C |
| Volatility: | Henry's law constant at 25°C: $2.3 \times 10^{-3}$ Pa · m³ / mol |
| Partition coefficient n-octanol / water: | log $P_{ow}$ at 25°C : 4.5 |
| Solubility in water: | 610 µg / litre at 25°C |

## PRODUCT SAFETY

**Mammalian toxicity:**

| | | |
|---|---|---|
| Acute oral $LD_{50}$ | Rat | > 5000 mg / kg |
| Acute dermal $LD_{50}$ | Rat | > 2000 mg / kg |
| Acute inhalation $LC_{50}$ | Rat | > 4646 mg / $m^3$ |
| Eye irritation | Rabbit | non irritating |
| Skin irritation | Rabbit | non irritating |
| Skin sensitisation (Buehler) | Guinea Pig | non-sensitising |
| Skin sensitisation (Maximisation) | Guinea Pig | sensitising |
| Mutagenicity | 5 tests | no mutagenic potential |
| Teratogenicity | Rat, Rabbit | no teratagenic potential |
| Chronic toxicity/Carcinogenicity | Rat, Mouse | no carcinogenic potential |
| Reproduction | Rat | no adverse effects |
| Metabolism | Rat | rapid absorption and elimination |

**Toxicity to Wildlife:**

| | | | |
|---|---|---|---|
| Birds | Bobwhite quail | $LD_{50}$ | > 2000 mg / kg |
| Fish | Rainbow trout | $LC_{50}$ | 0.015 mg / litre |
| Bees (oral) | | $LD_{50}$ | > 200 µg / bee |

**Environmental Fate:**

| | | |
|---|---|---|
| Hydrolysis in water | $DT_{50}$ | stable at pH 5,<br>11.4 weeks at pH 7 |
| Photolysis in water | $DT_{50}$ | 31.5 h at pH 7 and 25°C |
| Mobility in soil | $K_{oc}$ | 1642-3745 ml / g |
| Degradation in soil (field studies) | $DT_{50}$ | 5.4 days (range 1.9-16) |

## BIOLOGICAL PROPERTIES

CGA 279202 is particularly active against powdery mildews and leaf spot diseases but also gives significant control of rusts, downy mildews and other diseases. Early stages of fungal development, including spore germination, germ tube extension and appressorium formation are strongly inhibited, preventing infection from taking place. In the downy mildews, zoospore release is inhibited. Post-penetration stages, which are also affected, include haustoria formation and growth of surface mycelium in the powdery mildews and the growth of the subcuticular stroma in *Venturia inaequalis*.

The biochemical mode of action of CGA 279202 is by the inhibition of mitochondrial respiration. CGA 279202 does not show cross resistance with fungicides of any other chemical classes such as morpholines, triazoles, phenylamides, anilinopyrimidines and phenylpyroles.

On the plant surface, deposits of CGA 279202 provide a protective reservoir. The high affinity of the molecule for the waxy layers ensures a resistance to wash-off by rainfall. Small, but biologically effective, amounts penetrate the cuticle and provide curative activity against pathogens which are located close to the plant surface. Active ingredient which reaches the opposite leaf cuticle by means of diffusion, provides translaminar activity. The compound is also redistributed over small distances to untreated plant parts and within the crop canopy by superficial vapour movement and redeposition. The term "mesostemic" is used to describe all of these aspects of the behaviour of CGA 279202, both on and in the plant.

## FIELD TRIALS

### Methodology

Small plot field trials reported were carried out between 1995 and 1998 on Novartis experiment stations or in farmers' fields in regions where the target disease was of economic importance. Trials were laid down in complete randomised blocks with 3 or 4 replicates. Application of treatments was made with small plot precision sprayers or commercial sprayers.

### Cereals

CGA 279202 applied at 250 g a.i./ha provides good control of the most important foliar diseases of wheat and barley. When used alone, the activity of the compound is at an optimum when applied preventively. The use of mixtures of CGA 279202 with DMI fungicides provides greater flexibility. They also provide consistently good disease control if first symptoms of the diseases are already present at the time of application. In these situations, the DMI fungicides in the mixtures provide additional curative activity.

Typical results of a series of trials carried out in cereals in Europe with the formulated mixtures CGA 279202 + propiconazole at 125 + 125 g a.i./ha and CGA 279202 + cyproconazole at 187.5 + 80 g a.i./ha compared to standard triazole/morpholine mixtures and untreated controls are summarised in Tables 1-3.

Table 1. Control of diseases and yield of winter wheat in Europe 1997.

| Treatment | Rate g a.i./hl | Mean % disease control *E. graminis*[b] (3 trials) | *S. tritici*[b] (9 trials) | *P. recondita*[c] (4 trials) | Yield (dt/ha) (16 trials) | rel. % |
|---|---|---|---|---|---|---|
| Days after last treatment | | 55 | 42 | 25 | | |
| Check (attack) | | (36) | (55) | (166.2) | 72.4 | 100 |
| Standard[a] | | 55.4 | 66.4 | 98.7 | 78.6 | 108.5 |
| CGA 279202 + propiconazole 250EC | 125 + 125 | 81.3 | 87.3 | 92.8 | 83.7 | 115.6 |
| CGA 279202 + cyproconazole 267.5EC | 187.5 + 80 | 91.6 | 91.0 | 99.0 | 84.9 | 117.3 |

[a] propiconazole + fenpropimorph 125 + 375 g a.i./ha or tebuconazole + fenpropimorph + fenpropidin 250 + 562 + 188 g a.i./ha; [b] % leaf surface attacked; [c] number of pustules per leaf

Table 2. Control of diseases and yield of winter barley in Europe 1997.

| Treatment | Rate g a.i./hl | Mean % disease control *P.teres*[b] (7 trials) | *R. secalis*[b] (5 trials) | *P. hordei*[c] (2 trials) | Yield (dt/ha) (11 trials) | rel. % |
|---|---|---|---|---|---|---|
| Days after last treatment | | 39 | 31 | 35 | | |
| Check (attack) | | (43) | (23) | (68.3) | 68.9 | 100 |
| Standard[a] | | 50.3 | 75.9 | 80.7 | 73.8 | 107.1 |
| CGA 279202 + propiconazole 250EC | 125 + 125 | 79.4 | 88.5 | 96.1 | 77.9 | 113.1 |
| CGA 279202 + cyproconazole 267.5EC | 187.5 + 80 | 85.5 | 85.8 | 98.9 | 79.3 | 115.1 |

[a] propiconazole + fenpropimorph 125 + 300-375 g a.i./ha or flusilazole + carbendazim 200 + 100 g a.i./ha; [b] % leaf surface attacked; [c] number of pustules per leaf

Table 3. Influence on green leaf remaining in winter wheat and barley crops in Europe 1997.

| Treatment | Rate g a.i./hl | Wheat % green leaf area (4 trials) | Barley % green leaf area (2 trials) | Barley No. of green leaves (2 trials) |
|---|---|---|---|---|
| Days after last treatment | | 50 | 40 | 46 |
| Check | | 23.2 | 14.4 | 2.2 |
| Standard[a] | | 40.5 | 33.3 | 2.5 |
| CGA 279202 + propiconazole 250EC | 125 + 125 | 60.1 | 48.7 | 3.3 |
| CGA 279202 + cyproconazole 267.5EC | 187.5 + 80 | 63.0 | 52.1 | 3.5 |

[a] propiconazole + fenpropimorph 125 + 300-375 g a.i./ha or flusilazole + carbendazim 200 + 100 g a.i./ha or tebuconazole + fenpropimorph + fenpropidin 250 + 562 + 188 g a.i./ha

The results show that both mixtures based on CGA 279202 provide excellent disease control. The mixture with cyproconazole is preferred in situations where infection pressure of rust diseases is strong. Against all other diseases, both mixtures provide consistently better disease control than the triazole/morpholine standards. As a result of the long-lasting disease control provided by the mixtures based on CGA 279202, more green leaf area remains available for assimilation towards the end of the growing season. Consequently, yields from plots treated with the mixtures based on CGA 279202 are consistently higher than from plots treated with triazole/morpholine standards or from untreated plots.

## Grapes

CGA 279202 is active against all the major fruit and foliage diseases of grapes. A clear strength is its activity against powdery mildew (*Uncinula necator*) on both leaves and bunches. When applied in a preventive spray schedule, excellent disease control is obtained at rates of 6.25-7.5 g a.i./hl under high disease pressure conditions (Table 4).

Table 4. Control of powdery mildew of grapes in Europe 1995-1997.

| | | Mean % disease control | | |
|---|---|---|---|---|
| Treatment | Rate | Leaves | Bunches | Bunches |
| 14 day spray interval | g a.i./hl | (8 trials) | (18 trials) | (1 trial) |
| Mean number of sprays | | 4.3 | 5.4 | 15 DAT 7 |
| Check (% surface attack) | | (23) | (73) | (78) |
| DMI Standard[a] | | 96.3 | 87.3 | 92.7 |
| CGA 279202 50WG | 7.5 | 95.3 | 98.7 | 98.6 |
| CGA 279202 50WG | 6.25 | - | - | 95.2 |
| CGA 279202 50WG | 3.75 | - | - | 91.8 |

[a] penconazole at 1.5-3.5 g a.i./hl or tebuconazole at 10 g a.i./hl

A further strength of the compound is the protection offered to the berries against downy mildew (*Plasmopara viticola*) at 12.5 g a.i./hl when applied in 7-10 day intervals. The activity on leaves is weaker than on berries but the performance is stabilised and a curative property is added when used in a mixture with cymoxanil (Table 5).

Table 5. Control of downy mildew of grapes in Europe 1995-1997.

| | | Mean % Disease Control | |
|---|---|---|---|
| Treatment | Rate | Leaves | Bunches |
| 7-10 day spray interval | g a.i./hl | (11 trials) | (12 trials) |
| Mean number of sprays | | 8.9 | 9.1 |
| Check (% surface attack) | | (62) | (49) |
| Mancozeb + cymoxanil | 120/140 + 12 | 93.3 | 96.1 |
| CGA 279202 50WG | 12.5 | 87.7 | 98.7 |
| CGA 279202 + cymoxanil 49WG | 12.5 + 12 | 93.0 | 99.6 |

## Apples

CGA 279202 provides a high level of control of apple scab on leaves and fruit when applied preventively in 7-10 day intervals early in the season and then at intervals of 10-14 days when fruits have reached a diameter of 4 cm (Table 6). When used in this way, effective rates are 3.75-5.0 g a.i./hl (50-75 g a.i./ha).
Good control of secondary infections of powdery mildew is obtained at rates of 5.0-7.5 g a.i./hl (75 g-112.5 g a.i./ha) when applied preventively in 10-12 day intervals and then at 14-16 day intervals after fruits have reached a diameter of 4 cm. (Table 6). In southern Europe, where the disease pressure tends to be higher than in the north and where spray intervals tend to be long, the higher rate is favoured.
At harvest, treated fruits are of a high quality. Early indications are that the control of storage diseases caused by *Gloeosporium* spp. and *Venturia inaequalis* is equivalent to that of standard fungicides such as captan or dichlofluanid.

Table 6. Protective control of apple scab and powdery mildew in Europe 1996-1997.

| | | Mean % Disease Control | | |
|---|---|---|---|---|
| | | Scab | | Powdery mildew |
| Treatment | Rate g a.i./hl | Leaves ( 6 trials) | Fruit ( 6 trials) | Leaves ( 7 trials) |
| Mean number of sprays | | 7.0 | 11.6 | 7.8 |
| Check (incidence in %) | | (83) | (94) | (80) |
| Standard[a] | | 68.7 | 90.6 | 80.7 |
| CGA 279202 50WG | 3.75 | 96.2 | 96.9 | - |
| CGA 279202 50WG | 5.0 | 99.1 | 97.6 | 86.7 |
| CGA 279202 50WG | 7.5 | - | - | 91.5 |

[a]Dithianon at 75 g a.i./hl or captan at 125 g a.i./hl in scab trials; triadimefon at 5 g a.i./hl or penconazole at 2.5 g a.i./hl in powdery mildew trials

Curative use schedules against apple scab, in which the product was only applied 3-4 days after infection periods had occurred, resulted in very good disease control (Table 7). A more consistent performance was obtained at 5.0 g a.i./hl (75 g a.i./ha) compared with the 3.75 g a.i./hl (50 g a.i./ha) rate.

Table 7. Curative control of foliar apple scab in Europe 1995-1996.

| | | Mean % Disease Control | | | | |
|---|---|---|---|---|---|---|
| Treatment | g a.i./hl | Trial 1 8 DAT 2 | Trial 2 6 DAT 3 | Trial 3 6 DAT 3 | Trial 4 8 DAT 2 | Trial 5 6 DAT 2 |
| Days after first infection | | 3 | 3 | 3 | 3 | 4 |
| Spray intervals in days | | 10 | 10 ; 9 | 10 ; 20 | 10 | 11 |
| Check (incidence in %) | | (88) | (84) | (99) | (99) | (88) |
| CGA 279202 50WG | 3.75 | 92.2 | 96.7 | 80.5 | 84.8 | 78.8 |
| CGA 279202 50WG | 5.0 | 93.2 | 96.1 | 91.6 | 91.1 | 94.6 |

## Cucurbit Crops

CGA 279202 is highly effective against foliage powdery mildew diseases of cucurbit crops caused by *Sphaerotheca*, *Erysiphe* and *Microsphaera* spp. Under dry southern European conditions which favour the disease, the level of control on cucumber/marrow and melons exceeds that obtained with conventional fungicides. Optimum disease control is achieved when the product is applied in 10 day intervals. On cucumber and marrow, the effective rate is 6.25 g a.i./hl, whilst on melons, the performance is improved at 12.5 g a.i./hl (Table 8).

Table 8. Control of powdery mildew on cucurbits in Europe 1996-1997.

| Treatment | Rate g a.i./hl | Interval days | Mean % Disease Control: Cucumber / Marrow (5 trials) | Mean % Disease Control: Melon (6 trials) |
|---|---|---|---|---|
| Check (% surface attack) | | | (79) | (70) |
| Standard[a] | | 7-10 | 62.2 | 56.5 |
| CGA 279202 50WG | 6.25 | 10 | 90.4 | 84.2 |
| CGA 279202 50WG | 6.25 | 14 | 69.4 | 72.7 |
| CGA 279202 50WG | 12.5 | 10 | 96.8 | 96.7 |
| CGA 279202 50WG | 12.5 | 14 | 89.4 | 89.0 |

[a] ethirimol at 28 g a.i./hl or pyrazophos at 15 g a.i./hl

## Peanuts

CGA 279202 at 70-105 g a.i./ha provides control of the 3 peanut foliar diseases early leaf spot (*Cercospora arachidicola*), late leaf spot (*Cercosporidium personatum*) and rust (*Puccinia arachidis*). A mixture with propiconazole at 62.5 + 62.5 g a.i./ha, additionally offers greater application timing flexibility as well as providing a resistance management tool (Table 9).

Table 9. Control of peanut diseases in the USA 1995-1997.

| Treatment 10-14 day spray interval | Rate g a.i./ha | Mean % Disease Control: early leaf spot (3 trials) | Mean % Disease Control: early + late leaf spot (2 trials) | Mean % Disease Control: rust (4 trials) |
|---|---|---|---|---|
| Mean number of sprays | | 3.3 | 6.0 | 3.7 |
| Check (% surface attack) | | (51) | (55) | (51) |
| Chlorothalonil 720FS + propiconazole 3.6E | 841+ 62.5 | 90.0 | 85.9 | 75.3 |
| CGA 279202 50WG | 70 | - | - | 70.4 |
| CGA 279202 50WG | 105 | 88.7 | 86.4 | 78.8 |
| CGA 279202 50WG | 140 | 88.7 | 90.7 | - |
| CGA 279202 50WG + propiconazole 3.6E | 62.5+ 62.5 | 90.7 | 88.0 | 75.9 |