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(54) Title: SOLUBLE LIQUID COMPOSITIONS COMPRISING FLONICAMID AND USES THEREOF

(57) Abstract: The present invention provides an insecticide liquid stable composition comprising high concentration of flonicamid dissolved in a particular solvent system, and optionally one or more particular adjuvants, which is useful in controlling pest such as insects including an aphid, a mealybug, and a white fly.

SOLUBLE LIQUID COMPOSITIONS COMPRISING FLONICAMID AND USES THEREOF

TECHNICAL FIELD

[0001] The present invention provides an insecticide liquid stable composition comprising high concentration of flonicamid dissolved in a particular solvent system, and optionally one or more particular adjuvants, which is useful in controlling pest such as insects.

BACKGROUND ART

[0002] The extensive use of conventional insecticides (organochlorines, organophosphates, carbamates, and synthetic pyrethroids) has resulted in the development of severe pest resistance to insecticides, outbreaks of secondary pests, objectionable pesticide residues, direct hazard to the users, and adverse effect on environment and non-target organisms.

[0003] New insecticides, having good controlling properties of insect pests at low rates or doses, high level of selectivity, and greater specificity to target pests along with low toxicity to non-target organisms and the environment, replaced many old/conventional compounds. Such compounds are also less likely to cause outbreaks of secondary pests, extremely helpful for delaying resistance in key pests such as whiteflies and aphids, and have no cross-resistance with the old and already established insecticides (Kodandaram *et al.*, **2010**).

[0004] For instance, flonicamid (*N*-(cyanomethyl)-4-(trifluoromethyl)pyridine-3-carboxamide) is a highly selective insecticide belonging to the pyridine carboxamide group. Although it does not control coleopteran, lepidopteran, or dipteran insects and mites, it is effective against both nymph and adult stages of aphids. At the recommended doses under field conditions (50-100 gram active ingredient/hectare or 2.5-10 gram/100 L), this compound is highly effective in controlling a broad range of aphid species as well as other species of sucking insects such as greenhouse whitefly (*Trialeurodes vaporariorum*), yellow tea thrips (*Scirtothrips dorsalis*), Indian cotton leafhopper (*Amrasca biguttula*), tea green leafhopper (*Empoasca onukii*), tarnished plant bug (*Lygus lineolaris*), potato psyllid (*Bactericera cockerelli*), and brown rice planthopper (*Nilaparvata lugens*), while at the same time it does not negatively impact beneficial arthropods such as predatory mites,

parasitic wasps, predatory insects, and pollinators. Specifically, within 30 minutes after treatment, this compound inhibits the feeding behavior of aphids without noticeable poisoning symptoms such as convulsions or knockdown.

[0005] The precise mechanism of action of flonicamid is under investigation, yet it is clearly different from any conventional one, and its mode of action is different from other insecticides such as neonicotinoids, pymetrozine, and pyri-uquinazon. Actually, flonicamid exhibits no response against the existing insecticide targets such as acetylcholine esterase, and the sodium channel. In addition, although sharing structural similarities with neonicotinoid insecticides, flonicamid has no effect on nicotinic acetylcholine receptors from *Periplaneta americana*, *D. melanogaster*, or *Heliothis virescens* as well (Morita *et al.*, 2007).

[0006] Currently, flonicamid is the only insecticide that belongs to Insecticide Resistance Action Committee (IRAC) Group 29 with an undefined target site of action. It rapidly inhibits the feeding behavior of aphids, and has better action through ingestion than by contact.

[0007] Leaf dip assays in the laboratory showed that flonicamid is highly effective against every 15 field clones of *Aphis gossypii* tested, while having no cross-resistance to conventional insecticides such as organophosphates, carbamates, or pyrethroids. Flonicamid showed a long-lasting efficacy, controlling aphids for three to four weeks at 50 ppm. It possesses excellent translaminar and systemic activity through xylem vessels (Morita *et al.*, 2014).

[0008] Most of the currently available flonicamid-based products are solid formulations in the form of wettable or soluble granules (comprising 500 g/kg flonicamid); however, the main problem associated with using such solid formulations is the dust which is formed within the product-containing package prior to use.

[0009] As previously published (Ren *et al.*, 2018), flonicamid is soluble in anhydrous dimethyl sulfoxide (DMSO). Yet, and as in fact shown by the present inventors, DMSO-based formulations containing high concentration, e.g., about 22.5% by weight, of flonicamid freeze at low temperatures (e.g., at a temperature of -10°C) due to the melting point of DMSO (19°C).

SUMMARY OF INVENTION

[0010] It has now been found, in accordance with the present invention, that flonicamid in high concentrations dissolve in a particular solvent system consisting of DMSO and an additional solvent selected from Rhodiasolv® PolarClean (Rhodia Poliamida e Especialidades Ltd.), *N*-butyl-2-pyrrolidone (NBP), and Agnique® AMD 3L (BASF) to thereby form highly stable soluble liquid (SL) formulations comprising high concentrations, e.g., from about 15% to about 30% by weight, of said insecticide. Such SL formulations maintain their stability even after the addition of one or more particular agriculturally acceptable adjuvants, wherein the adjuvant-containing formulations obtained are highly effective in controlling insects such as tobacco whiteflies.

[0011] For example, a particular such formulation comprising 22.3% by weight flonicamid, dissolved in a solvent system consisting of DMSO and Rhodiasolv® PolarClean at a weight ratio of 1:1.6, respectively, was shown to be stable at room temperature as well as at a lower temperature of up to -10°C, and after the addition of an adjuvant, more specifically Lutensol® TO 8 (BASF), Atplus™ UEP-100 (Croda Crop Care), Silwet® L-77 (Momentive), or Tween 24, in an amount of 22.3% by weight, was found to be more effective, i.e., showed higher percentage in adult *Bemicia tabaci* mortality 72 hours after application to whole plants, as compared to the commercially available product Teppeki® (comprising wettable granules containing 500 g/kg flonicamid).

[0012] In one aspect, the present invention thus provides an insecticide composition comprising flonicamid in an amount of from about 15% to about 30%, preferably from about 20% to about 27%, by weight; and a solvent system (also referred to herein as a solvent combination) comprising DMSO and an additional solvent selected from pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester, *N*-(C_1-C_8)alkyl pyrrolidone, preferably *N*-(C_1-C_8)alkyl-2-pyrrolidone, an amide of the formula R-C(O)-N(CH_3)$_2$, wherein R is (C_1-C_{12})alkyl optionally substituted, preferably at position α to the amide group, with a group selected from -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2, a commercially available product comprising (e.g., consisting essentially of) it, and a mixture thereof.

[0013] In certain embodiments, said solvent system comprises DMSO and an additional solvent selected from pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester; NBP; *N*,*N*-dimethyl lactamide; a commercially available product comprising, or consisting

essentially of, pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester, NBP, or *N*,*N*-dimethyl lactamide; or a mixture thereof.

[0014] In a particular such aspect, said insecticide composition further comprises at least one adjuvant each independently selected from an alcohol ethoxylate, a sorbitan ester alkoxylate, an alkoxylated polyol ester, a trisiloxane ethoxylate, and a commercially available product comprising it; and optionally an anti-foaming agent, wherein preferred such compositions comprise, as said adjuvant, isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8), or a mixture of polyethylene glycol (C_{11}-C_{14})alkyl ethers enriched therewith or a commercially available product comprising it (e.g., Genapol® X-080).

[0015] In other aspects, the present invention relates to methods for using insecticide compositions as defined above, i.e., SL formulations containing high concentrations of flonicamid. In one particular such aspect, disclosed herein is a method of controlling pest, such as an insect, comprising applying to a locus where control of said pest is desired, such as a field of crop, an effective amount of an insecticide composition as defined herein. In another particular such aspect, disclosed herein is a method for the protection of a plant propagation material from an attack by a pest such as an insect, comprising treating the propagation material or the site where the propagation material is to be planted with an effective amount of an insecticide composition as defined herein.

BRIEF DESCRIPTION OF DRAWINGS

[0016] **Fig. 1** shows aphids' mortality (%) 72 hours post treatment with several flonicamid-based formulations (SL250) comprising various build-in adjuvants or mixed with tank mix adjuvants as compared to the commercial product Teppeki®, at two application rates (5 and 25 ppm) performed on detached cucumber leaves.

[0017] **Fig. 2** shows the biological efficacy (dose response) of various flonicamid (25 ppm)-based SL formulations having different ratios of Silwet® L-77 adjuvant (flonicamid:adjuvant 1:0.25-1) as compared to the commercial product Teppeki® on aphids' mortality (%) 72 hours post treatment.

DETAILED DESCRIPTION

[0018] In one aspect, disclosed herein is a composition comprising: (a) flonicamid as an insecticide, in an amount of from about 15% to about 30%, preferably from about 20% to

about 27%, by weight; and (b) a solvent system comprising DMSO and an additional agriculturally acceptable solvent selected from pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester; *N*-(C_1-C_8)alkyl pyrrolidone; an amide of the formula R-C(O)-$N(CH_3)_2$, wherein R is (C_1-C_{12})alkyl optionally substituted, preferably at position α to the amide group, with a group selected from -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2; a commercially available product comprising said pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester, said *N*-(C_1-C_8)alkyl pyrrolidone, or said amide of the formula R-C(O)-$N(CH_3)_2$; and a mixture thereof.

[0019] The term "alkyl" typically means a linear or branched hydrocarbyl having, e.g., 1-12 carbon atoms and includes, e.g., methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, sec-butyl, isobutyl, *tert*-butyl, *n*-pentyl, 2,2-dimethylpropyl, *n*-hexyl, *n*-heptyl, *n*-octyl, and the like. Preferred are (C_1-C_8)alkyls or (C_1-C_6)alkyls, more preferably methyl, ethyl, propyl, isopropyl, butyl, and *tert*-butyl. The alkyl may optionally be substituted by one or more groups (substituents) each independently selected from, e.g., -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2.

[0020] Particular solvents of the formula *N*-(C_1-C_8)alkyl pyrrolidone referred to herein are those of the formula *N*-(C_1-C_8)alkyl-2-pyrrolidone, preferably wherein said alkyl is (C_1-C_4)alkyl, e.g., NBP (wherein said alkyl is butyl).

[0021] Particular solvents of the formula R-C(O)-$N(CH_3)_2$ referred to herein are those wherein group R is (C_1-C_4)alkyl, e.g., methyl, ethyl, propyl, or butyl, substituted at any carbon atom thereof with one or more groups each independently selected from -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2, but preferably with one of said groups, e.g., -OH, at position α to the amide group, such as *N*,*N*-dimethyl lactamide.

[0022] In certain embodiments, the additional solvent composing, together with DMSO, the solvent system referred to herein, is a compound as defined above, i.e., pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester; *N*-(C_1-C_8)alkyl pyrrolidone, preferably *N*-(C_1-C_8)alkyl-2-pyrrolidone such as NBP; or an amide of the formula (C_1-C_{12})alkyl-C(O)-$N(CH_3)_2$ optionally substituted at the alkyl group, preferably at position α to the amide group, with a group as defined above, e.g., *N*,*N*-dimethyl lactamide, a commercially available product consisting essentially of said compound, or a mixture thereof. The term "consisting essentially of" as used herein with respect to said commercially available product means that said product comprises at least 90%, e.g., at least about 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, by weight, of said compound, such that any

other material if included within said solvent does not affect the basic physical and chemical properties of said compound.

[0023] The term "solvent system" or "solvent combination", used herein interchangeably, thus refers to a combination of two or more solvents, wherein one of said solvents is DMSO, and the other solvent is a compound selected from pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester, *N*-(C_1-C_8)alkyl pyrrolidone, preferably *N*-(C_1-C_8)alkyl-2-pyrrolidone, and an amide of the formula (C_1-C_{12})alkyl-C(O)-N(CH_3)$_2$ optionally substituted at the alkyl group, preferably at position α to the amide group, with a group selected from -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2; a commercially available product comprising, e.g., at least 90%, but preferably at least about 92%, 94%, 96%, 98%, or 99%, by weight, i.e., consisting essentially of, one of said compounds; and a mixture thereof. Examples of commercially available products consisting essentially of pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester include, e.g., Rhodiasolv® PolarClean; and examples of commercially available products consisting essentially of *N*,*N*-dimethyl lactamide include, e.g., Agnique® AMD 3L.

[0024] As shown herein, such a solvent system, e.g., a solvent combination comprising DMSO and Rhodiasolv® PolarClean at a weight ratio of about 1:1.6, respectively, is capable of dissolving high concentrations of flonicamid and to form a soluble liquid flonicamid formulation that is stable at both room temperature and freezing conditions (-10°C).

[0025] In certain embodiments, the ratio between the DMSO and the additional solvent(s) composing the solvent system referred to herein is from about 2:1 to about 1:4, e.g., about 1.8:1, about 1.6:1, 1.4:1, 1.2:1, about 1:1, about 1:1.2, about 1:1.4, about 1:1.5, about 1:1.6, about 1:1.75, about 1:1.8, about 1:2, about 1:2.2, about 1:2.4, about 1:2.6, about 1:2.8, about 1:3, about 1:3.2, about 1:3.4, about 1:3.6, or about 1:3.8, respectively, by weight.

[0026] In certain embodiments, the solvent system referred to herein comprises DMSO and pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester or a commercially available product comprising, or consisting essentially of, pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester (e.g., Rhodiasolv® PolarClean), as an additional solvent. In particular such embodiments, the ratio between the DMSO and the additional solvent is from about 2:1 to about 1:4, e.g., about 1.8:1, about 1.6:1, 1.4:1, 1.2:1, about 1:1, about 1:1.2, about 1:1.4, about 1:1.5, about 1:1.6, about 1:1.75, about 1:1.8,

about 1:2, about 1:2.2, about 1:2.4, about 1:2.6, about 1:2.8, about 1:3, about 1:3.2, about 1:3.4, about 1:3.6, or about 1:3.8, respectively, by weight.

[0027] In certain embodiments, the composition of the invention according to any one of the embodiments defined above further comprises at least one, e.g., two, three, four, or more, adjuvant each independently selected from an alcohol ethoxylate or a commercially available product comprising it, such as a polyethylene glycol (C_{11}-C_{14})alkyl ether, e.g., isotridecanol polyglycol ether 8 ethylene oxide (e.g., Lutensol® TO 8), or a mixture of polyethylene glycol (C_{11}-C_{14})alkyl ethers enriched therewith (e.g., Genapol® X-080), and polyethylene glycol octylphenyl ether (e.g., Triton™ X-100); a sorbitan ester alkoxylate or a commercially available product comprising it, such as Tween 20, Tween 21, Tween 22, Tween 23, Tween 24, and Tween 28; an alkoxylated polyol ester or a commercially available product comprising it, such as an ester of (C_{18})unsaturated fatty acid with a polyethylene glycol ether with trimethylolpropane (3:1) (e.g., Atplus™ UEP-100); and a trisiloxane ethoxylate or a commercially available product comprising it, such as 3-(2-methoxyethoxy)propyl-methyl-bis(trimethylsilyloxy) silane (e.g., Silwet® L-77) (referred to herein as "***SL flonicamid-adjuvant-based composition***").

[0028] Adjuvants are auxiliaries, which are added to agricultural compositions so as to increase the effectiveness of one or more of the agrochemical agents comprised therein, e.g., a herbicide, insecticide, and/or fungicide. The increase in the efficacy of said agrochemical agent induced by the presence of said adjuvant may be due to several possible modes of action such as facilitated wetting, penetration, or better retention. Adjuvants added to a spray liquid in a tank before application are called "tank-mix adjuvants", and adjuvants incorporated within the formulation as provided are called "built-in" or "in-can adjuvants".

[0029] In particular such embodiments, the at least one adjuvant comprised within the composition of the invention each independently is isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8), or a mixture of polyethylene glycol (C_{11}-C_{14})alkyl ethers enriched therewith or a commercially available product comprising it (e.g., Genapol® X-080). More specific such compositions are those comprising isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8) as the adjuvant.

[0030] In certain embodiments, the insecticide composition disclosed herein comprises a solvent system as defined above, and at least one adjuvant as defined in any one of the

embodiments above, e.g., isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8). Particular such compositions are those wherein the ratio between the flonicamid and the adjuvant in said composition is from about 1:0.5 to about 1:2, e.g., from about 1:0.7 to about 1:1.5, from about 1:0.8 to about 1:1.4, from about 1:0.9 to about 1:1.3, from about 1:1 to about 1:1.2, or about 1:1, respectively, by weight. More particular such compositions are those wherein the solvent system comprises DMSO in an amount of from about 17% to about 27%, preferably from about 20% to about 24%, or about 21.5%, by weight, and pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester or a commercially available product comprising (or consisting essentially of) it (e.g., Rhodiasolv® PolarClean), in an amount of from about 25% to about 40%, preferably from about 27% to about 37%, from about 30% to about 35%, or about 32%, by weight.

[0031] In certain embodiments, the SL flonicamid-adjuvant-based composition of the invention, as defined according to any one of the embodiments above, further comprises an anti-foaming agent.

[0032] The term "anti-foaming agent" or "defoamer" as used herein interchangeably refers to a chemical agent that is added to a composition so as to prevent, attenuate, or counter foam generation in the composition. Generally, such agents have surface active properties, are insoluble in the foaming medium, easily spreadable on the foamy surface, possess affinity to the air-liquid surface, and destabilize the foam lamellas which rupture the air bubbles and break down the surface foam.

[0033] Non-limiting examples of anti-foaming agents include a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling, or a commercially available product comprising it such as Geronol AF 80; a mineral oil-based defoamer or a commercially available product comprising it such as Lucrafoam® PDT; a blend of special wax, hydrophobic silica, and mineral oil or a commercially available product comprising it such as DEE FO® 3010E/50; a silicon emulsion or a commercially available product comprising it such as Silfoam® SE 47, Silfoam® SRE, Silcolapse® RG 12, and SAG 1572; a polydimethyl siloxane emulsion or a commercially available product comprising it such as SAG 10E; and a silicone-based compound or a commercially available product comprising it such as Silcolapse™ 910 and Xiameter® ACP-1000.

[0034] In certain embodiments, the anti-foaming agent comprised within the composition of the invention constitutes from about 0.5% to about 3%, e.g., from about

0.75% to about 2.5%, from about 1% to about 2%, from about 1.25% to about 1.75%, or about 1.5%, by weight of said composition.

[0035] In certain embodiments, disclosed herein is an insecticide composition comprising flonicamid in an amount of from about 15% to about 30% by weight; a solvent system comprising DMSO in an amount of about from 17% to about 27% by weight, and pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester or a commercially available product comprising (or consisting essentially of) it (e.g., Rhodiasolv® PolarClean), in an amount of from about 25% to about 40% by weight; isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8), as an adjuvant, in an amount of from about 15% to about 30% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling or a commercially available product comprising it such as Geronol AF 80, as an anti-foaming agent, in an amount of from about 0.5% to about 3% by weight. In particular such embodiments, the insecticide composition disclosed herein comprises flonicamid in an amount of from about 20% to about 27% by weight; DMSO in an amount of about from 20% to about 24% by weight; pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester or a commercially available product comprising (or consisting essentially of) it (e.g., Rhodiasolv® PolarClean), in an amount of from about 30% to about 35% by weight; isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8), in an amount of from about 20% to about 27% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling or a commercially available product comprising it such as Geronol AF 80, in an amount of from about 1.25% to about 1.75% by weight. More particular such compositions are those comprising flonicamid in an amount of about 22.5% by weight; DMSO in an amount of about 21.5% by weight; pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester or a commercially available product comprising (or consisting essentially of) it (e.g., Rhodiasolv® PolarClean), in an amount of about 32% by weight; isotridecanol polyglycol ether 8 ethylene oxide or a commercially available product comprising it (e.g., Lutensol® TO 8), in an amount of about 22.5% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling or a commercially available product comprising it such as Geronol AF 80, in an amount of about 1.5% by weight.

[0036] In other aspects, the present invention relates to methods for using an insecticide composition as defined in any one of the embodiments above, i.e., SL formulations containing high concentrations of flonicamid.

[0037] In one particular such aspect, disclosed herein is a method of controlling pest comprising applying to a locus where control of said pest is desired an effective amount of an insecticide composition as defined in any one of the embodiments above. In certain embodiments, the pest controlled by this method is an insect such as an aphid, a mealybug, and a white fly.

[0038] In another particular such aspect, disclosed herein is a method for the protection of a plant propagation material from an attack by a pest such as an insect, comprising treating the propagation material or the site where the propagation material is to be planted with an effective amount of a composition as defined herein.

[0039] The term “locus” as used herein refers not only to areas where the pest such as an insect may already be developed, but also to areas that have not yet been attacked by said pest, and to areas under cultivation. Locus includes the crop and propagation material of the crop (all the generative parts of the crop such as seeds and vegetative plant material such as cuttings and tubers, which can be used for the multiplication of the plant). Examples of propagation material of the crop include seeds, tubers, spores, corms, bulbs, rhizomes, sprouts basal shoots, stolons, buds and other parts of plants, including seedlings and young plants, which could be transplanted after germination or after emergence from soil. Locus also includes the area surrounding the crop and the growing media of the crop, such as soil and crop field.

[0040] In certain embodiments, the locus treated by the method disclosed herein above is a field of crop. The term “crop” (or “plant”) as used herein refers to whole plants, plant organs (e.g., leaves, stems, twigs, roots, trunks, limbs, shoots, fruits, etc.), plant cells, or plant seeds. Non-limiting examples of crops are oilseed rape (OSR), cotton, rice, banana, potato, coffee, sugar cane, citrus, beans, sunflower, apple, corn, soybean, wheat, barley, oats, chickpeas, fruit trees, nut trees, lentils, and grain sorghum.

[0041] Unless otherwise indicated, all numbers expressing, e.g., amounts of components or ratios between components, used in this specification, are to be understood as being modified in all instances by the term "about". Accordingly, unless indicated to the contrary, the numerical parameters set forth in this specification are approximations that

may vary by up to plus or minus 10% depending upon the desired properties to be obtained by the present invention.

[0042] The invention will now be illustrated by the following non-limiting Examples.

EXAMPLES

Materials and Methods

[0043] ***Materials***. Dimethyl sulfoxide (DMSO; >99% purity) was purchased from Hubei Xingfa Chemicals Group Co; *N*-butyl-2-pyrrolidone (NBP) was purchased from Clariant AG; Agnique® AMD 3L (*N*,*N*-dimethyl lactamide) was purchased from BASF; Armid® FMPC (consisting of 80.0% by weight *N*-formyl morpholine and 20.0% by weight propylene carbonate) was purchased from Nouryon; flonicamid was purchased from Jingbo Agrochemicals Technology Co., Ltd.; and Rhodiasolv® PolarClean was purchased from Rhodia Poliamida e Especialidades Ltd.

[0044] ***Preparation of flonicamid-based soluble liquid (SL) formulations***. A solid flonicamid was added to a stirred mixture of the appropriate solvent system, and the stirring continued until complete dissolution of the solid occurred. Then, if desired, an appropriate adjuvant was added with continuous stirring followed by the addition of a defoamer. The obtained clear solution was then filtered through a 5-micron filter.

Example 1. Solubility of flonicamid in various solvents

[0045] The solubility of flonicamid in various solvents was tested and shown in **Table 1**.

Table 1

Solvent	Solubility w/w (%)
butyl lactate	negative
acetophenone	negative
dipropylene glycol	negative
Agnique® AMD 3L	~29%
carbitol (diethylenglycol ethyl ether)	~15%
Stepsol® MET-10U	~10%
Rhodiasolv® PolarClean	23%
Armid® FMPC	23%
2-ethylhexanol	negative
butyl carbitol (diethylenglycol butyl ether)	slightly dissolved
Genagen® 4166	~15%
N-butyl-2-pyrrolidone (NBP)	~29%
propylene glycol	negative
N-octyl-2-pyrrolidone (NOP)	15%
DMSO	43%

Example 2. The stability of flonicamid-based soluble liquid (SL) formulations comprising different solvent systems

[0046] The stability of flonicamid-based SL formulations comprising flonicamid in an amount of 22.3% and various solvent systems is shown in **Table 2**.

Table 2

Solvent system	stability at 22°C	stability at 0°C	stability at -10°C	stability at diluted conditions
DMSO	stable	pass	freeze	pass
DMSO+PolarClean (1:1.6 by weight, respectively)	stable	pass	pass	pass
DMSO+NBP (1:1.6 by weight, respectively)	stable	pass	pass	pass
DMSO+Armid® FMPC (1:1.6 by weight, respectively)	stable	fail	fail	pass
DMSO+Agnique® AMD 3L (1:1.6 by weight, respectively)	stable	pass	pass	pass
Agnique® AMD 3L	precipitate	fail	fail	N/A
PolarClean	insoluble	N/A		
NBP	stable	fail	fail	pass
Armid® FMPC	insoluble	N/A		
PolarClean+Armid® FMPC (1:1.6 by weight, respectively)	insoluble	N/A		
PolarClean+Agnique® AMD 3L (1:1.6 by weight, respectively)	insoluble	N/A		
PolarClean+NBP (1:1.6 by weight, respectively)	insoluble	N/A		
NBP+Armid® FMPC (1:1.6 by weight, respectively)	precipitate	fail	fail	pass

N/A - not available.

Example 3. Preparation of a particular flonicamid-based SL formulation

[0047] A flonicamid-based formulation comprising DMSO and Rhodiasolv® PolarClean as a solvent system; Lutensol® TO 8 as an adjuvant; and Geronol AF 80 as an antifoaming agent (see **Table 3**), was prepared as described in Materials and Methods.

Table 3

Component	v/w (%)	w/w (%)
flonicamid	250	22.32
Geronol AF 80	16.8	1.5
Lutensol® TO 8	250	22.32
DMSO	240	21.43
Rhodiasolv® PolarClean	up to 100%	up to 100%

Example 4. The stability of flonicamid-based SL formulation with various adjuvants

[0048] The stability of flonicamid-based SL formulations comprising flonicamid (22.3%), DMSO (21.4%), Rhodiasolv® PolarClean (34%), and different adjuvants (22.3%) was evaluated, and the results are summarized in **Table 4**. The cold stability was evaluated at -10ºC and 0ºC, and the "compatibility" parameter indicates whether the tested formulation is compatible, i.e., clear at room temperature for at least one week, or is non-compatible, i.e., hazy, turbid and/or contains precipitants.

Table 4

Adjuvant	Chemical class	Compatibility	Cold stability	Dilution stability
Emulsogen EL-360 (Clariant AG)	Castor oil ethoxylate	Yes	pass	fail
Adsee 1250 HV	Quaternary amine ethoxylate blend	Yes	fail	N/A
Genapol® X-080	Alcohol ethoxylate	Yes	pass	pass
Tween 23	Sorbitan ester alkoxylate	Yes	pass (0ºC) fail (-10ºC)	pass
Lutensol® TO 8	Alcohol ethoxylate	Yes	pass	pass
Break thru SP133	Polyglycerol ester	Yes	fail	N/A
Atplus® 245	Alkoxylated alcohol	Yes	pass	fail
Ethylan 995	Fatty alcohol alkoxylate	Yes	pass	fail
Adsee C80W	Cocoamine propyl amide	Yes	fail	N/A
Synergen® 848	Alkylated copolymers of ethylene oxide and propylene oxide	Yes	pass	fail
Synergen GL 5	Copolymer of glycerol/coconut fatty acid/phthalic acid anhydride	No	N/A	N/A
Synergen® OS	Cross-linked polyglycerol ester in methylated seed oil	No	N/A	N/A
Synergen® SOC	Blend of fatty acid esters and fatty alcohol ethoxylates	No	N/A	N/A
Synergen™ GA	Glucamide in aqueous/glycolic solution	No	N/A	N/A
Atplus™ UEP-100	Alkoxylated polyol ester	Yes	pass	pass
Synergen™ ME	Microemulsion of alkylpolyglucoside (APG) and alcohol ethoxylates	No	N/A	N/A
Silwet® L-77	Trisiloxane ethoxylate	Yes	pass	pass

Example 5. Bio-efficacy trials of flonicamid-based SL formulations

[0049] In the first trial, the biological efficacies of various flonicamid-based SL formulations having different adjuvants (either adjuvants comprised within the

formulation, i.e., built-in adjuvants, or tank mix adjuvants), wherein the ratio between the flonicamid and the adjuvant is about 1:1 by weight have been compared to that of the commercially available flonicamid-based product Teppeki® (water dispersible granules (WG) containing 500g/kg flonicamid), when applied on detached leaves on aphids' mortality.

[0050] ***Preparation of the tested flonicamid-based SL formulations comprising build-in adjuvants***. The tested formulations comprising build-in adjuvants were prepared as described above and the content of the tested formulations is shown in **Table 5**. After preparation, the formulations were diluted with water to obtain samples wherein the final concentration of flonicamid was 5 and 25 ppm, respectively.

[0051] ***Preparation of the tested flonicamid-based SL formulations with tank mix adjuvants***. The SL250 formulation depicted in **Table 5** was diluted with water to obtain a diluted formulation comprising flonicamid in a concentration of 5 or 25 ppm. Then, an appropriate adjuvant, i.e., methyl soyate or SK Enspray 99 (Hanyu Energy), at the same concentration (i.e., 5 or 25 ppm) was added.

Table 5

Component	Name of formulation				
	SL250	SL250+ Lutensol	SL250+ Silwet L-77	SL250+ Tween 24	SL250+ Atplus™ UEP-100
Flonicamid	22.3%	22.3%	22.3%	22.3%	22.3%
DMSO	30%	21.4%	21.4%	21.4%	21.4%
PolarClean	47.7%	34%	34%	34%	34%
Silwet® L-77			22.3%		
Lutensol® TO 8		22.3%			
Tween 24				22.3%	
Atplus™ UEP-100					22.3%

[0052] ***Results***. **Fig. 1** shows the mortality of aphids following the different treatments at two application rates (5 and 25 ppm) performed on detached cucumber leaves. The SL250+Silwet L-77, SL250+Lutensol, and SL250+SK Enspray 99 (tank mix adjuvant) formulations showed about 70-90% of aphids mortality at a rate of 25 ppm and were more potent as compared to the commercial product tested at this rate. The other tested formulations showed an improved efficacy of about 50-70% of aphids mortality at a rate of 5 ppm as compared to the commercial product at this rate.

[0053] In the second trial, the biological efficacy of various flonicamid-based SL formulations having different ratios of Silwet® L-77 adjuvant on aphids' mortality was tested.

[0054] ***Preparation of flonicamid-based SL formulations having different ratios of Silwet® L-77 adjuvant***. The SL250 and SL250+Silwet L-77 formulations depicted in **Table 5** were diluted with water and mixed in appropriate ratios to obtain formulations with 25 ppm flonicamid and various ratios of adjuvant, i.e., from 0 to 25 ppm.

[0055] ***Results***. **Fig. 2** shows that there is a threshold for efficacy improvement, i.e., the efficacy of the tested formulations containing various amounts of adjuvant was constant and significantly increased only when the ratio between the flonicamid and adjuvant was 1:1.

[0056] In the third trial, the biological efficacies of four flonicamid-based formulations containing four different build-in adjuvants, two flonicamid-based formulations containing two different tank mix adjuvants, and a flonicamid-based formulation without an adjuvant, have been compared to that of the commercially available flonicamid-based product Teppeki®, in a contact and sucking assay with adult silverleaf whitefly *Bemisia tabaci*. The content of the tested flonicamid-based formulations is depicted in **Table 5**.

[0057] ***Assay method***. 20 adult whiteflies were used and 4-6 replicates per treatment were performed. Foliar dip prior to the introduction of the pest by "leaf on-clip" cages.

[0058] ***Formulation preparation***. Formulations with and without build-in adjuvants and commercial standard were prepared with tap water only by mixing all the components of the formulation with magnetic stirrer until homogeneous solutions were obtained.

[0059] ***Preparation of formulations containing tank mix adjuvants***. An appropriate adjuvant was added to water under stirring until a stable emulsion was obtained. Then, flonicamid was added to obtain a final concentration of 2000 ppm of flonicamid.

[0060] ***Tank mix ratios***. Ratios of flonicamid to adjuvant of 1-3.6:1 were used.

[0061] ***Assessment times***. Mortality was determined 72 hours after the exposure of the whiteflies to the treated plants.

[0062] ***Results***. **Table 6** shows the effect of the commercial Teppeki®, containing only flonicamid, compared to that of each one of the formulations (the adult mortality was

determined 72h after treatment). As clearly shown, the effect of the flonicamid-based formulations was faster than the that of the commercial Teppeki®. Adding an adjuvant to flonicamid-based formulations significantly increased the effectiveness of the flonicamid. It seems that treatment number 3 was the most effective one; however, the other formulations were not statistically different from each other. As further shown, the effect of each one of the adjuvants alone did not differ significantly from the water control.

Table 6

Entry	Treatment (2000 ppm)	comment	Adult mortality ± SEM (%)
1	Teppeki® (WG containing 500 g/kg flonicamid)	Commercial standard	53±6
2	SL 250	No adjuvant (blank)	70±5.8
3	SL 250+Silwet L-77		93±3.4
4	SL 250+Atplus UEP 100		78±7.5
5	SL 250+Lutensol		87±3
6	SL 250+Tween 24		88±2
7	SL 250+methyl soyate as tank mix adjuvant	flonicamid:adjuvant 3:1	91±2
8	SL 250+SK oil as tank mix adjuvant	flonicamid:adjuvant 3.6:1	88±3
9	methyl soyate		12±1.5
10	SK Enspray 99		11±0.5
0	Tap water	control	11.2±0.6

Percentage mortality was corrected for control mortality with Abbott's formula. The effect of the formulations on *B. tabaci* adults was compared 72h after treatment. Treatments were subjected to one-way analysis of variance (ANOVA); Percentage data were transformed (angular transformation=Arcsine) before statistical analysis. Means followed by a common letter do not differ significantly at $p>0.05$.

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CLAIMS

1. An insecticide composition comprising flonicamid in an amount of from about 15% to about 30% by weight; and a solvent system comprising dimethyl sulfoxide (DMSO) and an additional solvent selected from pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester, *N*-(C_1-C_8)alkyl pyrrolidone, an amide of the formula R-C(O)-N(CH_3)$_2$ wherein R is (C_1-C_{12})alkyl, and a mixture thereof.

2. The composition of claim 1, wherein said *N*-(C_1-C_8)alkyl pyrrolidone is *N*-(C_1-C_8)alkyl-2-pyrrolidone; and/or R is substituted, preferably at position α to the amide group, with a group selected from -OH, -O-(C_1-C_6)alkyl, -CN, and -NO_2.

3. The composition of claim 2, wherein said additional solvent is pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester; *N*-butyl-2-pyrrolidone (NBP); *N*,*N*-dimethyl lactamide; or a mixture thereof.

4. The composition of claim 3, wherein said additional solvent is pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester.

5. The composition of any one of claims 1-4, wherein the ratio between the DMSO and the additional solvent in said solvent system is from about 2:1 to about 1:4, from about 1:1 to about 1:2, or from about 1:1.5 to about 1:1.75, respectively, by weight.

6. The composition of any one of claims 1-5, further comprising at least one adjuvant each independently selected from an alcohol ethoxylate such as a polyethylene glycol (C_{11}-C_{14})alkyl ether and polyethylene glycol octylphenyl ether, a sorbitan ester alkoxylate, an alkoxylated polyol ester such as an ester of (C_{18})unsaturated fatty acid with a polyethylene glycol ether with trimethylolpropane (3:1), and a trisiloxane ethoxylate such as 3-(2-methoxyethoxy)propyl-methyl-bis(trimethylsilyloxy)silane.

7. The composition of claim 6, wherein said at least one adjuvant each independently is isotridecanol polyglycol ether 8 ethylene oxide, or a mixture of polyethylene glycol (C_{11}-C_{14})alkyl ethers enriched therewith.

8. The composition of claim 7, wherein said adjuvant is isotridecanol polyglycol ether 8 ethylene oxide.

9. The composition of any one of claims 6-8, wherein the ratio between said flonicamid and said adjuvant is from about 1:0.5 to about 1:2, respectively, by weight.

10. The composition of any one of claims 6-9, wherein the solvent system comprises DMSO in an amount of from about 17% to about 27% by weight, and pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester in an amount of from about 25% to about 40% by weight.

11. The composition of claim 10, wherein the solvent system comprises DMSO in an amount of from about 20% to about 24% by weight, and pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester in an amount of from about 30% to about 35% by weight.

12. The composition of any one of claims 6-11, further comprising an anti-foaming agent.

13. The composition of claim 12, wherein said anti-foaming agent is a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling; a mineral oil-based defoamer; a blend of wax, hydrophobic silica, and mineral oil; a silicon emulsion; a polydimethyl siloxane emulsion; a silicone-based compound; or a mixture thereof.

14. The composition of claim 12 or 13, wherein said anti-foaming agent constitutes from about 0.5% to about 3% by weight of said composition.

15. The composition of claim 14, comprising flonicamid in an amount of from about 15% to about 30% by weight; DMSO in an amount of about from 17% to about 27% by weight; pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester in an amount of from about 25% to about 40% by weight; isotridecanol polyglycol ether 8 ethylene oxide in an amount of from about 15% to about 30% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling in an amount of from about 0.5% to about 3% by weight.

16. The composition of claim 15, comprising flonicamid in an amount of from about 20% to about 27% by weight; DMSO in an amount of about from 20% to about 24% by weight; pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester in an amount of from about 30% to about 35% by weight; isotridecanol polyglycol ether 8 ethylene oxide

in an amount of from about 20% to about 27% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling in an amount of from about 1.25% to about 1.75% by weight.

17. The composition of claim 16, comprising flonicamid in an amount of about 22.5% by weight; DMSO in an amount of about 21.5% by weight; pentanoic acid 5-(dimethylamino)-2-methyl-5-oxo-methyl ester in an amount of about 32% by weight; isotridecanol polyglycol ether 8 ethylene oxide in an amount of about 22.5% by weight; and a mixture of alkenes, C_{11}-C_{12}, hydroformylation products, low boiling in an amount of about 1.5% by weight.

18. A method of controlling pest comprising applying to a locus where control of said pest is desired an effective amount of a composition according to any one of claims 1-17.

19. The method of claim 18, wherein said pest is an insect such as an aphid, a mealybug, or a white fly.

20. The method of claim 18 or 19, wherein said locus is a field of crop.

21. The method of claim 20, wherein said crop is selected from oilseed rape (OSR), cotton, rice, banana, potato, coffee, sugar cane, citrus, beans, sunflower, apple, corn, soybean, wheat, barley, oats, chickpeas, fruit trees, nut trees, lentils, and grain sorghum.

22. A method for the protection of a plant propagation material from an attack by a pest such as an insect, comprising treating the propagation material or the site where the propagation material is to be planted with an effective amount of a composition according to any one of claims 1-17.

Fig. 1

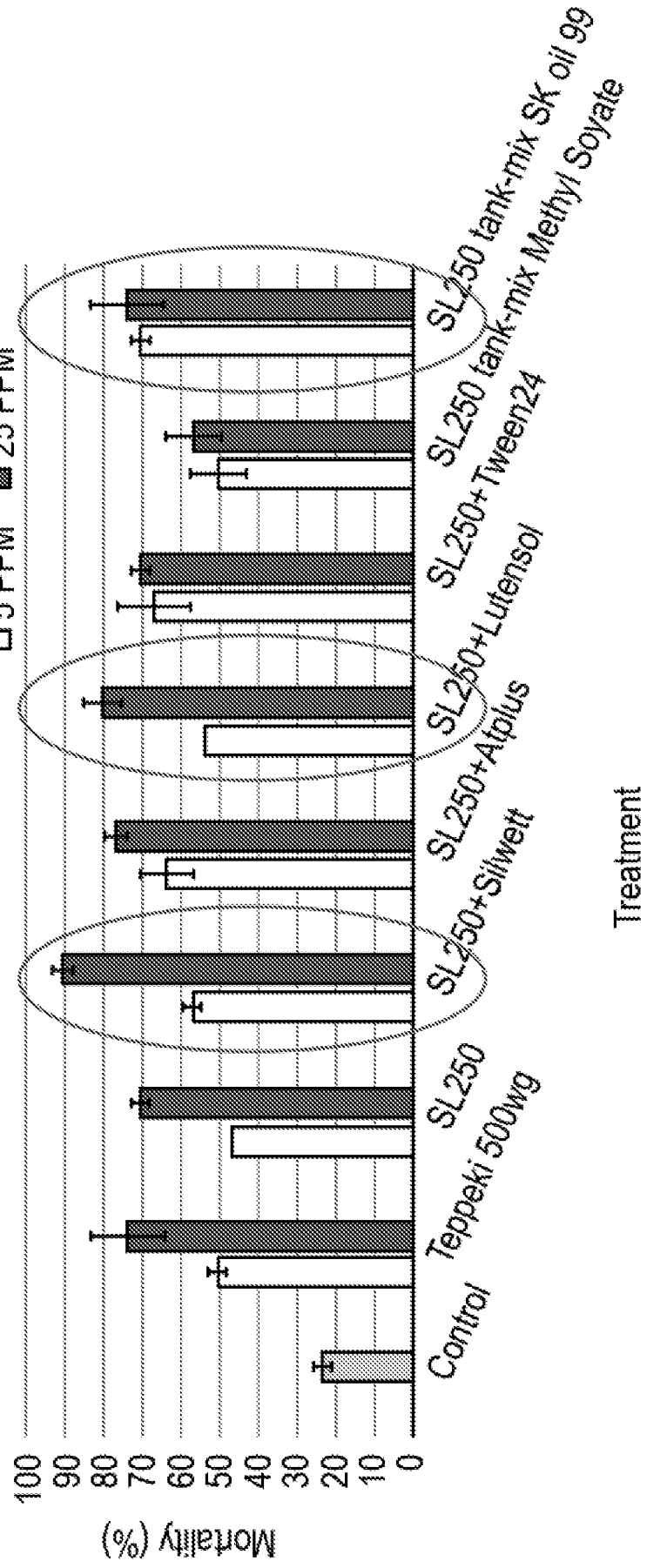
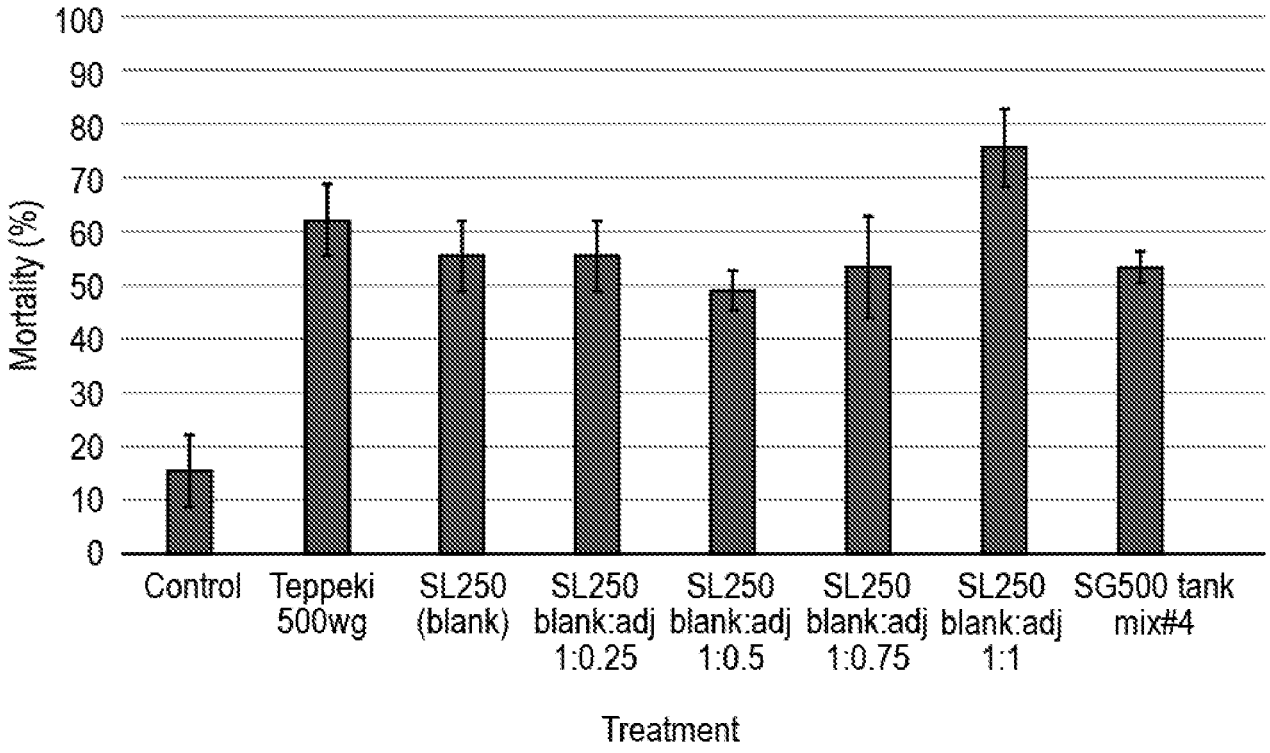

5 PPM
25 PPM
Mortality (%)
100
90
80
70
60
50
40
30
20
10
0
Control
Teppeki 500wg
SL250
SL250+Silwett
SL250+Atplus
SL250+Lutensol
SL250+Tween24
SL250 tank-mix Methyl Soyate
SL250 tank-mix SK oil 99
Treatment

Fig. 2


100
90
80
70
60
50
40
30
20
10
0
Mortality (%)
Control
Teppeki 500wg
SL250 (blank)
SL250 blank:adj 1:0.25
SL250 blank:adj 1:0.5
SL250 blank:adj 1:0.75
SL250 blank:adj 1:1
SG500 tank mix#4
Treatment