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(71) Applicant: BAYER CROPSCIENCE LP [US/US]; 2 T.
W. Alexander Drive, Research Triangle Park, NC 27709
(US).

(72) Inventors: WU, Tai-Teh; 200 Collinson Drive, Chapel
Hill, NC 27514 (US). ROGERS, Dick; 197 Tobacco Farm
Way, Chapel Hill, NC 27516 (US).

(74) Agent: MCBEE, Susan E., Shaw; McBee Moore Wood-
ward & Vanik IP, LLC, 510 South Market Street, Freder-
ick, MD 21701 (US).

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(54) Title: METHOD FOR CONTROLLING PARASITIC MITES

(57) Abstract: The present disclosure is directed to a method of directing or repelling mites away from bees and/or a beehive in proximity to the bees. In particular, the method is directed to protecting bees and bee colonies from mites. The method requires a step of exposing the mites to an effective amount of a composition comprising at least one ketone compound having 8 or more carbon atoms.



METHOD FOR CONTROLLING PARASITIC MITES

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is an international application under the Patent Cooperation Treaty, which claims priority to U.S. provisional application 62/294,608 (filed February 12, 2016), the contents of which are incorporated herein by reference in their entirety.

BACKGROUND

[0002] Bees, such as honey bees, play a vital role in an agricultural ecosystem. For instance, bees are necessary for the pollination of certain crops and thus have a substantial impact on the agricultural economy. In addition, honey bees also produce honey and wax for consumption. However, bees are threatened worldwide due to various reasons, such as pathogens and parasites. These parasites include at least two species of mites, *Varroa* mites and tracheal mites, which are deadly and can cause the death of an entire colony. In particular, the mites can affect the health of bees and a colony as they can feed on the bees and are also a vector for diseases.

[0003] Various miticides have been employed to eradicate mites. However, some of these miticides can be toxic to bees and to humans while others are simply not as effective. In addition, certain miticides can only be employed during certain times of the year, for instance, when honey supers are not on the hives (typically before and after nectar flow periods) or when a colony is broodless (typically in the late fall through the mid to later winter). Also, some miticides will only kill phoretic *Varroa* mites while others may kill phoretic mites as well as mites in sealed brood cells.

[0004] As a result, there is a need for an improved method for controlling, directing, and/or repelling mites from beehives and preventing mite infestation in such hives. In particular, there is a need for a method with improved efficacy and selectivity and one that is less toxic, in particular to bees and beekeepers.

SUMMARY

[0005] In general, the present disclosure is directed to a method for directing or repelling mites away from bees and/or a beehive in proximity to the bees. The method comprises a step of exposing the mites to an effective amount of a composition comprising at least one ketone compound having 8 or more carbon atoms.

[0006] Other features and aspects of the present disclosure are discussed in greater detail below.

DETAILED DESCRIPTION

[0007] Reference now will be made in detail to the embodiments of the invention, one or more examples of which are set forth below. Each example is provided by way of explanation of the invention, not limitation of the invention. In fact, it will be apparent to those skilled in the art that various modifications and variations can be made in the present invention without departing from the scope or spirit of the invention. For instance, features illustrated or described as part of one embodiment, can be used on another embodiment to yield a still further embodiment. Thus, it is intended that the present invention cover such modifications and variations.

[0008] In general, the present invention is directed to a method for controlling, directing, and/or repelling mites from bees and/or beehives containing bees. In one aspect, the method is directed to preventing and/or reducing a mite infestation in a beehive. In another aspect, the method is directed to treating, preventing and/or reducing a disease, such as varroaosis, of bees and bee colonies. In this regard, the present invention is directed to protecting bees, bee colonies, and/or beehives from mites.

[0009] In general, the methods herein can be used to protect bees of any genus and species affected by mites. For instance, these bees may include bumblebees (genus *Bombus*), mason bees (genus *Osmia*), alfalfa leafcutter bees (genus *Megachile*), honey bees (genus *Apis*), and wild bees.

[00010] In general, the mites referenced herein are parasitic mites that prey on bees, such as honey bees, and/or can cause an infestation in a beehive. These mites include those of the genus *Varroa* (e.g., species include *Varroa destructor* and *Varroa jacobsoni*), honey bee tracheal mites (e.g., *Acarapis woodi*), and *Tropilaelaps* spp. *Varroa* mites and *Tropilaelaps* mites are ectoparasites that feed on bee hemolymph and infest feral and managed honey bee colonies. Honey bee tracheal mites are microscopic mites that inhabit the respiratory tubes of bees.

[00011] In general, *Varroa* mite reproduction begins when the adult female mite enters a brood cell, preferentially a drone brood cell but may also include worker and queen cells, shortly before it is capped. The female mite feeds on the pupal hemolymph prior to depositing the eggs. The *Varroa* eggs eclose under the sealed cell, and the

developing mites feed on the bee hemolymph of the pupa. The mites develop within the sealed cell and are released from the capped cell when the new bee emerges from the cell. The mites can also attach to the bees, which may serve as intermediate hosts and provide a means of transport to new sites of infestation. Thus, there is a need to prevent mites from being carried and transported by bees and to prevent mites from entering the beehive. By preventing mites from entering the hive, there can be a less likelihood of disease and death of the bee colony.

[00012] In this regard, the presently disclosed method is directed to exposing the mites to a composition containing a specific ketone compound and optionally other additives (e.g., surfactant, solvent, etc.). In particular, when applied at a certain rate or concentration (i.e., effective amount), the method disclosed herein can effectively control, direct, and/or repel mites so that they do not attach to bees, will detach from bees, and/or will not enter a beehive containing bees. In particular, when employed at the specific rate or concentration, the method disclosed herein can effectively control, direct, and/or repel mites without harming the bees. Thus, while the mites are controlled, directed, and/or repelled away from the bees and/or a beehive containing bees, the bees still continue to perform normal tasks and/or will continue to enter/exit the beehive. In addition, the method disclosed herein may also have no adverse effects on the beekeepers or on honey produced from the bees.

[00013] Composition

[00014] A. Ketone Compound

[00015] As indicated above, the composition contains a specific ketone compound. According to the present inventors, when employed in an effective amount, the ketone compound can control, direct, and/or repel a mite. In this regard, the ketone compound can alter the behavior of the mite.

[00016] As disclosed herein, the ketone compound is a compound comprising a carbonyl group. According to the method disclosed herein, the ketone compound is one having at least 8 carbon atoms. For instance, the ketone compound may have from 8 or more carbon atoms, such as 9 or more carbon atoms, such as 10 or more carbon atoms to 20 or less carbon atoms, such as 15 or less carbon atoms, such as 12 or less carbon atoms. For instance, the ketone compound may have from 8 to 20 carbon

atoms, such as from 9 to 20 carbon atoms, such as from 9 to 15 carbon atoms, such as from 10 to 13 carbon atoms, such as from 10 to 12 carbon atoms.

[00017] In one embodiment, the ketone compound may have a structure according to Formula (I):



[00018] In one embodiment, R₁ and R₂ are independently selected from alkyl, aryl, phenyl, substituted phenyl, fused phenyl, heterocyclic ring, aryl alkyl, vinyl, acetyl, vinyl alkyl, propargyl, and allyl group.

[00019] In one embodiment, R₁ and R₂ are independently selected from methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, iso-butyl, tert-butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and substituted or non-substituted C₂-C₂₀-alkyl (such as C₅-C₁₅ alkyl, such as a C₆-C₁₂ alkyl, such as C₇-C₁₀ alkyl), substituted or non-substituted C₂-C₂₀ alkenyl (such as C₅-C₁₅ alkenyl, such as a C₆-C₁₂ alkenyl, such as C₇-C₁₀ alkenyl), and substituted or non-substituted C₂-C₂₀ alkynyl (such as C₅-C₁₅ alkynyl, such as a C₆-C₁₂ alkynyl, such as C₇-C₁₀ alkynyl), alkyl substituted with halogen, F, Cl, Br, I, oxygen, hydroxyl, alkoxy, cyano, aryloxy, C=C, C≡C; nitrogen, NH₂, alkyl amino, dialkyl amine trialkylamino; SH, alkylthio or where R¹ and R² are linked together to form a substituted or unsubstituted (CH₂)₇, (CH₂)₈, (CH₂)₉, (CH₂)₁₀, (CH₂)₁₁, (CH₂)₁₂, (CH₂)₁₃ ring structure

[00020] In one embodiment, R₁ and R₂ are independently selected from methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, iso-butyl, tert-butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and substituted or non-substituted C₂-C₂₀-alkyl (such as C₅-C₁₅ alkyl, such as a C₆-C₁₂ alkyl, such as C₇-C₁₀ alkyl), substituted or non-substituted C₂-C₂₀ alkenyl (such as C₅-C₁₅ alkenyl, such as a C₆-C₁₂ alkenyl, such as C₇-C₁₀ alkenyl), and substituted or non-substituted C₂-C₂₀ alkynyl (such as C₅-C₁₅ alkynyl, such as a C₆-C₁₂ alkynyl, such as C₇-C₁₀ alkynyl). For instance, in one embodiment R₁ is H and R₂ is an alkyl or aryl or R₁ is alkyl or aryl and R₂ is H. In another embodiment, both R₁ and R₂ are alkyl, such as linear/unbranched alkyl.

[00021] In one embodiment, R_1 is methyl or ethyl and R_2 is selected from the group consisting of pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and substituted or non-substituted C_2 - C_{20} -alkyl (such as C_5 - C_{15} alkyl, such as C_6 - C_{10} -alkyl), substituted or non-substituted C_2 - C_{14} alkenyl (such as C_5 - C_{15} alkenyl, such as C_6 - C_{10} -alkenyl), and substituted or non-substituted C_2 - C_{14} -alkynyl (such as C_5 - C_{15} alkynyl, such as C_6 - C_{10} -alkynyl), or vice versa.

[00022] It should be understood that the alkyl group may be straight chain, branched, cyclic, or cyclic alkyl. The alkyl may be optionally substituted with halogen (e.g., F, Cl, Br, I), oxygen, hydroxyl, alkoxy, cyano, aryloxy, $C=C$, $C\equiv C$; nitrogen, NH_2 , alkyl amino, dialkyl amine trialkylamino; SH, alkylthio and oxidation states, arylthio and oxidation states; amido, monoalkylamino, dialkylamino, and ureido.

[00023] In one embodiment, R_1 and R_2 can form a ring, such as a cycloalkyl ring, for example, a cyclooctyl, cyclononyl, cyclodecyl, or the like, fused alkyl ring, such as camphor. In another aspect, the R_1 and R_2 ring is a phenyl ring optionally substituted with one or more of halogen, OH, alkoxy, cyano, amino alkylamino, dialkylamino, SH, alkylthio and oxidation states, phenoxy, formyl, alkylcarbonyl, alkoxy carbonyl, haloalkyl, haloalkoxy, polyhaloalkyl, polyhaloalkoxy, perhaloalkyl, perhaloalkoxy, amido, alkylamino, amino, dialkylamino, hydroxycarbonyl, alkyl carbonyl, aryl carbonyl, and alkoxy carbonyl groups.

[00024] In one embodiment, R_1 and R_2 can be linked together to form a substituted or unsubstituted $(CH_2)_7$, $(CH_2)_8$, $(CH_2)_9$, $(CH_2)_{10}$, $(CH_2)_{11}$, $(CH_2)_{12}$, and a $(CH_2)_{13}$ ring structure.

[00025] In one embodiment, the disclosure provides for optically active and/or geometric isomers and/or salts thereof of compounds of Formula I. In one embodiment, the disclosure provides for metabolites, analogues, homologues, isomers, diastereomers, conjugate isomers, tautomers, and salts thereof of compounds of Formula I. In one embodiment, the methodology described herein can be practiced with one or more compounds represented by Formula I.

[00026] In one embodiment, the ketone compound comprises a C_8 - C_{20} ketone, such as a C_9 - C_{15} ketone, such as a C_{10} - C_{13} ketone, such as a C_{10} - C_{12} ketone. In one embodiment, the ketone compound comprises a methyl ketone. In one embodiment,

the ketone compound comprises one or more of 2-octanone, 3-octanone, cyclooctanone, 2-nonanone, cyclononanone, 2-decanone (methyl-n-octyl ketone), 2-undecanone (methyl-n-nonylketone), 2-dodecanone, 1,3-dioxolane, 2-methyl-2-octyl, 2-tridecanone, 2-tetradecanone, 2-pentadecanone, 2-hexadecanone, 2-heptadecanone, 2-nonanethione, cyclodeconone, decane, 2,2-dimethoxy, sulfur analog of 2-decanone, 2-decanimine, (+)-2-decanol, 2-decanol, 2,9-decanedione, 2,11-dodecanedione, 2,5-dodecanedione, 2,2-decanediol, 1-undecen-2-ol, 3-decanone, 4-decanone, 5-decanone, 9-methyl, decanal, ethanone, 1-[3-methyl-4-(trifluoromethyl) phenyl], ethanone, 2,2,2-trifluoro-1-phenyl, 5,9-undecadien-2-one, 6,10-dimethyl-, (5E)-, 2-pentadecanone, 4-methylcyclohexanone, p-methylacetophenone, propionphenone, 2-Hydroxyacetophenone, 2,9-decanedione, 2,11-dodecanedione, 2,5-dodecanedione, and 2-hydroxy acetophenone.

[00027] In one embodiment, the ketone compound comprises one or more of 2-octanone, 3-octanone, cyclooctanone, 2-nonanone, cyclononanone, 2-decanone, 3-decanone, 4-decanone, 5-decanone, 2-undecanone, 2-dodecanone, 2-tridecanone, 2-tetradecanone, 2-pentadecanone, 2-hexadecanone, 2-heptadecanone, cyclodeconone, and sulfur analogs of 2-decanone. In one particular embodiment, the ketone compound comprises one or more of 2-decanone, 3-decanone, 4-decanone, 5-decanone, 2-undecanone, 2-dodecanone.

[00028] In one embodiment, the ketone compound does not include a C₃-C₇ ketone compound. In one embodiment, the ketone compound does not include a heptanone, such as 2-heptanone, 3-heptanone, 4-heptanone, and/or cycloheptanone.

[00029] According to the present method, the ketone compound may not be volatile. For instance, the ketone compound can be present for a sufficient amount of time for exposure to a mite. In this regard, the ketone compound may have a boiling temperature, at atmospheric pressure, of 160°C or greater. For instance, the boiling temperature can be from 160°C or greater, such as 180°C or greater, such as 200°C or greater, such as 220°C or greater, such as 240°C or greater to 500°C or less, such as 400°C or less, such as 350°C or less, such as 300°C or less, such as 250°C or less, such as 240°C or less.

[00030] In one embodiment, the ketone compound comprises, consists of, or consists essentially of any of ketone compounds described herein. In addition, in one embodiment, the composition comprises, consists of, or consists essentially of any of ketone compounds described herein.

[00031] In one embodiment, the disclosure provides for a composition comprising, consisting essentially of, or consisting of 2-decanone. In another aspect, the disclosure provides for a composition comprising, consisting essentially of, or consisting of 2-undecanone and camphor. In yet another aspect, the disclosure provides for a composition comprising, consisting essentially of, or consisting of 2-dodecanone. In yet another aspect, the disclosure provides for a composition comprising, consisting essentially of, or consisting of 2-tridecanone.

[00032] In addition, it should be understood that the composition may include more than one ketone compound. For instance, the composition may include at least two ketone compounds as described herein, such as at least three ketone compounds as described herein.

[00033] As indicated above, the composition may consists of the ketone compound. Thus, the ketone compound may be 100 wt.% of the composition. Alternatively, the ketone compound may be present in the composition in an amount of from 0.01 wt.% to 99.99 wt.%. The ketone compound may be present in an amount of from 0.01 wt.% or more, such as 0.1 wt.% or more, such as 1 wt.% or more, such as 5 wt.% or more, such as 10 wt.% or more, such as 25 wt.% or more, such as 50 wt.% or more, such as 75 wt.% or more, such as 90 wt.% or more, such as 95 wt.% or more to 99.99 wt.% or less, such as 99.9 wt.% or less, such as 99 wt.% or less, such as 95 wt.% or less, such as 90 wt.% or less, such as 75 wt.% or less, such as 50 wt.% or less, such as 25 wt.% or less, such as 10 wt.% or less, such as 5 wt.% or less, such as 1 wt.% or less, such as 0.5 wt.% or less.

[00034] B. Solvents/Carriers

[00035] Optionally, the composition may also comprise a solvent. The solvent may include any known solvent in the art that can be combined with the aforementioned ketone compounds and if any, surfactants. In addition, the solvent should not harm the bees, bee colonies, and/or beehives.

[00036] The solvent may include water, an aromatic hydrocarbon, an aliphatic hydrocarbon (e.g., paraffin), an alcohol and its ester/ether (e.g., ethanol), a glycol and its ester/ether (e.g., ethylene glycol, ethylene glycol monomethyl or monoethyl ether, propylene glycol), strong polar solvents (e.g., NMP), as well as oils (e.g., vegetable oil such as coconut oil or soybean oil).

[00037] However, it should be understood that a solvent may not be necessary. For instance, the ketone compound may be employed directly without the presence of a solvent.

[00038] C. Surfactants/Adjuvants

[00039] Optionally, the composition may also comprise a surfactant. In general, the surfactant can be employed to enhance the emulsifying and wetting properties of the components and composition. The surfactant may be a non-ionic surfactant, a cationic surfactant, an anionic surfactant, and/or an amphoteric surfactant. The surfactant may include any known surfactant in the art that can be combined with the aforementioned ketone compounds and if any, solvent. In addition, the surfactant should not harm the bees, bee colonies, and/or beehives.

[00040] Surfactants include alkali metal salts, alkaline earth metal salts, or unsubstituted or substituted ammonium salts of higher fatty acids (e.g., C₁₀-C₂₂). Surfactants also include fatty sulfonates, fatty sulfates, and alkylarylsulfonates. Non-ionic surfactants include polyglycol ether derivatives of aliphatic or cycloaliphatic alcohols, saturated or unsaturated fatty acids and alkylphenols, water soluble adducts of polyethylene oxide with polypropylene glycol, etc. Cationic surfactants include quaternary ammonium salts which contain, as N-substituent, at least one C₆-C₂₂ alkyl radical and, as further substituents, unsubstituted or halogenated lower alkyl, benzyl or hydroxy-lower alkyl radicals.

[00041] If employed, the surfactant is present in the composition in an amount of from 0.01 wt.% to 50 wt.%, such as from 0.1 wt.% to 25 wt.%, such as from 0.5 wt.% to 15 wt.%. However, it should be understood that a surfactant may not be necessary. For instance, the ketone compound may be employed directly without the presence of a surfactant.

[00042] D. Other Additives

[00043] The composition may also comprise other additives generally employed in the art. These additives may include stabilizers, viscosity regulators, binders, pH adjusters, etc. However, it should be understood that these additives should not harm the bees or the bee colonies.

[00044] In one embodiment, the composition may also optionally include pine oil, tea tree oil, essential oil of tea tree, densifolia leaf essential oil, essential oil of ocimum santum, systox, phenol, alkaloids, carum copticum oil, propionic anhydride, butyric anhydride, methyl salicylate, 6-hexatriacontene, stenpcereol, 27,28,29-trisnor-13-15-17-meratriene, samaderine E, phenylacetaldehyde, benzaldehyde, *Swertia densifolia* leaf essential oil, linalool, ambrette seed oil, cascarilla bark oil, leaf oil, cascarilla bark oil, rue oil, rue flower oil, terpineol, stearic acid, hydroquinone and octadecanal, methyl anthranilate, methyl anthranilate, creosote, acetic acid and propionic acid, N,N-diethyltoluamide, dimethyl phthalate, and isopropyl cinnamate. In one embodiment, the composition may also optionally include citronella (for example, *Cymbopogon* spp., *Cymbopogon nardus*, *Cymbopogon winterianus* and *Cymbopogon citratus*), *eucalyptus* (*Eucalyptus* spp.), lemon *eucalyptus* (*Corymbia citriodora*), cinnamon (*Cinnamomum verum*), castor (*Ricinus communis*), rosemary (*Rosmarinus officinalis*), cedar (*Cedrus* spp.), peppermint (*Mentha piperita*), clove (*Syzygium aromaticum*), geranium (*Pelargonium graveolens*), verbena (*Verbenaspp.*, *Verbena officinalis*), pennyroyal (*Mentha pulegium*), lavender (*Lavandula* spp.), pine (*Pinus* spp.), cajeput (*Melaleuca* spp.; *Melaleuca leucadendra*), basil (*Ocimum basilicum*), thyme (*Thymus vulgaris*), pandan (*Pandanus amaryllifolius*), allspice (*Pimenta dioica*), soybean (*Glycine max*), garlic (*Allium sativum*), DEET, Picaridin, p-Mentane-3,8-diol, Permethrin, Allethrin, Metofluthrin, Geraniol, Eugenol, Cinnamaldehyde, Alkaloids, p-cymene, linalool, α -pinene, β -pinene, sabinene, myrcene, α -phellandrene, α -terpinene, α -terpineol, α -ter, limonene, 1,8-cineole, γ -terpinene, terpinolene, terpinen-4-ol and α -terpineol, copticum, and Ptychotis oil. These compounds may be able to provide a synergistic influence when combined with the ketone compound describe herein.

[00045] Mite Control

[00046] As disclosed herein, the present invention is directed to a method for controlling, directing, and/or repelling mites. In particular, the present invention is

directed to controlling, directing, and/or repelling mites so that they do not attach to bees, will detach from bees, and/or will not enter a beehive containing bees. In one aspect, the method is directed to preventing and/or reducing a mite infestation in a beehive. In another aspect, the method is directed to preventing and/or reducing a disease, such as varroaosis, of bees and bee colonies.

[00047] In one embodiment, a method of “repelling” refers to the ability of the composition and/or ketone compound described herein to influence or alter the behavior of a mite away from an area, location, structure, article, or substance of interest. In order to be classified as “repelling” according to an aspect of the disclosure, it is not necessary that 100% of the mites be directed away from an area, location, structure, article, or substance of interest. In one embodiment, a mite is “repelled” if at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% of the mites are directed away from an area, location, structure, article, or substance of interest.

[00048] In one embodiment, a method of “directing” refers to the ability of the composition described herein to influence the behavior or movement of a mite in a given direction. In order to be classified as “directing” according to an aspect of the disclosure, it is not necessary that 100% of the mites be directed away from an area, location, structure, article, or substance of interest. In one embodiment, a mite is “directed away” if at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% of the mites are directed away from an area, location, structure, article, or substance of interest.

[00049] In one embodiment, a method of “controlling” refers to the ability of the composition described herein to control or alter the behavior of a mite. In order to be classified as “controlling” according to an aspect of the disclosure, it is not necessary that 100% of the mites are controlled relative to an area, location, structure, article, or substance of interest. In one embodiment, a mite is “controlled” if at least 50%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% of the mite behavior is altered or controlled relative to an area, location, structure, article, or substance of interest.

[00050] In an aspect, a composition or ketone compound described herein has the ability to repel or direct a mite away from a structure. Without being limited, a “structure” is an area or locus capable of contacting or being infested by a mite. In another aspect, a “structure” can be man-made or naturally occurring. Without being limited, a “structure” can be a building, for example a commercial or residential building, the interior or exterior of a building, an outdoor space, including but not limited to a field, a park area, a golf course or the like, a car, a boat, a patio, a deck, a table, a chair, a window, a container, a container designed to hold a mite, a container designed to repel, direct, or control a mite, a trashcan or a trash receptacle, an indoor space, such as a room in a commercial or residential building, an outdoor space, or structures oftentimes present in an outdoor space, such as a tree, a bush, a clover, a shrub, a flowering plant, a lawn, a shed, or other such structure.

[00051] In an aspect, a composition or ketone compound described herein has the ability to repel or direct a mite away from an article. Without being limited, an “article” is an element that is capable of being contacted, influenced, or infested by a mite. In another aspect, without being limited, an “article” can be bait, a bait mechanism or holder, a device, garment, belt, air freshener, candle, other scented article, fiber, bedding, sheet, cloth, clothing, net, insect netting, fabric, paper, glass, paint, ink, clay, cotton, woods, furniture, carpet, sanitary good, plastic, polymer, biological or synthetic material, spray product, fogging system, fogger, foam, gel, evaporator product, evaporator system, granule, or dust.

[00052] Stated in another manner, the mites are controlled, directed, and/or repelled so that it changes trajectory, is prevented or inhibited from attaching to a bee and/or entering a beehive, and/or is caused to detach itself from a host bee. In one aspect, the mites are controlled, directed, and/or repelled so as to inhibit mite survival and/or reduce, slow, or stabilize the growth of a mite population.

[00053] As indicated herein, the method requires a step of exposing mites to the composition and/or ketone compound described herein. Thus, the ketone compound should be present in an amount effective to control, direct, and/or repel mites. For instance, the ketone compound should be present in an amount to cause a mite to change trajectory, prevent or inhibit the mite from attaching to a bee and/or enter a

beehive, and/or cause a mite to detach itself from a host bee. However, the ketone compound should not be present in an amount that would also repel bees from entering a beehive modify their behavior.

[00054] According to the present method, the mites can be exposed to the composition and/or ketone compound as described herein using any method generally known in the art. In this regard, the composition and/or ketone compound should be applied so as to contact the mite and/or be sensed by the mite.

[00055] For instance, the mites can be exposed when the ketone compound is applied to a desired area upon or through which the mites will traverse or travel.

[00056] For instance, in one embodiment, the composition can be applied (e.g., by spraying, misting, and the like) on or around a beehive. In one embodiment, the composition and/or ketone compound can be applied on at least a portion of a beehive. In one aspect, the composition and/or ketone compound can be applied to an entrance of a beehive, such as a portion of the entrance of a beehive or the entire entrance of a beehive. In one particular embodiment, the composition and/or ketone compound can be applied to the entrance of a beehive as illustrated in US Patent Application Publication No. 2008/0280528 to Mudd, which is incorporated herein by reference in its entirety. However, it should be understood that the entrance to the beehive may be configured in any manner that allows for bees to enter/exit the beehive.

[00057] If applied around a beehive, the ketone compound can be applied within about 0.1 meters, about 0.5 meters, about 1 meter, about 3 meters, about 5 meters, about 10 meters, about 25 meters, about 50 meters, about 100 meters, about 200 meters, or about 300 meters within the beehive, such as the entrance of a beehive.

[00058] In one embodiment, a dispensing device, such as a strip/substrate containing the composition and/or ketone compound can be placed at or adjacent a beehive, such as the entrance of the beehive. The strip/substrate may be made of paper, wood, cardboard, plastic, or other absorbent material that can be moistened, soaked, or impregnated with the composition and/or ketone compound. In this regard, the strip/substrate can be placed within about 0.1 meters, about 0.5 meters, about 1 meter, about 3 meters, about 5 meters, about 10 meters, about 25 meters, about 50

meters, about 100 meters, about 200 meters, or about 300 meters within a beehive, such as the entrance of a beehive.

[00059] In one embodiment, the ketone compound can be provided via a controlled release mechanism. For instance, the ketone compound can be combined or surrounded by a permeable release rate controlling mechanism that permits the compound to permeate through at a desired rate. The ketone compound can be provided with a complexation agent and/or with a chelating agent or the compound, can be encapsulated or provided as a host-guest complex. The ketone compound can be released based on temperature or moisture controlling factors/methods. When provided in such manner, it can be placed within about 0.1 meters, about 0.5 meters, about 1 meter, about 3 meters, about 5 meters, about 10 meters, about 25 meters, about 50 meters, about 100 meters, about 200 meters, or about 300 meters within a beehive, such as the entrance of a beehive.

[00060] In one embodiment, the composition and/or ketone compound can be applied (e.g., sprayed) directly on a bee. For instance, the composition and/or ketone compound can be applied to the bee via a misting process. In such instance, the ketone compound is applied at a low concentration sufficient for controlling, directing, and/or repelling mites but not to modify the behavior of the bees.

[00061] When exposed to the ketone compound, the mites are controlled, directed, and/or repelled so that they do not attach to bees, will detach from bees, and/or will not enter a beehive containing bees. Thus, as an example, when mites are on the bees and the bees enter the beehives, the mites can be exposed to the ketone compound and detach from the bees and/or not enter a beehive. Alternatively, mites may not even attach to a bee when sensing the ketone compound. For this to occur, the mites would have been exposed to the ketone compound in any manner, such as when applied around the beehive, applied on the beehive (e.g., the entrance), applied on the bees, supplied through a delivery mechanism, etc.

[00062] As indicated herein, the ketone compound should be applied or delivered in an amount effective to control, direct, and/or repel or disrupt a mite biological function such as a behavioral activity. For instance, the activity may include repelling a mite so that it does not enter a beehive with the bee, control a mite so that it does not attach to

a bee or so that it does detach from a bee, etc. However, the behavior of the bee should not be modified. That is, bees should still enter/exit a beehive. In this regard, the ketone compound is delivered at a concentration below a level that may have a detrimental effect on the bees.

[00063] In this regard, when applied to the beehive an area around the beehive, or on a delivery mechanism such as a strip/substrate, the ketone compound can be applied at a rate of from about 0.01 $\mu\text{g}/8\text{ cm}^2$ or more, such as about 0.1 $\mu\text{g}/8\text{ cm}^2$ or more, such as about 0.5 $\mu\text{g}/8\text{ cm}^2$ or more, such as about 1 $\mu\text{g}/8\text{ cm}^2$ or more, such as about 10 $\mu\text{g}/8\text{ cm}^2$ or more, such as about 100 $\mu\text{g}/8\text{ cm}^2$ or more to about 1000 $\mu\text{g}/8\text{ cm}^2$ or less, such as about 750 $\mu\text{g}/8\text{ cm}^2$ or less, such as about 500 $\mu\text{g}/8\text{ cm}^2$ or less, such as about 250 $\mu\text{g}/8\text{ cm}^2$ or less. For instance, the ketone compound should be applied at a rate of from about 0.1 $\mu\text{g}/8\text{ cm}^2$ to about 1000 $\mu\text{g}/8\text{ cm}^2$, such as from about 1 $\mu\text{g}/8\text{ cm}^2$ to about 500 $\mu\text{g}/8\text{ cm}^2$.

[00064] By exposing the mites to the ketone compound, without intending to be limited by theory, it should be understood that such exposure can come via any means so long as the mites are exposed to the compound. Thus, "exposing" may mean touching/contacting, associating with, or having proximity to. Without intending to be limited by theory, controlling, directing, and/or repelling activity may be the result of (1) physical transfer of the composition and/or ketone compound to the mite or (2) mites sensing the presence of the composition and/or ketone compound.

[00065] In one embodiment, the composition and/or ketone compound described herein work by influencing or altering the senses of a mite. In another aspect, the composition and/or ketone compound can alter the olfactory senses, sight, or other physical characteristics of a mite or combinations thereof. Thus, the mite can be controlled, directed, and/or repelled based on sight (e.g., color), tactile sensations, taste, or other physical characteristics such as sound, vibrations, and combinations of any of the foregoing.

[00066] In addition, the composition and/or ketone compound can be delivered, whether applied/sprayed/misted, through a strip/substrate or other delivery mechanism, to the selected area once or more than once. For instance, the composition and/or ketone compound may be applied two to three times over an interval of 1 to 2 weeks. In

order to prevent mites from entering the beehive, cause mites to detach from bees, and/or prevent mites from attaching to bees, it may be desired to apply the composition and/or ketone compound two or three times over a complete brood cycle (21 days for workers or 28 days for drones).

[00067] The composition and/or ketone compound can be applied manually, such as by an individual (e.g., a beekeeper). Alternatively, a mechanism may be created that allows for remote applications/deliveries. For instance, a remote unit containing a reservoir with the composition and/or ketone compound can be attached to a delivery device (e.g., sprayer, mister, etc.) and placed on or adjacent a beehive or selected area. The delivery device can be connected to a wireless network. A remote user at another location can then transfer a signal to the delivery device through the wireless network and cause the delivery device to deliver the composition and/or ketone compound at a desired rate/concentration from the reservoir. Such delivery mechanism is generally referred to as remote sensing and digital application technology.

[00068] In general, the beehives referenced herein may refer to man-made structures that contain a bee colony. The hives can include a bottom board, a cover, and one more boxes stacked one above the other. The boxes contain movable frames of comb or foundation. However, the beehives may have any sort of construction/configuration. Other beehive designs and constructions, including natural cavities inhabited by bees may also be included.

[00069] As indicated herein, the treatment can be applied directly to the bees, a beehive in proximity to the bees, or a selected area adjacent to the beehive. Thus, in proximity or within a selected area adjacent to the beehive can mean within about 1 cm, about 5 cm, about 10 cm, about 100 cm, about 0.2 meters, about 0.5 meters, about 1 meter, about 2 meters, about 5 meters, about 10 meters, about 25 meters, about 50 meters, about 100 meters, about 200 meters, or about 300 meters.

[00070] It should be understood that the quantity of mites can be determined using any method generally known in the art. In particular, one method is referred to as the alcohol wash method. Such method can provide the number of mites per a certain quantity of bees (e.g., per 100 bees). According to this method, each sample of bees is placed in a strainer basket and washed using a non-sudsing or low-sudsing fluid (e.g.,

isopropyl alcohol, low sudsing soap, windshield washer fluid). During the process, mites are dislodged from the bees. The number of mites washed off are counted and recorded. The number of bees that were washed are also counted and recorded. To calculate the number of mites per 100 bees, the total number of mites per sample is divided by the total number of bees in the sample and then multiplied by 100. The result provides the number of mites per 100 bees of the sample. In making such determination, a statistically significant number of bees should be sampled, such as at least about 50 bees, such as 100 bees, such as 150 bees, such as 200 bees, such as 250 bees, such as 300 bees. The bees can be sampled from the desired location (e.g., from within the beehive, immediately prior to the entrance to a beehive, etc.) based on the location upon which the mites are exposed to the composition and/or ketone compound.

[00071] According to any or all of these methods, when employing the composition and/or ketone compound as described herein, the method can provide a reduction in the number of mites (i.e., prevent or inhibit a mite infestation) in a beehive in comparison to a second beehive where mites were not exposed to the composition and/or ketone compound described herein. In particular, relative to the second beehive without the presence of or exposure to the composition and/or ketone compound, the beehive where mites are exposed to the composition and/or ketone compound will have at least about 10% less, such as at least about 25% less, such as at least about 50% less, such as at least about 75% less, such as at least about 90% less, such as at least about 95% less mites. The level of infestation or mite quantity used to determine these percentages can be based on any or all of the aforementioned tests.

[00072] In addition, various parameters can also be indicative of the level of mite infestation present in a bee colony. These include the number of mites present in a sample of bees from an infested hive, bee size and weight because those reared in an infested hive are on average smaller than those in a hive without infestation, amount of honey produced in an infected hive may be less than that produced in a healthy hive.

[00073] As indicated herein, the method can be used to control, direct, and/or repel a mite. In particular, the method disclosed herein can effectively control, direct,

and/or repel mites so that they do not attach to bees, will detach from bees, and/or will not enter a beehive containing bees.

[00074] In one embodiment, the composition and/or ketone compound described herein control, direct, and/or repel a mite for at least about 10 minutes, about 30 minutes, about 1 hour, about 4 hours, about 8 hours, about 12 hours, about 24 hours, about 2 days, about 3 days, about 7 days, about 14 days, about 21 days, about 1 month, about 2 months, about 3 months or more, or a designated time frame or growing or harvesting season. In one embodiment, the composition and/or ketone compound can control, direct, and/or repel a mite such that the mite is not in direct contact for at least the aforementioned times with a treated substance, such as a structure or article, including a beehive, or a treated area. In one embodiment, the composition and/or ketone compound can control, direct, and/or repel a mite away from a structure or article, including a beehive, for at least the aforementioned times.

[00075] In one embodiment, the composition and/or ketone compound described herein controls, directs, and/or repels mites from about 20% or more, about 30% or more, about 40% or more, about 50% or more, about 60% or more, about 75% or more, about 80% or more, about 90% or more, about 95% or more, about 98% or more, or about 99% or more to about 100% or less, such as about 90% or less, such as about 80% or less, such as about 70% or less relative to a composition that does not contain an effective amount of the ketone compound described herein. In one embodiment, the composition and/or ketone compound described herein controls, directs, and/or repels a mite by at least the aforementioned percentages and for at least about 5 minutes, about 10 minutes, about 30 minutes, about 1 hour, about 2 hours, about 3 hours, about 4 hours, about 8 hours, about 10 hours, about 15 hours, about 24 hours, about 48 hours, about 72 hours, about 7 days, about two weeks, about one month, about two months, about three months or more, or during a complete or partial season relative to a composition that does not contain an effective amount of the ketone compound described herein.

[00076] In one embodiment, the quantity of mites in a beehive before and after providing the composition and/or ketone compound described herein can be determined. Relative to before the composition and/or ketone compound is provided, a

beehive may have about 20% or less, such as about 30% or less, such as about 40% or less, such as about 50% or less, such as about 60% or less, such as about 70% or less, such as about 80% or less, such as about 90% or less, such as about 95 % or less, such as about 98% or less mites.

[00077] In one embodiment, the composition and/or ketone compound reduces mite interaction with a structure (e.g., beehive), article, and/or bees. For instance, the composition and/or ketone compound described herein is capable of reducing the interaction of a mite with a structure (e.g., beehive), article, and/or bees for at least about 5 minutes, about 10 minutes, about 30 minutes, about 1 hour, about 2 hours, about 3 hours, about 4 hours, about 8 hours, about 10 hours, about 15 hours, about 24 hours, about 48 hours, about 72 hours, about 7 days, about two weeks, about one month, about two months, about three months or more, or a designated time frame, for example, a growing or harvesting season. In one embodiment, the composition and/or ketone compound is capable of reducing the interaction by at least about 20% or more, about 30% or more, about 40% or more, about 50% or more, about 60% or more, about 75% or more, about 80% or more, about 90% or more, about 95% or more, about 98% or more, or about 99% or more relative to a composition that does not contain an effective amount of the ketone compound described herein.

[00078] In one embodiment, the composition and/or ketone compound is capable of controlling, directing, and/or repelling 20% or more, about 30% or more, about 40% or more, about 50% or more, about 60% or more, about 75% or more, about 80% or more, about 90% or more, about 95% or more, about 98% or more, or about 99% or more mites away from a structure, article, and/or bees for at least about 5 minutes, about 10 minutes, about 30 minutes, about 1 hour, about 2 hours, about 3 hours, about 4 hours, about 8 hours, about 10 hours, about 15 hours, about 24 hours, about 48 hours, about 72 hours, about 7 days, about two weeks, about one month, about two months, about three months or more, or a designated time frame, for example, a growing or harvesting season.

[00079] As disclosed herein, to control, direct, and/or repel may also mean to eliminate or reduce the number of mites that are available to affect honey bees.

[00080] In addition, the method employed herein should not cause bees to be repelled or directed away from a beehive. In this regard, 75% or less, such as 50% or less, such as 40% or less, such as 30% or less, such as 20% or less, such as 10% or less, such as 5% or less bees are repelled or directed away from a structure or article, including a beehive. For instance, such percentages apply whether the structure or article is treated, the area adjacent the structure or article is treated, the bee is treated, or a delivery mechanism is placed adjacent to such structure or article. In particular, such bees are not repelled or directed for at least about 10 minutes, about 30 minutes, about 1 hour, about 4 hours, about 8 hours, about 12 hours, about 24 hours, about 2 days, about 3 days, about 7 days, about 14 days, about 21 days, about 1 month, about 2 months, or about 3 months.

[00081] These and other modifications and variations to the present invention may be practiced by those of ordinary skill in the art, without departing from the spirit and scope of the present invention, which is more particularly set forth in the appended claims. In addition, it should be understood that aspects of the various embodiments may be interchanged both in whole or in part.

[00082] Furthermore, those of ordinary skill in the art will appreciate that the foregoing description is by way of example only, and is not intended to limit the invention so further described in such appended claims.

CLAIMS

1. A method for directing or repelling mites away from bees and/or a beehive in proximity to the bees, the method comprising
 exposing the mites to an effective amount of a composition comprising at least one ketone compound having 8 or more carbon atoms.
2. The method according to claim 1, wherein the ketone compound has a structure according to formula (I):



wherein R₁ and R₂ are independently selected from methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, iso-butyl, tert-butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and substituted or non-substituted C₂-C₂₀-alkyl, substituted or non-substituted C₂-C₂₀ alkenyl, a substituted or non-substituted C₂-C₂₀-alkynyl, alkyl substituted with halogen, F, Cl, Br, I, oxygen, hydroxyl, alkoxy, cyano, aryloxy, C=C, C≡C; nitrogen, NH₂, alkyl amino, dialkyl amine trialkylamino; SH, alkylthio or where R¹ and R² are linked together to form a substituted or unsubstituted (CH₂)₇, (CH₂)₈, (CH₂)₉, (CH₂)₁₀, (CH₂)₁₁, (CH₂)₁₂, (CH₂)₁₃ ring structure

3. The method according to claim 2, wherein R₁ is methyl.
4. The method according to any of claims 2-3, wherein R₂ is a C₅-C₁₅ alkyl.
5. The method according to any of claims 1-3, wherein the ketone compound contains from 9 to 15 carbon atoms.
6. The method according to any of claims 1-5, wherein the ketone compound has a boiling temperature at atmospheric pressure of from 180°C to 350°C.
7. The method according to any of claims 1-6, wherein the ketone compound comprises 2-decanone.
8. The method according to any of claims 1-6, wherein the ketone compound comprises 2-undecanone.
9. The method according to any of claims 1-6, wherein the ketone compound comprises 2-dodecanone.

10. The method according to any of claims 1-6, wherein the ketone compound comprises 2-tridecanone.

11. The method according to any of claims 1-10, wherein the composition comprises at least two ketone compounds having 8 or more carbon atoms.

12. The method according to any of claims 1-11, wherein the mites are of the genus *Varroa*.

13. The method according to any of claims 1-12, wherein the mites are of the species *Varroa destructor*.

14. The method according to any of claims 1-13, wherein the composition is applied to at least a portion of the beehive.

15. The method according to claim 14, wherein the ketone compound is applied at a rate of from 0.1 $\mu\text{g}/8\text{ cm}^2$ to 1000 $\mu\text{g}/8\text{ cm}^2$.

16. The method according to claim 15, wherein the ketone compound is applied at a rate of from 500 $\mu\text{g}/8\text{ cm}^2$ to 1000 $\mu\text{g}/8\text{ cm}^2$.

17. The method according to any of claims 1-16, wherein the composition is provided on a substrate that is placed in proximity to the beehive.

18. The method according to any of claims 1-17, wherein the composition is applied around the beehive.

19. The method according to any of claims 1-18, wherein the composition is applied to the bees.

20. The method according to any of claims 1-19, wherein the mites are repelled or directed away from entering a beehive.

21. The method according to any of claims 1-20, wherein the mites are repelled or directed away from the bees.

22. The method according to any of claims 1-21, wherein the ketone compound contacts the mites.

23. The method according to any of claims 1-21, wherein the ketone compound does not contact the mites.

24. The method according to any of claims 1-23, wherein relative to prior to exposing the mites to the composition containing the ketone compound, at least 50% of the mites are repelled or directed away from the bees and/or the beehive.

25. The method according to claims 1-23, wherein less than 75% of the bees are repelled or directed away from the beehive for at least 4 hours.

26. The method according to any of claims 1-23, wherein the beehive contains at least 50% less mites relative to a second beehive where mites are not exposed to the ketone compound.

27. Use of a composition comprising at least one ketone compound having 8 or more carbon atoms for directing or repelling mites away from bees and/or a beehive in proximity to the bees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/016820

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01N35/02
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

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, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/044443 A1 (ERICKSON ERIC H [US] ET AL) 6 March 2003 (2003-03-06)	1-4,12,14,17-23,27
Y	paragraphs [0015] - [0041]; claims; examples; table 1	1-27
Y	US 2015/257384 A1 (WU TAI-TEH [US] ET AL) 17 September 2015 (2015-09-17) paragraphs [0122] - [0127], [0167] - [0172], [0425] - [0448]; claims; examples 6-9,11; tables	1-27
Y	ZA 9 806 236 A (CHRISTOFFEL JAKOBUS SMIT) 13 August 1999 (1999-08-13) abstract; claims 1,3,6,9; examples 4.1,4.4.	1-27



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

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"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

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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

Butkowskyj-Walkiw, T

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2017/016820

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