DESCRIPTION

Title of Invention: LARVICIDE, BIOCONTROL AGENT AND BIOCONTROL METHOD

Technical Field

[0001] The present disclosure relates to a larvicide, a biocontrol agent and a biocontrol method.

Background Art

[0002] Mosquitos are harmful insects that mediate severe diseases such as malaria and dengue fever, and the control thereof is an important issue in the region of Southeast Asia.

Various kinds of products are used as insecticides for mosquitos. For example, Bti (Bacillus thuringiensis), a bacterial insecticide that kills mosquito larvae, and bifenthrin, a pyrethroid insecticide that kills adult mosquitos, are widely used in the countries of Southeast Asia in combination.

However, it has been reported that mosquitos are building a resistance to the combination of Bti and bifenthrin, and alternative insecticides that are effective for mosquito control are anticipated. For example, Non-patent document 1 studies insecticidal activity of table salt and iodine salt with respect to larvae of Aedes aegypti and Aedes albopictus.

[Prior Art Document]

[Non-patent document]

[0003] Non-patent document 1: World Journal of Pharmaceutical and Life Sciences, 2018, Vol. 4, Issue 9, 36-40

[Summary]

[Problem to be Solved]

[0004] In view of the current circumstances that the existing biocontrol agents are losing their control activity due to the acquired resistance by the target organism, it is essential to find a new biocontrol agent that can replace the existing ones for the establishment of a sustainable biocontrol system.

An embodiment of the present disclosure aims to provide a new larvicide and a new biocontrol agent that are useful for controlling harmful organisms such as mosquito larvae; and a biocontrol method using the larvicide and the biocontrol agent.

[Means for Solving Problem]

[0005] The means for solving the aforementioned problem include the following embodiments.

<1> A larvicide for controlling mosquito larvae, the larvicide comprising diiodomethyl-p-tolylsulfone as an active ingredient.

<2> The larvicide according to <1>, wherein the diiodomethyl-p-tolylsulfone is solubilized with respect to water.

<3> The larvicide according to <1> or <2>, wherein the diiodomethyl-p-tolylsulfone forms an inclusion compound with a cyclodextrin.

<4> The larvicide according to any one of <1> to <3>, wherein the mosquito larvae is at a fourth larval stage.

<5> A biocontrol agent comprising diiodomethyl-p-tolylsulfone as an active ingredient, the diiodomethyl-p-tolylsulfone being solubilized with respect to water.

<6> The biocontrol agent according to <5>, wherein the diiodomethyl-p-tolylsulfone forms an inclusion compound with a cyclodextrin.

<7> The biocontrol agent according to <5> or <6>, which is for controlling a target that lives in an environment in which water is present.

<8> A biocontrol method, comprising applying the larvicide according to any one of <1> to <4> or the biocontrol agent according to any one of <5> to <7> to an environment in which water is present.

[0006] According to an embodiment of the present disclosure, a new larvicide and a new biocontrol agent that are useful for controlling harmful organisms such as mosquito larvae; and a biocontrol method using the larvicide and the biocontrol agent are provided.

[Embodiments for Implementing Invention]

[0007] Embodiments for carrying out the present invention will now be described in detail. However, the invention is in no way limited to the following embodiments. In the present disclosure, the functional mechanisms described therein may include presumptive mechanisms, and validness thereof does not limit the present invention.

[0008] In the present disclosure, any numerical range described using the expression “from * to” represents a range in which numerical values described before and after the “to” are included in the range as a minimum value and a maximum value, respectively.

[0009] In a numerical range described in stages, in the present disclosure, an upper limit value or a lower limit value described in one numerical range may be replaced with an upper limit value or a lower limit value in another numerical range described in stages. Further, in a numerical range described in the present disclosure, the upper limit value or the lower limit value in the numerical range may be replaced with a value shown in the Examples.

[0010] In the present disclosure, the definition of the term “step” includes not only an independent step which is distinguishable from another step, but also a step which is not clearly distinguishable from another step, as long as the purpose of the step is achieved.

[0011] In the present disclosure, each component may include plural kinds of substances corresponding to the component. In a case in which plural kinds of substances corresponding to

each component are present in a composition, the content ratio or content of each component refers to the total content ratio or content of the plural kinds of substances present in the composition, unless otherwise specified.

[Embodiments for Implementing Invention]

[0012] <Larvicide>

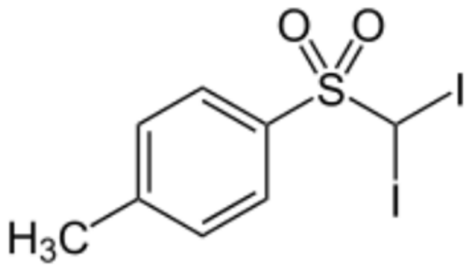
A first embodiment of the present disclosure is a larvicide for controlling mosquito larvae, the larvicide comprising diiodomethyl-p-tolylsulfone as an active ingredient.

[0013] The present inventor has discovered that diiodomethyl-p-tolylsulfone exhibits an insecticidal activity with respect to mosquito larvae. Accordingly, a larvicide comprising diiodomethyl-p-tolylsulfone as an active ingredient is useful for controlling mosquito larvae.

Further, a larvicide comprising diiodomethyl-p-tolylsulfone as an active ingredient is effective on older mosquito larvae, such as those at a fourth larval stage, in contrast to most of the commercial larvicides.

[0014] Diiodomethyl-p-tolylsulfone is a compound represented by the following structural formula.

[0015]



[0016] As necessary, the larvicide may include other active ingredients than diiodomethyl-p-tolylsulfone. Examples of the other active ingredients include insecticidal components such as pyrethroid compounds, phosphoroorganic compounds, neonicotinoid compounds and carbamate compounds; insect growth regulators (IGR); and insect repellents.

[0017] As necessary, the larvicide may include other components than an active ingredient. Examples of the other components include a surfactant, a moistening agent, a fixing agent, a thickening agent, an antiseptic agent, a colorant, a stabilizer, and a carrier in solid or liquid form.

The larvicide may be in any form such as liquid, wettable powder, flowable, dust, emulsion, tablets, granules and capsules.

[0018] The diiodomethyl-p-tolylsulfone included in the larvicide may be solubilized with respect to water. Mosquito larvae live in an environment in which water is present. Therefore, if diiodomethyl-p-tolylsulfone included in the larvicide is solubilized with respect to water,

diiodomethyl-p-tolylsulfone being dissolved in water can contact with mosquito larvae in an efficient manner.

[0019] In the present disclosure, "diiodomethyl-p-tolylsulfone is solubilized with respect to water" refers to that a degree of water solubility of diiodomethyl-p-tolylsulfone is enhanced as compared with a degree of water solubility of diiodomethyl-p-tolylsulfone in itself.

[0020] The means for solubilizing diiodomethyl-p-tolylsulfone with respect to water is not particularly limited.

For example, diiodomethyl-p-tolylsulfone that is solubilized with respect to water may form an inclusion compound with cyclodextrin. Specifically, the larvicide may include an inclusion compound that is formed from cyclodextrin as a host compound and diiodomethyl-p-tolylsulfone as a guest compound.

[0021] The cyclodextrin used for the formation of an inclusion compound is a cyclic oligosaccharide formed from a plurality of D-glucose that are bonded via α-1,4-glycoside linkages, such as α-cyclodextrin formed from six D-glucoses, β-cyclodextrin formed from seven D-glucoses, and γ-cyclodextrin formed from eight D-glucoses.

Specific examples of cyclodextrin include methyl-β-cyclodextrin, hydroxypropyl-β-cyclodextrin, methyl-γ-cyclodextrin and methyl-α-cyclodextrin. Among these, methyl-β-cyclodextrin and hydroxypropyl-β-cyclodextrin are preferred.

In the present disclosure, the inclusion compound may be formed using a single kind of cyclodextrin or two or more kinds thereof in combination.

[0022] The method for producing an inclusion compound from diiodomethyl-p-tolylsulfone and cyclodextrin is not particularly limited. For example, an inclusion compound may be produced by mixing diiodomethyl-p-tolylsulfone and cyclodextrin in a solvent.

[0023] From the viewpoint of production efficiency, the inclusion compound is preferably produced by a method comprising:

preparing a solution A, including diiodomethyl-p-tolylsulfone and a water-soluble organic solvent;

preparing a solution B, including cyclodextrin and water; and

mixing the solution A and the solution B.

[0024] In the aforementioned method, the solution A is prepared using a water-soluble organic solvent to dissolve diiodomethyl-p-tolylsulfone that is slightly soluble to water, and the solution B is prepared using water to dissolve cyclodextrin that is highly soluble to water. Therefore, a sufficient degree of opportunity is secured for diiodomethyl-p-tolylsulfone and cyclodextrin to contact with each other in a mixture of the solvent A and the solvent B, thereby producing an inclusion compound in an efficient manner.

[0025] In the aforementioned method, the water-soluble organic solvent used for the preparation of the solution A is not particularly limited. For example, the water-soluble organic solvent preferably includes at least one selected from the group consisting of a nitrile compound, an alcohol compound, a ketone compound and an ether compound.

[0026] The nitrile compound is preferably acetonitrile or propionitrile, more preferably acetonitrile.

The alcohol compound is preferably methanol, ethanol, propanol or isopropanol, more preferably methanol or ethanol, further preferably methanol.

The ketone compound is preferably acetone, methyl ethyl ketone, methyl propyl ketone or diethyl ketone.

The ether compound is preferably diethyl ether, dipropyl ether, diisopropyl ether, tetrahydrofurane, 1,4-dioxane or 1,2-dimethoxyethane, more preferably tetrahydrofurane or 1,2-dimethoxyethane.

[0027] The temperature of the solution A and the solution B when mixing the same may be independently selected from 5°C to 50°C for example, preferably from 10°C to 40°C, more preferably from 15°C to 30°C.

[0028] The time for mixing the solution A and the solution B is preferably 1 hour or more, more preferably 5 hours or more, further preferably 10 hours or more, yet further preferably 15 hours or more.

The upper limit for the time for mixing may be determined in view of productivity or the like. For example, the time for mixing may be up to 50 hours.

[0029] In the mixture of the solution A and the solution B, the value of CD/DMTS, which is a molar ratio of cyclodextrin (CD) to diiodomethyl-p-tolylsulfone (DMTS), is preferably 0.3 or more, more preferably 0.5 or more, further preferably 0.7 or more, yet further preferably 1.0 or more.

In the mixture of the solution A and the solution B, the value of CD/DMTS, which is a molar ratio of cyclodextrin (CD) to diiodomethyl-p-tolylsulfone (DMTS), is preferably 10 or less, more preferably 7 or less, further preferably less than 7, yet further preferably 5 or less.

[0030] It is possible to obtain an aqueous solution including an inclusion compound by removing a water-soluble organic solvent from a mixture of the solution A and the solution B, after the formation of an inclusion compound.

Examples of the method for removing a water-soluble organic solvent from a mixture include a method in which the water-soluble organic solvent is evaporated by heating the mixture including an inclusion compound at a temperature lower than that of water. Accordingly, the water-soluble organic solvent used for the preparation of the solution A preferably has a boiling point of lower than the boiling point of water (100°C).

[0031] As necessary, an inclusion compound may be obtained in a dried state by removing water from the aqueous solution including the inclusion compound.

[0032] <Biocontrol agent>

A second embodiment of the present disclosure is a biocontrol agent comprising diiodomethyl-p-tolylsulfone as an active ingredient, the diiodomethyl-p-tolylsulfone being solubilized with respect to water.

[0033] The biocontrol agent including diiodomethyl-p-tolylsulfone as an active ingredient exhibits an effective biocontrol activity. Further, the diiodomethyl-p-tolylsulfone included in the biocontrol agent is solubilized with respect to water. Therefore, the biocontrol agent can contact with an organism living in an environment in which water is present in an effective manner, and exhibit an excellent control activity with respect to the organism. Further, the biocontrol agent is highly compatible with human bodies or natural environments because the biocontrol agent can be used without a means for dissolving diiodomethyl-p-tolylsulfone, such as an organic solvent.

[0034] As necessary, the biocontrol agent may include other active ingredients than diiodomethyl-p-tolylsulfone. Examples of the other active ingredients include insecticidal components such as pyrethroid compounds, phosphoroorganic compounds, neonicotinoid compounds and carbamate compounds; insect growth regulators (IGR); and insect repellents.

[0035] As necessary, the biocontrol agent may include other components than an active ingredient. Examples of the other components include a surfactant, a moistening agent, a fixing agent, a thickening agent, an antiseptic agent, a colorant, a stabilizer, and a carrier in solid or liquid form.

The biocontrol agent may be in any form such as liquid, wettable powder, flowable, dust, emulsion, tablets, granules and capsules.

[0036] The means for solubilizing diiodomethyl-p-tolylsulfone with respect to water is not particularly limited.

For example, diiodomethyl-p-tolylsulfone may form an inclusion compound with cyclodextrin. Specifically, the biocontrol agent may include an inclusion compound that is formed from cyclodextrin as a host compound and diiodomethyl-p-tolylsulfone as a guest compound.

The details and preferred embodiments of the inclusion compound are the same as the details and preferred embodiments of the inclusion compound that may be included in the larvicide as described above.

[0037] The organism as the target of the biocontrol agent is not particularly limited. The organism is preferably an animal, and examples of the organism include insects such as mosquitos, houseflies, blackflies, horseflies, ants, cockroaches, ground beetles, locusts, lice, fleas and weevils; and organisms other than insects such as spiders, ticks, centipedes, millpedes and woodlice. The

organism as the target of the biocontrol agent may be in any form such as adults, larvae, eggs or pupae.

[0038] The biocontrol agent is suitable for controlling an organism living in an environment in which water is present, and examples thereof include mosquito larvae.

[0039] <Biocontrol method>

A third embodiment of the present disclosure is a biocontrol method comprising applying the larvicide or the biocontrol agent according to the present disclosure to an environment with water.

[0040] The method for applying the larvicide or the biocontrol agent to an environment in which water is present is not particularly limited, and may be performed by any known method.

For example, the larvicide or the biocontrol agent may be applied to an environment in which water is present in a direct manner, or may be diluted with water or the like prior to the application thereof.

The amount of the larvicide or the biocontrol agent to apply to an environment in which water is present is not particularly limited, and may be determined in consideration of a state of propagation of the organism to be controlled, possible effects on human bodies or natural environments, and the like.

The environment in which water is present is not particularly limited, and examples thereof include rivers, lakes, ponds, marshes, puddles, farmlands, wastewater-treatment facilities, water-and-sewage systems, wells, kitchens and bathrooms.

[Examples]

[0041] In the following, embodiments of the present disclosure are explained by referring to the Examples. The details of the Examples may be altered without departing from the scope of the present disclosure. Therefore, the scope of the present disclosure should not be limited to the specific embodiments described therein.

[0042] <Test Example 1>

Larvicidal activity of diiodomethyl-p-tolylsulfone was evaluated by conducting the following test. In the test, an inclusion compound formed of methyl-β-cyclodextrin as a host compound and diiodomethyl-p-tolylsulfone as a guest compound (DMTS-CD, Mitsui Chemicals, Inc.) was used.

In each of Samples 1-1 to 1-6, four replicates of mosquito larvae at a late third larval stage (n=100) were introduced into treatment cups containing a mixture of water (249 mL) and ethanol (1mL), and DMTS-CD was added to the treatment cups at different DMTS concentrations shown in Table 1. Larval mortality was recorded at 1 hour, 3.5 hours and 24 hours after the addition of DMTS-CD at a temperature of 25-30°C and a relative humidity of 70 to 90%. The results are shown in Table 1.

[0043] Table 1

Sample No.	DMTS in DMTS-CD		Mortality [%]		
	mg/L	μmoles/L	After 1h	After 3.5h	After 24h
1-1	31	72.97	0	4	96
1-2	62	145.93	4	20	100
1-3	123	291.86	16	72	100
1-4	185	437.79	28	84	100
1-5	246	583.72	32	76	100
1-6	308	729.65	48	92	100

[0044] As shown in Table 1, almost 100% mortality was recorded after 24 hours for all of the samples tested. Further, larvae were killed in shorter times in samples with higher DMTS concentration. These results indicate that DMTS exhibits an effective biocontrol activity with respect to mosquito larvae.

[0045] <Test Example 2>

Four replicates of test larvae at a late third larval stage (n=100) were introduced into treatment cups containing a mixture of water (249 mL) and ethanol (1mL), and DMTS (diiodomethyl-p-tolylsulfone), DMTS-CD and CD (methyl-β-cyclodextrin) were added to the treatment cups at the concentrations as shown in Table 1, respectively. Larval mortality was recorded at 24 hours after the addition of DMTS, DMTS-CD or CD, at a temperature of 25-30°C and a relative humidity of 70 to 90%. The results are shown in Table 2.

[0046] Table 2

	mg/L	μmoles/L	Mortality [%]
DMTS	50	118.47	100
DMTS in DMTS-CD	50	118.47	100
CD	593	454.69	0

[0047] As shown in Table 2, 100% mortality of mosquito larvae was recorded in the samples containing DMTS or DMTS-CD, whereas 0% mortality of mosquito larvae was recorded in the sample containing CD. These results indicate that DMTS exhibits an effective biocontrol activity with respect to mosquito larvae.

Further, an LC99 (Lethal Concentration for 99% mosquito) test was conducted on DMTS-CD, which was found 56.38 mg/L.

[0048] <Test Example 3>

Larvicidal activity on iodine was tested by using potassium iodide as source of iodine.

In each of Samples 1-1 and 1-2, four replicates of mosquito larvae at a late third larval stage (n=100) were introduced into treatment cups containing a mixture of water (249 mL) and

ethanol (1mL), and potassium iodide was added to the treatment cups at different concentrations shown in Table 3. Larval mortality was recorded at 24 hours' exposer after the addition of potassium iodide at a temperature of 25-30°C and a relative humidity of 70 to 90%.

The amount of potassium iodide in Sample 1-1 is determined such that the amount of iodine contained therein is 30 mg/L, which corresponds to the amount of iodine contained in 50 mg/L of DMTS that demonstrates 100% mortality in Test Example 2.

The amount of potassium iodide in Sample 1-2 corresponds to the result of LC99 test conducted on DMTS-CD in Test Example 2 (56.38 mg/L).

[0049] Table 3

Sample No.	Potassium iodide concentration [mg/L]	Number of death larvae				Mean Mortality [%]
		R1	R2	R3	R4	
1-1	39.32	0	0	0	0	0
1-2	56.38	0	0	0	0	0

[0050] As shown in Table 3, potassium iodide did not show any effects against mosquito larvae at above studied doses. The results show the effectiveness of DMTS as a larvicide over potassium iodide, even though the compounds contain iodine in common.

[0051] <Test Example 4>

Most of the commercial larvicides are not effective over older larvae, such as those at a fourth larval stage. While Test Examples 1, 2 and 3 were carried out on mosquito larvae at a third larval stage, Test Example 4 was carried out in order to demonstrate the effect of DMTS on mosquito larvae at a forth larval stage.

Four replicates of mosquito larvae at a late fourth larval stage (n=100) were introduced into treatment cups containing a mixture of water (249 mL) and ethanol (1mL), and LC99 which was found 56.38 mg/L was added to the treatment cups. Larval mortality was recorded at 24 hours' exposer after the addition of DMTS-CD at a temperature of 25-30°C and a relative humidity of 70 to 90%. The results are shown in Table 4.

[0052] Table 4

DMTS in DMTS-CD (56.38 mg/L)	Number of death larvae				Mean Mortality [%]	SD (±)
	R1	R2	R3	R4		
Larvae, L4	25	25	25	25	100	0
Control	0	0	0	0	0	0

[0053] As shown in Table 4, DMTS was found effective towards mosquito larvae at a fourth larval stage. The results show the advantage of DMTS over commercial larvicides to control older larvae.

CLAIMS

Claim 1. A larvicide for controlling mosquito larvae, the larvicide comprising diiodomethyl-p-tolylsulfone as an active ingredient.

Claim 2. The larvicide according to claim 1, wherein the diiodomethyl-p-tolylsulfone is solubilized with respect to water.

Claim 3. The larvicide according to claim 1 or claim 2, wherein the diiodomethyl-p-tolylsulfone forms an inclusion compound with a cyclodextrin.

Claim 4. The larvicide according to any one of claim 1 to claim 3, wherein the mosquito larvae is at a fourth larval stage.

Claim 5. A biocontrol agent comprising diiodomethyl-p-tolylsulfone as an active ingredient, the diiodomethyl-p-tolylsulfone being solubilized with respect to water.

Claim 6. The biocontrol agent according to claim 5, wherein the diiodomethyl-p-tolylsulfone forms an inclusion compound with a cyclodextrin.

Claim 7. The biocontrol agent according to claim 5 or claim 6, which is for controlling a target that lives in an environment in which water is present.

Claim 8. A biocontrol method, comprising applying the larvicide according to any one of claim 1 to claim 4 or the biocontrol agent according to any one of claim 5 to claim 7 to an environment in which water is present.