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(54) Title: METHOD OF CONTROLLING PHYTOPATHOGENIC FUNGI USING JAWSAMYCIN

(57) Abstract: The present disclosure relates to a method of controlling or preventing phytopathogenic fungi belonging to *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia equalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*, on a plant or on plant propagation material thereof, the method comprising applying to the plant, plant propagation material or locus thereof, a composition comprising jawsamycin..



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METHOD OF CONTROLLING PHYTOPATHOGENIC FUNGI USING JAWSAMYCIN

The present invention relates to a method for controlling phytopathogenic fungi using jawsamycin.

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Background

Jawsamycin is a natural compound, indicated as FR-900848, that is produced by *Streptoverticillium* or *Streptomyces* bacteria. The compound was first discovered in 1990 by Yoshida et al (1990), J. of Antibiotics, p. 748-754. Yoshida et al (1990) discloses that the compound was active against *Aspergillus niger*, *Mucor rouxianus*, *Aureobasidium*, *Penicillium chrysogenum*, *Fusarium oxysporum*, *Sclerotinia arachidis* and *Trichophyton* species.

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JP2101006 discloses that jawsamycin was active against apple leaf spot *Alternaria* and against cucumber *Botrytis* grey mold.

Fu et. al. (2020), Nature Communications 11-3387, discloses that jawsamycin was active against some yeasts, fungi such as *Aspergillus sp.*, *Fusarium oxysporum*, *Scedosporium sp.*, and some Mucorales fungi. Fu et al. (1990) suggests that jawsamycin would have a broad-spectrum fungicidal activity, however, there is no teaching or suggestion which fungi are affected, nor whether by jawsamycin would be fungicidally active on which planta.

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Due to development of resistance by phytopathogenic fungi to known pesticides, regulations by governments and societal pressure there is a continuous need for improved products or compounds from biological origin that have activity against phytopathogenic fungi.

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Summary of the invention

The present invention relates to a method of controlling or preventing phytopathogenic fungi belonging to *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*, on a plant or on plant propagation material thereof, the method comprising applying to the plant, plant propagation material or locus thereof, a composition comprising jawsamycin.

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In another aspect the present invention relate to the use of jawsamycin for controlling or preventing phytopathogenic fungi, wherein the fungus is selected from *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia equalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora kikuchii*, and *Cercospora sojina*.

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Detailed description

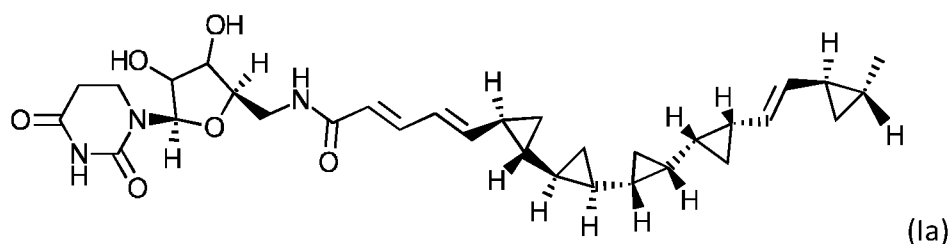
A method of controlling or preventing phytopathogenic fungi belonging to *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*, on a plant or on plant propagation material thereof, the method comprising applying to the plant, plant propagation material or locus thereof, a composition comprising jawsamycin, preferably a fungicidally effective amount of jawsamycin.

The term "fungicidally effective amount" where used means the quantity of such a compound or combination of such compounds that is capable of producing an effect on the growth of fungi. Controlling or modifying effects include all deviation from natural development, such as killing, retardation and the like, and prevention includes barrier or other defensive formation in or on a plant to prevent fungal infection. Controlling or preventing means reducing infestation by phytopathogenic fungi to such a level that an improvement is demonstrated. A fungicidally effective amount of jawsamycin, comprises 0.1 to 500 ppm, preferably 0.5 to 250 ppm of jawsamycin.

Surprisingly it was found that jawsamycin was surprisingly effective to control the fungi *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum* (syn. *Parastagonospora nodorum*), *Pyrenophora teres*, *Venturia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*. Accordingly, jawsamycin has a surprising fungicidal activity against these fungi.

To the contrary, we found that jawsamycin showed very little or no activity against oomycetes, such as *Phytophthora infestans*, *Pythium ultimum*, and *Plasmopora viticola*, Basidiomycetes, such as *Puccinia recondita*, and *Rhizoctonia solani* (syn. *Thanatephorus cucumeris*) and the Ascomycetes *Blumeria graminis*, and *Uncinula necator*. Accordingly, it appears the teaching of Fu, Y. *et al.* in Nat Commun 11, 3387 (2020) cannot be applied to all fungi.

Jawsamycin is a known compound and has a structural formula according to Formula (Ia)



The jawsamycin of formula (Ia) is an oligocyclopropyl-containing natural product, also noted as FR-900848. Jawsamycin is a polyketide comprising a 5'-amino-5'-deoxy-3,4,5,6-tetrahydrouridine in which

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one of the hydrogens of the amino group is substituted by a (1E,3E)-1-[(1R,1'R,1''R,1'''R,2S,2'R,2''R,2'''S)-2'''-(E)-2-[(1R,2R)-2-methylcyclopropyl]ethenyl][1,1':2',1'':2'',1'''-quater(cyclopropan)]-2-yl]-5-oxopenta-1,3-dien-5-yl group.

The structure of jawsamycin is $C_{32}H_{43}N_3O_6$, comprising a 5'-amino-5'-deoxy-5, 6-dihydrouridine with an unsaturated fatty acid comprising four serial and one isolated cyclopropane rings.

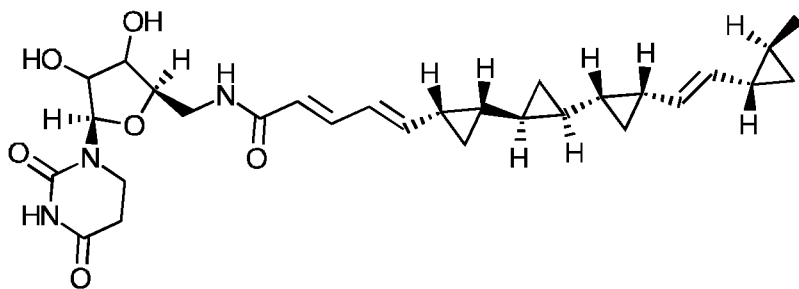
Its IUPAC name of jawsamycin is (2E,4E)-N-[[[(2R,3S,4R,5R)-5-(2,4-dioxo-1,3-diazinan-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl]-5-[(1S,2R)-2-[(1R,2R)-2-[(1R,2R)-2-[(1R,2S)-2-[(E)-2-[(1R,2R)-2-methylcyclopropyl]ethenyl]cyclopropyl]cyclopropyl]cyclopropyl]penta-2,4-dienamide.

While the total synthesis of jawsamycin entitled "pentacyclopentane antifungal agent FR-900848" has been disclosed by A. Barrett et al., J. Am. Chem. Soc. 1996, 118, 45, 11030–11037, the compound is preferably accessible, and employed, as the metabolite obtained from, or isolated from *Streptoverticillium* or *Streptomyces* bacteria.

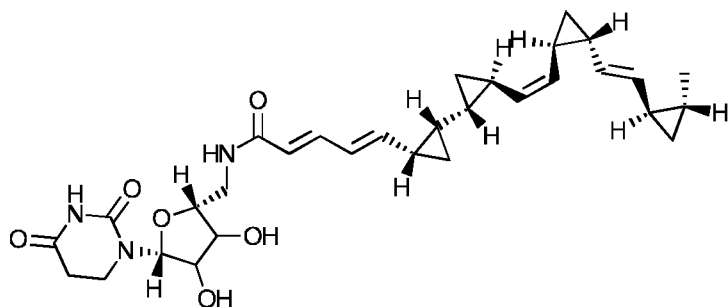
A microorganism expressing a compound according to formula (Ia) may be a *Streptoverticillium* and/or a *Streptomyces*, preferably *Streptoverticillium fervens*, and/or *Streptomyces luteoverticillatus*, or their spores, as these microorganisms express the compounds of formula (Ia) as metabolites.

A particularly suitable route to produce jawsamycin may be by cultivating *Streptoverticillium fervens* and isolating jawsamycin, for instance according to the methods disclosed in Masaru et al, The Journal of Antibiotics, 1990, Volume 43, Issue 7, Pages 748-754.

Congeners of jawsamycin are compounds Ib and Ic according to following formulae:



(Ib); and



(Ic),

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These congeners according to formula Ib) and Ic) are expressed by the above microbial cultures in varying, but usually small or negligible amounts.

The method according to the present invention comprises applying a composition comprising Jawsamycin to a plant, plant propagation material or locus thereof. Applying jawsamycin to a plant may
5 be performed by spraying, dusting or any suitable other means.

A suitable method of controlling or preventing an infestation of crop plants by *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturiainia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and / or *Cercospora sojina* comprises the application of an agrochemical composition
10 comprising jawsamycin is foliar application. The frequency of application and the rate of application will depend on the risk of infestation by the phytopathogenic fungi. However, jawsamycin can also penetrate the plant through the roots via the soil by drenching the locus of the plant with a liquid formulation, or by applying the compounds in solid form to the soil, e.g. in granular form (soil application).

It may be possible to use a composition comprising jawsamycin as dressing agents for the
15 treatment of plant propagation material, e.g., seed, such as fruits, tubers or grains, or plant cuttings, for the protection against infections by *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*. The propagation material can be treated with a composition comprising jawsamycin before planting: seed, for example,
20 can be dressed before being sown. Jawsamycin can also be applied to grains (coating), either by impregnating the seeds in a liquid formulation or by coating them with a solid formulation. The composition can also be applied to the planting site when the propagation material is being planted, for example, to the seed furrow during sowing.

The method according to the present invention comprises applying compositions, wherein the
25 composition may be employed in any conventional form, for example in the form of a twin pack, a powder for dry seed treatment (DS), an emulsion for seed treatment (ES), a flowable concentrate for seed treatment (FS), a solution for seed treatment (LS), a water dispersible powder for seed treatment (WS), a capsule suspension for seed treatment (CF), a gel for seed treatment (GF), an emulsion concentrate (EC), a suspension concentrate (SC), a suspo-emulsion (SE), a capsule suspension (CS), a water
30 dispersible granule (WG), an emulsifiable granule (EG), an emulsion, water in oil (EO), an emulsion, oil in water (EW), a micro-emulsion (ME), an oil dispersion (OD), an oil miscible flowable (OF), an oil miscible liquid (OL), a soluble concentrate (SL), an ultra-low volume suspension (SU), an ultra-low volume liquid (UL), a technical concentrate (TK), a dispersible concentrate (DC), a wettable powder (WP) or any technically feasible formulation in combination with agriculturally acceptable adjuvants.
35 Such compositions may be produced in conventional manner, e.g., by mixing the active ingredients with

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at least one appropriate inert formulation adjuvant (for example, diluents, solvents, fillers, and optionally other formulating ingredients such as surfactants, biocides, anti-freeze, stickers, thickeners, and compounds that provide adjuvancy effects). Also, conventional slow-release formulations may be employed where long lasting efficacy is intended. Particularly formulations to be applied in spraying forms, such as water dispersible concentrates (e.g. EC, SC, DC, OD, SE, EW, EO and the like), wettable powders and granules, may contain surfactants such as wetting and dispersing agents and other compounds that provide adjuvancy effects, e.g. the condensation product of formaldehyde with naphthalene sulphonate, an alkylarylsulphonate, a lignin sulphonate, a fatty alkyl sulphate, and ethoxylated alkylphenol and an ethoxylated fatty alcohol.

Any suitable plant may be treated to prevent or control infestation by *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *enturiainia inaequalis*, *Botrytis eliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora kikuchii*, and / or *Cercospora sojina*. A suitable plant includes ornamental plants such as trees, shrubs, flowers and houseplants, and also fruits, vegetables, herbs and forages. Preferably wherein the plant is selected from vegetables, such as cucumber, tomato, fruits, such as apple, pear, grapes, cereals, such as barley, wheat, corn, peanut, rice and soya.

A plant in method as disclosed herein for controlling or preventing infestation by *Glomerella lagenarium*, comprises or is cucumber. *Glomerella lagenarium* was effectively controlled at a fungicidally effective amount of jawsamycin of 0.1 to 500 ppm , preferably 0.2 to 300 ppm, preferably 0.3 to 200 ppm.

A plant in method as disclosed herein for controlling or preventing infestation by *Magnaporthe grisea* comprises or is rice. *Magnaporthe grisea* was surprisingly effectively controlled at a fungicidally effective amount of jawsamycin of 1 to 500 ppm , preferably 2 to 300 ppm, preferably 5 to 200 ppm.

A plant in method as disclosed herein for controlling or preventing infestation by *Mycosphaerella arachidis* comprises or is peanut. *Mycosphaerella arachidis* was surprisingly effectively controlled on planta at a fungicidally effective amount of jawsamycin of 20 to 500 ppm, preferably 30 to 300 ppm, preferably 40 to 250 ppm.

A plant in method as disclosed herein for controlling or preventing infestation by *Pyrenophora teres* comprises or is barley. *Pyrenophora teres* was surprisingly effectively controlled at a fungicidally effective amount of jawsamycin of 0.5 to 500 ppm , preferably 1 to 300 ppm, preferably 2to 200 ppm.

A plant in method as disclosed herein for controlling or preventing infestation by *Venturia inaequalis* comprises or is fruit, preferably apple. *Venturia inaequalis* was surprisingly effectively controlled at a fungicidally effective amount of jawsamycin of 0.1 to 500 ppm , preferably 0.2 to 300 ppm, preferably 0.3 to 200 ppm.

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A plant in method as disclosed herein for controlling or preventing infestation by *Phaeosphaeria nodorum* comprises or is wheat. *Phaeosphaeria nodorum* is effectively controlled at a fungicidally effective amount of jawsamycin of 50 to 500 ppm, preferably 60 to 400 ppm

5 The term "plants" refers to all physical parts of a plant, including seeds, seedlings, saplings, roots, tubers, stems, stalks, foliage, and fruits.

A plant as used herein also includes useful plants. The term "useful plants" is to be understood as also including useful plants that have been rendered tolerant to herbicides.

10 The term "useful plants" is to be understood as also including useful plants which have been so transformed by the use of recombinant DNA techniques that they are capable of synthesising one or more selectively acting toxins, such as are known, for example, from toxin-producing bacteria, especially those of the genus *Bacillus*.

15 The term "plant propagation material" is understood to denote generative parts of the plant, such as seeds, which can be used for the multiplication of the latter, and vegetative material, such as cuttings or tubers, for example potatoes. There can be mentioned for example seeds (in the strict sense), roots, fruits, tubers, bulbs, rhizomes and parts of plants. Germinated plants and young plants which are to be transplanted after germination or after emergence from the soil, may also be mentioned. These young plants can be protected before transplantation by a total or partial treatment by immersion. Preferably "plant propagation material" is understood to denote seeds.

In one embodiment a composition comprising jawsamycin is an agriculturally acceptable composition.

20 The term "locus" as used herein means fields in or on which plants are growing, or where seeds of cultivated plants are sown, or where seed will be placed into the soil. It includes soil, seeds, and seedlings, as well as established vegetation.

25 Throughout this document the expression "composition" stands for the various mixtures or combinations of jawsamycin, for example in a single "ready-mix" form, in a combined spray mixture composed from separate formulations of the single active ingredient components, such as a "tank-mix", and in a combined use of the single active ingredients when applied in a sequential manner, i.e. one after the other with a reasonably short period, such as a few hours or days.

30 The composition comprising jawsamycin in a method according to the present invention preferably is an agriculturally acceptable composition. Preferably, the composition further comprises at least one agriculturally acceptable carrier, additive, formulation adjuvant, and / or a surfactant.

Suitable carriers and adjuvants, e.g. for agricultural use, can be solid or liquid and are substances useful in formulation technology, e.g. natural or regenerated mineral substances, solvents, dispersants, wetting agents, tackifiers, thickeners, binders or fertilizers.

35 In another embodiment, the composition comprises one or more further biologically active compound(s), preferably one or more further pesticide, such as fungicides, insecticides, or herbicides.

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Such one or more further pesticidal components are known and are referred to hereinabove by their so-called ISO common name or their IUPAC name. Typical pesticidal components are included in the Pesticide Manual Online ("E-pesticide Manual") by the British Crop Production Council and in the Compendium of Pesticide Common Names by Alan Wood.

5 In one embodiment of method according to the present invention, jawsamycin is applied at a rate of from 5 to 2000 g a.i./ ha, particularly 1 g a.i./ha to 1000 g a.i. / ha, preferably at a rate 5 g a.i./ha to 500 g a.i./ha, preferably at a rate 1 g a.i./ha to 250 g a.i./ha. As used herein, the abbreviation "a.i." stands for "active ingredient", and the active ingredient comprises or is jawsamycin,

10 In another embodiment of the method according to the present invention jawsamycin is applied at a rate of, 0.001 to 50 g of a.i. per kg of plant propagation material, in particular per kg of seeds. Preferably, jawsamycin is applied at a rate of, 0.01 to 40 g, preferably at a rate of 0.1 to 30 g of a.i. per kg of plant propagation material.

The present invention also relates to the use of jawsamycin for controlling or preventing phytopathogenic fungi, wherein the fungus is selected from *Glomerella lagenarium*, *Magnaporthe*
15 *grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia inaequalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora kikuchii*, and *Cercospora sojina*.

Preferably, the use of jawsamycin for controlling or preventing phytopathogenic fungi is on a plant or on plant propagation material. The method and use of the present invention excludes methods and uses for the treatment of the human or animal body by surgery or therapy.

Examples

Materials and methods

Jawsamycin employed in the examples was produced by cultivating *Streptovercillium fervens* and isolating jawsamycin according to the methods disclosed in Masaru et al, The Journal of Antibiotics,
25 1990, Volume 43, Issue 7, Pages 748-754.

Example 1. *In vitro* liquid culture assays.

Conidia or mycelial fragments from the fungus / oomycetes listed in Table 1 were mixed into nutrient broth (potato dextrose broth (PDB) / Vogel's minimal media (Microbial Genetics Bulletin 13:42-43, 1956)). A 10 µL solution of jawsamycin and DMSO was dispensed into a well of a 96-well microtiter
30 plate, before 90 µL of the nutrient broth containing the conidia or mycelial fragments was added to the well. The assay plate was then incubated at 24 °C and assessed photometrically at 620 nm after 2 to 7 days incubation. The efficacy of jawsamycin was assessed by comparing test wells to non-treated inoculated wells and non-inoculated wells and allocating efficacy on a scale of 0-100 %.

The results in Table 1 show that *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora*
35 *kikuchii*, *Cercospora sojina*, *Glomerella lagenarium*, and *Mycosphaerella arachidis* were effectively

controlled by jawsamycin in liquid culture assays. However, jawsamycin did not affect the growth of *Pythium ultimum* and *Rhizoctonia solani*.

5 **Table 1.** Efficacy (%) of jawsamycin against fungal and oomycete species at different concentrations in liquid culture assays

Rate (ppm)	<i>Mycosphaerella arachidis</i>	<i>Pythium ultimum</i>	<i>Glomerella lagenarium</i>	<i>Rhizoctonia solani</i>	<i>Corynespora cassicola</i>	<i>Cercospora kikuchii</i>	<i>Cercospora soja</i>	Rate (ppm)	<i>Botrytis elliptica</i>	<i>Botrytis tulipae</i>
20	100	0	100	0	90	100	100	25	100	93
2.2	100	0	100	0	70	50	100	12.5	100	77
0.2	70	0	100	0	20	0	0	6.25	100	83

Example 2. Efficacy of jawsamycin against fungi and oomycetes in leaf disc assays

Leaf disc assays

Leaf discs efficacy was assessed on a scale of 0 – 100 % by comparing test discs to non-treated, inoculated leaf discs representing 0 % control and leaf discs treated with a known standard that completely controls the pathogen representing 100 % control.

***Phytophthora infestans* (late blight of potato/tomato):**

Tomato leaf disks were placed on water agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed 4 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

***Plasmopara viticola* (downy mildew of grapevine):**

Grape vine leaf disks were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After

appropriate incubation the activity of a compound was assessed 7 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

***Blumeria graminis f.sp. tritici* (Wheat powdery mildew):**

- 5 Barley leaf segments were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with spores of the fungus. After appropriate incubation the activity of a compound was assessed 7 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 66-22 ppm.

10 ***Pyrenophora teres* (Net blotch):**

Barley leaf segments were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed 4 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

15 ***Puccinia recondita* (Brown rust):**

Wheat leaf segments were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed 8 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

20 ***Phaeosphaeria nodorum* (syn. *Parastagonospora nodorum*, Glume blotch):**

Wheat leaf segments were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed 4 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

***Magnaporthe oryzae* (Rice blast):**

Rice leaf segments were placed on agar in multiwell plates (24-well format) and sprayed with test solutions. After drying, the leaf disks are inoculated with a spore suspension of the fungus. After appropriate incubation the activity of a compound was assessed 5 dpi (days post inoculation) as preventive fungicidal activity. Dose range: 200-22 ppm.

The results in Table 2 show that jawsamycin showed activity in the leaf disc assay against the ascomycetes *Pyrenophora teres*, *Phaeosphaeria nodorum* and *Magnaporthe grisea*, but showed no

activity against the Ascomycete *Blumeria graminis* and the Basidiomycete *Puccinia recondite*, nor against oomycetes.

Table 2. Efficacy (%) of jawsamycin against several fungi and oomycetes in leaf disc assay

	Efficacy (%)							
	Fungus or oomycete	<i>Phytophthora infestans</i>	<i>Plasmopara viticola</i>	<i>Blumeria graminis</i>	<i>Puccinia recondita</i>	<i>Phaeosphaeria nodorum</i>	<i>Pyrenophora teres</i>	<i>Magnaporthe grisea</i>
Rate (ppm)	Plant leaf	Tomato	Grape	Barley	Barley	Wheat	Barley	Rice
200		0	0	/	0	70	100	100
66.6		0	0	0	0	0	0	100
22.2		0	0	0	0	0	20	0

5

Example 3. Efficacy of jawsamycin against fungi and oomycetes on plants

Whole plant assays

- 10
- Whole plant disease efficacy was assessed by comparing symptom coverage on the plant and scoring it on a scale of 0 – 100%. Plants were compared to an untreated control plant and to plants treated with a standard that has complete control acting as an example of 100 % coverage.

***Blumeria graminis* f. sp. *tritici* (*Erysiphe graminis* f. sp. *tritici*) on wheat with a preventative application.**

1-week old wheat plants cv. Arina were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spreading powdery mildew spores over them in an inoculation chamber two days after application. The inoculated test plants were incubated at 20° C / 18°C (day/night) and 60% rh in a greenhouse and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (7 – 9 days after application).

***Glomerella lagenarium* (*Colletotrichum lagenarium*) on cucumber with a preventative application.**

1-week old cucumber plants cv. Wisconsin were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension one day after application. After an incubation period of 30 h in darkness at 23° C and 100% rh, the inoculated test plants were kept at 23° C / 21° C (day/night) and 70% rh in a greenhouse. The percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (6 – 8 days after application).

***Magnaporthe grisea* (*Pyricularia oryzae*) on rice with a preventative application.**

3-weeks old rice plants cv. Koshihikari were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension two days after application. The inoculated test plants were incubated at 25° C and 95% rh and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (7 – 9 days after application).

***Mycosphaerella arachidis* (*Cercospora arachidicola*) on peanut with a preventative application**

3-weeks old peanut plants cv. Georgia Green were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension on their lower leaf surface one day after application. After an incubation period of 4 days under a plastic hood at 23° C and 100% rh, the inoculated test plants were kept at 23° C / 20° C (day/night) and 70% rh in a greenhouse. The percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (12 – 14 days after application).

***Phytophthora infestans* on potato with a preventative application.**

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2-weeks old potato plants cv. Bintje are sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a sporangia suspension 2 days after application. The inoculated test plants were incubated at 18° C with 14 h light/day and 100 % rh in a growth chamber and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (5 – 7 days after application).

***Plasmopara viticola* on grape with a preventative application.**

5-weeks old grape seedlings cv. Gutedel were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying a sporangia suspension on their lower leaf surface one day after application. The inoculated test plants were incubated at 22° C and 100% rh in a greenhouse and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (6 – 8 days after application).

***Puccinia recondita* f. sp. *tritici* on wheat with a preventative application.**

2-weeks old wheat plants cv. Arina were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension one day after application. After an incubation period of 1 day at 20° C and 95% rh, the inoculated test plants were kept at 20° C / 18° C (day/night) and 60% rh in a greenhouse. The percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (12 – 14 days after application).

***Pyrenophora teres* (*Helminthosporium teres*) on barley with a preventative application.**

1-week old barley plants cv. Regina were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension 2 days after application. The inoculated test plants were incubated at 20° C and 95% rh and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (5 – 7 days after application).

***Venturia inaequalis* on apple with a preventative application.**

3-weeks old apple seedlings were sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by spraying them with a spore suspension 1 day after application. After an incubation period of 2 days at 20° C and 95% rh, the inoculated test plants were placed at 20°C/19°C (day/night) and 60% rh in a greenhouse. The percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (11 – 13 days after application).

***Uncinula necator* on grape with a preventative application.**

5-weeks old grape seedlings cv. Gutedel are sprayed in a spray chamber with the formulated test compound diluted in water. The test plants were inoculated by shaking plants infected with grape powdery mildew above them 1 day after application. The inoculated test plants were incubated at 24/22 °C (day/night) and 70% rh under a light regime of 14/10 h (light/dark) and the percentage leaf area covered by disease was assessed when an appropriate level of disease appeared on untreated check plants (7 – 9 days after application).

The results in Table 3 show that jawsamycin showed surprising efficient fungicidal activity against *Pyrenophora teres*, *Mycosphaerella arachidis*, *Venturia inaequalis*, *Glomerella lagenarium*, *Magnaporthe grisea* on the plants as indicated, but no activity was found against the ascomycete *Blumeria graminis* and *Uncinula necator* and the Basidiomycete *Puccinia recondita* and the oomycetes *Phytophthora infestans*, *Plasmopora viticola*.

Table 3. Efficacy (%) of jawsamycin against fungi and oomycetes

	Fungus or oomycete	<i>Phytophthora infestans</i>	<i>Plasmopara viticola</i>	<i>Blumeria graminis</i>	<i>Puccinia recondita</i>	<i>Pyrenophora teres</i>	<i>Mycosphaerella arachidis</i>	<i>Venturia inaequalis</i>	<i>Glomerella lagenarium</i>	<i>Magnaporthe grisea</i>	<i>Uncinula necator</i>
Rate (ppm)	Plant	Potato	Grape	Wheat	Wheat	Barley	Peanut	Apple	Cucumber	Rice	Grape
200		0	0	0	0	93.8	71.4	/	/	/	0
60		0	0	0	0	93.8	35.7	100	97.4	73.2	0
20		0	0	0	0	87.5	0	91.1	95.5	19.6	0
6		0	0	0	0	81.3	0	88.1	92.3	46.4	0
2		0	0	0	0	50	0	98.8	80.8	1.8	0
0.6		/	/	/	/	/	/	100	67.9	0	/

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Claims

- 5 1. A method of controlling or preventing phytopathogenic fungi belonging to *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia equalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassicola*, *Cercospora kikuchii*, and / or *Cercospora sojina* on a plant or on plant propagation material thereof, the method comprising applying to the plant, plant propagation material or locus thereof, a composition comprising jawsamycin.
- 10 2. The method according to claim 1, wherein the composition comprises a fungicidally effective amount of jawsamycin.
- 15 3. The method according to claim 1 or 2, wherein the plant is selected from vegetables, such as cucumber, tomato, fruits, such as apple, pear, grapes, cereals, such as barley, wheat, or corn, peanut, rice and soya.
- 20 4. The method according to any one of the claims 1 to 3, wherein the composition is an agriculturally acceptable composition.
- 25 5. The method according to any one of the claims 1 to 4, wherein the composition further comprises at least one agriculturally acceptable carrier, additive, formulation adjuvant, and / or a surfactant.
- 30 6. The method according to any one of the claims 1 to 5, wherein the composition comprises one or more further biologically active compound(s), preferably one or more further pesticide, such as fungicides, insecticides, or herbicides.
7. The method according to any one of the claims 1 to 6, wherein the fungicidally effective amount of jawsamycin comprises 5 g a.i./ha to 2000 g a.i. / ha.
8. The method according to any one of claims 1 to 6, wherein the fungicidally effective amount of jawsamycin comprises 0.001 to 50 g of a.i. per kg of plant propagation material, preferably per kg of seeds.

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9. Use of jawsamycin for controlling or preventing phytopathogenic fungi, wherein the fungus is selected from *Glomerella lagenarium*, *Magnaporthe grisea*, *Mycosphaerella arachidis*, *Phaeosphaeria nodorum*, *Pyrenophora teres*, *Venturia equalis*, *Botrytis elliptica*, *Botrytis tulipae*, *Corynespora cassiicola*, *Cercospora kikuchii*, and *Cercospora sojina*.

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10. Use according to claim 9, wherein said controlling or preventing phytopathogenic fungi is on a plant or on plant propagation material.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER INV. A01N43/54 A01N63/22 A01N63/28 A01P3/00 C07H19/067 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A01N C07H A01P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, CHEM ABS Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/13487 A2 (GREEN CARE LAB LTD [IL]; ELIYAHU NITZAN [IL]; SHOKHEN MICHAEL [IL]) 16 March 2000 (2000-03-16) page 1, last paragraph -----	1 - 10
A	US 2023/081771 A1 (BIERI STÉPHANE [CH] ET AL) 16 March 2023 (2023-03-16) the whole document -----	1 - 10
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 29 November 2024		Date of mailing of the international search report 18/12/2024
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Bertrand, Franck

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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