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(54) **COMPOSITION FOR DISSOLVING AN OILY COMPOUND IN WATER**

(57) The present invention relates to a composition for dissolving a water-insoluble active compound comprising: an alcohol, a surfactant, being a quaternary ammonium salt according to Formula I, and water, wherein R3 of Formula I is a C1-18 alkyl or alkene. The invention further relates to the composition comprising an active ingredient. The invention also relates to the use of the composition with the active ingredient as an insect repellent insecticide, antimicrobial composition, antibacterial composition, fragrance or fungicide. Additionally, the invention relates to a method for repelling insects and the invention relates to a method of manufacturing the composition of the invention.

Dit octrooi is verleend ongeacht het bijgevoegde resultaat van het onderzoek naar de stand van de techniek en schriftelijke opinie. Het octrooischrift wijkt af van de oorspronkelijk ingediende stukken. Alle ingediende stukken kunnen bij Octrooicentrum Nederland worden ingezien.

COMPOSITION FOR DISSOLVING AN OILY COMPOUND IN WATER

The present invention relates to a composition for dissolving a water-insoluble active compound. The invention further relates to the composition comprising an active ingredient. The invention further relates to the use of the composition with the active ingredient as an insect repellent.

Insect repellents can prevent and control the outbreak of insect-borne, and other arthropod-borne, diseases such as malaria, Lyme disease, dengue fever, bubonic plague, river blindness, and West Nile fever. Most insect repellents are insecticides (bug killers), but some additionally discourage insects and send them flying or crawling away. Common insect repellents are DEET (N,N-diethyl-m-toluamide), permethrin and icaridin, also known as picaridin or saltidin. Icaridin is effective against the greatest range of insects, this chemical is a synthetic version of piperine, a repellent found in pepper plants. Icaridin also has minimal odor, no damaging effect on plastics and other synthetics and meets all requirements for human and environmental safety and effective use. Together with DEET, icaridin is therefore one of the most popular insect repellents.

Icaridin is often sold under its product name, Picaridin. This product is icaridin dissolved in a neat oil. A neat oil is a water-undiluted mineral or vegetable oil blended with certain additives in order to generate certain beneficial properties. Picaridin can further be diluted in organic solvents such as ethanol, dimethylsulfoxide (DMSO), and dimethyl formamide (DMF).

Due to its hydrophobic properties, it is impossible to dissolve an effective amount of icaridin in water. It is therefore impossible to prepare an aqueous solution comprising icaridin, which can be used as an insect repellent. Icaridin can therefore not be used in for example sprayable non-dangerous and non-harmful insect repellents such as active wall sprays, clothing sprays and topical skin formulations. The lack of a safe sprayable formulation comprising icaridin severely hampers the effectiveness of the compound. Furthermore, on a surface, the compound evaporates quicker thus limiting the time of action. Currently available icaridin products are based on alcohol, which makes the product flammable. This leads to logistical restrains and more implementation issues.

An alternative way of dissolving compounds having hydrophobic characteristics in water is dissolving these compounds by using cosolvents. Cosolvent techniques are however only deployed to solubilize solids or hydrophobic compound but not for compounds which are water-insoluble, such as oily compounds. Also, as another alternative, surfactants are often applied to dissolve oily compounds, however, adding surfactants only provides solubility to oily compounds in (very) low concentrations.

It is therefore an object of the invention to provide a composition for dissolving hydrophobic compounds in water.

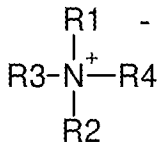
It was surprisingly found that a composition comprising an alcohol, which is liquid at room temperature, and a surfactant, being a quaternary ammonium salt provides the ability to dissolve water-insoluble active compounds in water.

The alcohol is this composition is a cosolvent. Cosolvents are added to compositions to increase the solubility of a poorly soluble compound. Cosolvents are utilized in dissolving solubilize solids or hydrophobic compounds in aqueous systems but not in oily solvents.

The term surfactant is derived from the term surface-active agent. This means that the compound can lower the surface tension of a liquid or the interfacial tension between two liquids, between a gas and a liquid or between a solid and a liquid. Surfactants can therefor act as detergents, wetting agents, emulsifiers, foaming agents, or dispersants. In the context of this of the present invention, the surfactant acts as an emulsifier, which means that the surfactant will form a micelle or micelle like structure around the water-insoluble active compound.

The invention therefore relates to a composition for dissolving a water-insoluble active compound, comprising:

- an alcohol,
- a surfactant, being a quaternary ammonium salt according to Formula I, and
- water,



Formula I

wherein R3 is a C1-18 alkyl or alkene.

This composition comprising the combination of a surfactant and a cosolvent enables to dissolve a water-insoluble compound in water.

The surfactant of the composition of the present invention is a quaternary ammonium salt according to Formula I. The surfactant forms a corona like structure with its hydrophobic side turned towards the water-insoluble compound and its hydrophilic sides turned towards the water molecules. Such surfactants allow the oily substance to form a stable mixture with the aqueous solution.

The invention provides a system which enables dissolving water-insoluble active compounds. The invention therefore further relates to the above composition further comprising an effective amount of water-insoluble active compound, preferably an oily active compound.

The active compound of the composition of the present invention can be a naturally or synthetic insect repellent, insecticide, antimicrobial compound, antibacterial compound or fungicide, an aniline-based molecule, such as a dye, aroma, or odorant.

According to the invention, the active compounds can be selected from the group consisting of icaridin, DEET (N,N-diethyl-meta-toluamide), citronellal, citronellol, eucalyptol, nepetalactone, azadirachtin, A-terpineol, carvacrol, thymol, cinnamaldehyde, rosemary oil, cedarwood oil, myrcene, citral, geranyl acetate, nerol, geraniol, limonene, permethrin, zinc-pyrithione, or derivatives thereof, preferably, icaridin and derivatives thereof.

The surfactant of the composition of the invention can be split in four embodiments based on the definition of the R-groups. The first embodiment further defines R4.

The invention therefore further relates to the above composition, wherein R4 of Formula I is a methyl group, an alkyl shorter than the alkyls in R1, R2 and R3 or wherein R4 of Formula I is one to three carbons with a carboxylic acid, hydroxy, sulfonate, quaternary silane group or phenyl group.

The second embodiment is directed to the composition of the invention, wherein R1, R2 and R3 are the same.

Further, in the third embodiment, all R-groups are further defined. The invention therefore also relates to the above composition, wherein R1, R2 are a methyl group, R3 is C_nH_{2n+1} with n=1-18 and R4 is an alkyl shorter than the alkyls in R1, R2 and R3, or R4 is one to three carbons and a carboxylic acid, hydroxy, sulfonate or phenyl group.

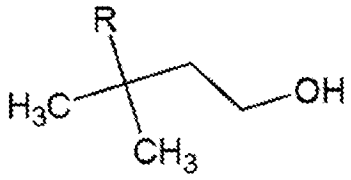
Finally, in the fourth embodiment, the invention relates to the above composition, wherein each of R1, R2, R3 and R4 are the same.

The invention therefore also relates to the above composition wherein the counter ion of the quaternary ammonium salt is a halide anion, preferably a chloride ion or a bromide ion.

The surfactants of the composition of the invention can be a compound selected from the list consisting of trimethyloctadecylammonium chloride, stearyltrimethylammonium chloride, hexadecyltrimethylammonium chloride, cetyltrimethylammonium chloride, tetradecyltrimethylammonium bromide, myristyltrimethylammonium bromide, tetradecyltrimethylammonium chloride, dodecyltrimethylammonium bromide, dodecyltrimethylammonium chloride, trimethylactylammonium chloride, tetramethylammonium chloride, dimethyloctadecyl[3-(trimethoxysilyl)propyl]ammonium chloride, cetyl dimethyl betaine, benzalkalkonium chloride, 3-(dimethyl(octadecyl)ammonio)propane-1-sulfonate, N-dodecyl-N,N-(dimethylammonio)butyrate (DDMAB), bezyldimethyldodecylammonium chloride, zephirol, N-dodecyl-N,N-dimethyl-3- ammonio-1-propanesulfonate, domiohen bromide, (lauryldimethylammonio)acetate, didecyldimethylammonium bromide, didodecyldimethylammonium bromide, methyltrioctylammonium chloride,

tridodecylmethylammonium chloride, tetraoctylammonium bromide, tetradodecylammonium bromide, preferably trimethyloctadecylammonium chloride.

Alcohols are organic compounds with at least one hydroxy group. In the context of the present invention, the alcohol acts as a cosolvent. The alcohol as present in the composition of the present invention can be divided into four main categories that work in the cosolvent principle. The first category are the linear alcohols, these are hydrocarbons with one hydroxy group. The linear alcohols have variation in carbon chain length, however these linear alcohols do not possess branches. The second category are the branched alcohols, these are hydrocarbon chains with at least one branch, which has the length of at least a methyl group. The third category is depicted as Formula II. Each compound of this category of Formula II comprises a 1-butanol backbone, with two methyl groups and an R-group at the 3-position.



Formula II

The final category involves the same alcohols as in the first three categories, however these alcohols contain at least two hydroxy groups instead of one.

The invention also relates to the above composition, wherein the alcohol is liquid at room temperature, and wherein the alcohol in particular is methanol, ethanol, propanol, propanol derivatives, butanol, or butanol derivatives.

In a further embodiment, the propanol derivative of the composition of the invention is 2-propanol or isopropyl ether-ethyl alcohol.

In another embodiment, the butanol derivative of the composition of the invention is selected from the list consisting of tert-butanol, isobutanol, 2-methoxy-3-methyl-1-butanol (MMB), 3-ethoxy-3-methyl-1-butanol, 3-benzyloxy-3-methyl-1-butanol, 3-methyl-3-methyl-1-butanol, 3-methyl-1,3-butanediol, and is preferably 2-methoxy-3-methyl-1-butanol (MMB).

According to the invention, the active compound is present in the composition in about 0.1 wt.% to about 44.9 wt.%, preferably about 0.1 wt.% to about 20 wt.%, more preferably in about 0.1 wt.% to about 10 wt.%, even more preferably in about 0.5 wt.% to about 7 wt.%, most preferably in about 1 wt.% to about 5 wt.%, most preferably in about 2 wt.% to about 3 wt.% with respect to the total weight of the composition.

The surfactant can be present in the composition of the invention in about 0.1 wt.% to 6 wt.%, preferably in about 0.5 wt.% to 4 wt.%, more preferably in about 0.75 wt.% to 3 wt.%, most preferably in about 1 wt.% to 2 wt.% with respect to the total weight of the composition.

The alcohol can be present in the composition in about 5 wt.% to 49.9 wt.%, preferably in about 7 wt.% to 40 wt.%, more preferably in about 9 wt.% to 30 wt.%, more preferably in about 10 wt.% to 25 wt.%, most preferably in about 12.5 wt.% to 15 wt% with respect to the total weight of the composition, with the proviso that water is present in the composition in a higher wt.% than any other component of the composition separately.

In the context of the present invention a solution is defined as a solute being dissolved in the solvent and resulting in a homogeneous mixture that is stable over time and will remain a homogenous stable mixture when passed through a filter.

Also, in the context of this invention the solvent in an aqueous solution is always liquid water. Therefore, a composition having multiple components is considered an aqueous solution when water is present in the composition in a higher wt.% than any other component of the composition separately.

Therefore, in another embodiment, the invention relates to the composition of the invention, wherein the water is present in the composition in a higher wt.% than any other component of the composition separately.

Also, in an embodiment of the invention, the water is deionized water.

In a further embodiment of the invention, the water is present in the composition in a higher wt.% than the other components of the composition together.

According to a preferred embodiment of the invention the water is present in the composition in more than 50 wt.%, preferably more than 60 wt.%, more preferably in more than 70 wt.%, most preferably in more than 80 wt.% with respect to the total weight of the composition or wherein the water is present in about 80 wt.% with respect to the total weight of the composition.

In a preferred embodiment, the invention relates to the above composition, wherein the composition comprises 2-methoxy-3-methyl-1-butanol, trimethyloctadecylammonium chloride, icaridin and water.

In this more preferred embodiment, the composition of the invention may comprise at least 12.5 wt.% methoxy-3-methyl-1-butanol and at least 1 wt.% trimethyloctadecylammonium chloride with respect to the total weight of the composition.

The composition of the invention can comprise an active compound, however the invention also relates to the composition in which the active compound is not present, i.e. wherein the composition solely consists of the system for dissolving oily compounds. This latter composition comprises the alcohol in a different wt.% than the composition which does comprise the active compound. Therefore, the composition of the invention in which the active compound is not present can comprise alcohol in at least 12.5 wt.%, preferably between 12.5 wt.% and 50 wt.%, more preferably between 15 wt.% and 40 wt.%, even more preferably between 15 wt.% and 25 wt.%, most preferably in about 20 wt.% with respect to the total weight of the composition.

In the embodiment in which the composition of the invention does not comprise the active compound, the composition can also comprise the surfactant in a different wt.% than the composition which does not comprise the active compound. The composition of the invention in which the active compound is not present can comprise the surfactant in about 0.1 wt.% to 12 wt.%, preferably in about 0.5 wt.% to 8 wt.%, more preferably in about 0.75 wt.% to 4 wt.%, most preferably in about 1 wt.% to 2 wt.% with respect to the total weight of the composition.

Further, the composition of the invention with the active compound can be used as an insect repellent, insecticide, antimicrobial composition, antibacterial composition fragrance, or fungicide. In particular, the composition of the invention can be used to repel insects, in particular in particular insects that have the potential to carry communicable diseases, more in particular mosquitoes, ticks, cockroaches, bed bugs, ants, biting flies, fleas and chiggers.

In another embodiment, the invention relates to the above composition for use on a building, part of a building, building material such as concrete, plastic, brick, foam, or polyester. Implementing the composition of the invention into homes or building materials of homes enables a convenient application of the active compound present in the composition of the invention. When active compounds are in an aqueous solution, such compound are better implementable in homes or building materials of homes.

In a further embodiment, the invention relates to the above composition, for use in a coating, paint, epoxy, wood, brick, fibers, composite materials, or textile.

Also, in another embodiment, the composition of the invention can be used on human or animal skin. The composition of the application is an aqueous solution and is therefore not flammable and less hazardous. Consequently, application of the composition of the invention on the human or animal skin is more convenient and safer.

In addition, a further embodiment of the invention is that the composition can be used as topical skin composition, in particular a cosmetic lotion, spray, or cream or as part of topical skin composition, such as a lotion, spray or cream.

The invention further relates to a method for repelling insects, comprising:

- applying the composition of the invention on a surface, wherein the surface is preferably human or animal skin, a surface of a building, or part of a building, building material or a coating.

The invention also relates to a method of manufacturing the composition of the invention without the active compound, comprising:

- dissolving the alcohol and surfactant as described above in water to obtain a solution.

The invention also relates to a method of manufacturing the composition of the invention with the active compound, comprising:

- dissolving the alcohol and surfactant as described above in water to obtain a solution.
- adding the in water in soluble active compound as described above to the solution.

The invention also relates to the use of the composition of the invention as an insect repellent, insecticide, antimicrobial composition, antibacterial composition, or fungicide.

The invention will now be illustrated by means of the following examples, which do not limit the scope of the invention in any way.

5

EXAMPLES

Example 1

A general procedure to prepare the solution of an active compound in the composition of the invention is applied:

Deionized water was brought in a beaker equipped with a stirring bar and placed on a stirring plate. The cosolvent was added to the solution whilst stirring. Subsequently, the surfactant was added, and before the surfactant was dissolved also icaridin was added. Stirring is stopped when all components of the composition are dissolved.

The experiments are summarized in **Table 1** below. The first column lists the cosolvent and surfactant that were used. The second column describes the results, and the third column provides the weight percentages of the various components.

Table 1

Description experiment	Result	Compounds (Wt.%)
MMB and Trimethyloctadecyl ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 1)	Deionized water: 81.5 MMB: 12.5 Trimethyloctadecyl ammonium chloride: 1.0 Icaridin: 5.0
MMB and Dimethyloctadecyl [3-trimethoxysilyl)propyl] ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 2)	Deionized water: 80.5 MMB: 12.5 Dimethyloctadecyl [3-trimethoxysilyl)propyl] ammonium chloride: 2.0 Icaridin: 5.0
MMB and Tetradecyltrimethyl ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution.	Deionized water: 79.0 MMB: 15.0 Tetradecyltrimethyl ammonium chloride: 1.0

	It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 3)	Icaridin: 5.0
MMB and 3-(dimethyl(octadecyl) ammonio)propane-1-sulfonate	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 4)	Deionized water: 79.0 MMB: 15.0 3-(dimethyl(octadecyl) ammonio)propane-1-sulfonate: 1.0 Icaridin: 5.0
MMB and Domiohen bromide	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 5)	Deionized water: 79.0 MMB: 15.0 Domiohen bromide: 1.0 Icaridin: 5.0
MMB and Didodecyldimethyl ammonium bromide	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 6)	Deionized water: 79.0 MMB: 15.0 Didodecyldimethyl ammonium bromide: 1.0 Icaridin: 5.0
IPA and Trimethyloctadecyl ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an	Deionized water: 79 IPA: 15 Trimethyloctadecylammonium chloride: 1.0 Icaridin: 5.0

	aqueous Icaridin solution. (Figure 7)	
Methanol and Trimethyloctadecyl ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 8)	Deionized water: 79 IPA: 15 Trimethyloctadecylammonium chloride: 1.0 Icaridin: 5.0
Ethanol and Trimethyloctadecyl ammonium chloride	All compounds were mixed together which yielded a colourless translucent solution. It can thus be concluded that the combination of the used surfactant and MMB leads to an aqueous Icaridin solution. (Figure 9)	Deionized water: 79 IPA: 15 Trimethyloctadecylammonium chloride: 1.0 Icaridin: 5.0

Example 2

In this experiment, it is tested if the combination of the cosolvent and the surfactant is required to dissolve icaridin or if individual components can also dissolve icaridin in water.

Deionized water was brought in a beaker equipped with a stirring bar and placed on a stirring plate. The (when applicable) cosolvent was added to the solution whilst stirring. Subsequently (when applicable) the surfactant was added, before this dissolved also (when applicable) icaridin was added. Stirring is stopped when everything is dissolved.

Table 2

Description experiment	Result	Compounds (Wt.%)
Icaridin in water	Deionized water and icaridin were mixture together. Upon initial mixing this resulted in a milky white solution that was only 'Stable' for a few hours. After wards face separation occurred. This can be seen in the picture. Icaridin and water are present as layers above each other. Icaridin can thus not be dissolved in water in our desired concentration. (Figure 10)	Deionized water: 95.0 Icaridin: 5.0
Icaridin in a mixture of water and MMB	All compounds were mixed together which yielded a colorless translucent solution. It can thus be concluded that a relative high concentration of MMB leads to an aqueous Icaridin solution. (Figure 11)	Deionized water: 50 MMB: 45 Icaridin: 5.0
Icaridin in a mixture of water and MMB	All compounds were mixed together which yielded a colorless translucent solution. It can thus be concluded that a relative high concentration of MMB leads to an aqueous Icaridin solution. (Figure 12)	Deionized water: 70 MMB: 25 Icaridin: 5.0
Icaridin in a mixture of water and MMB	All compounds were mixed together which yielded a milky white solution. It can thus be concluded that a	Deionized water: 82.5 MMB: 12.5 Icaridin: 5.0

	relative low concentration of MMB without a surfactant leads to an unstable solution and thus not an aqueous Icaridin solution. (Figure 13)	
Icaridin with a surfactant in water	All compounds were mixed together which yielded a milky white solution with flakes in it. It can thus be concluded that only a surfactant without solvent leads to an unstable solution and thus not an aqueous Icaridin solution. (Figure 14)	Deionized water: 93.0 Trimethyloctadecylammonium chloride: 2.0 Icaridin: 5.0
MMB and Tetradodecylammonium bromide	All compounds were mixed together which yielded a milky white solution with flakes in it. It can thus be concluded that an unstable solution is present and thus not an aqueous Icaridin solution. Therefor this surfactant is not useful. (Figure 15)	Deionized water: 79.0 MMB: 15.0 Tetradodecylammonium bromide: 1.0 Icaridin: 5.0

From **Table 2** it can be concluded that icaridin is only soluble in water using the combination cosolvent and surfactants.

Example 3

The same test was applied to determine if the composition of the invention is also able to dissolve alternative water-insoluble compounds. In this experiment icaridin was switched for DEET and the general procedure was applied.

Table 3

Description experiment	Result	Compounds (Wt.%)
General procedure was followed. Icaridin was switched for DEET	All compounds were mixed together which yielded a clear translucent solution. It can thus be concluded that a stable solution is present and thus possible to obtain an aqueous solution with other non-water solvable compounds. (Figure 16)	Deionized water: 81.5 MMB: 12.5 Trimethyloctadecylammonium chloride: 1.0 DEET: 5.0

In **Table 3,** it is demonstrated that the composition of the invention also enables dissolving DEET in 5 wt.% in water.

Example 4. GC-method and NMR-method

The GC-method is performed to demonstrate that the active compound is present in the solution. The GC-method experiment is performed according to the following steps:

1. Prepare an internal standard solution (IS) via dilution of EBAP (Ethyl butylacetylaminopropionate, cas# 52304-36-6) with IPA (2-propanol, cas# 67-63-0) to obtain a 1% EBAP solution in IPA.
2. Prepare a rinse solution. Dilute the IS solution 100 times with IPA to 0.01% EBAP.
3. Cut pieces of Whatman no. 1 paper (25 mm x 40 mm + 10 mm (10 cm2 + 2.5 cm2)).
4. Cut pieces 100% cotton shirts (25mm x 40 mm + 10 mm (10 cm2 + 2.5 cm2))
5. Prepare a to be tested solution as stated in section 3.1.
6. Apply to each of five papers and five textile pieces, 20 µL of the to be tested solution with a micro pipette in a spot like pattern of ~2 µL per spot.
7. Before a sample is taken. Prepare 10 sample vials (25 mL) by filling them with 10 mL rinse solution each.
8. Transfer the papers/textile sheets to their corresponding sample vials and make sure they are full emerged in solution.

9. Once all the papers and textile pieces are in a sample vial, leave them for at least 8h. Next transfer 1 mL of each solution into a GC vial and measure GC following the specifics in the table below.

10. Check if the compound peak is present at the expected retention time.

Table 4

Equipment and information of GC-chromatography.

Equipment	Information		
Gas Chromatography (GC)	Shimadzu 2010	Injector	250 °C
GC Software	GC solution version 2.30.00	Detector temperature	325 °C
Column	Thermo TG-5SILMS; 30 m; ID 0.25 mm; film 0.25 um	Make up flow	nitrogen/air 30 mL/min
Program	0:00 – 2:00 (min:sec) - 150 °C, 2:00 – 10:30 ramp to 320 °C (20 °C /min)	Hydrogen flow	60 mL/min
Ionization mode	EI	Air flow	400 mL/min
Split	10	Sampling rate	40 ms
Injection Volume	1 µL	Retention time IS	4.3 - 4.5 min
Carrier gas	1 bar, 21 mL/min	Retention time Icaridin	5.0 - 5.1 min
Column flow	1.77 mL/min	GC vials + Caps	1.5 mL, septa caps
		Gilson pipette	2 – 10 µL, 10 – 200 µL, 100 – 1000 µL

An NMR-method is also performed to demonstrate that the active compound is present in the solution. The NMR-method experiment is performed according to the following steps:

Dissolve 25 µg of the solution in 0.7 mL of DMSO-d6 or CDCl3 depending on the active compound and measure an NMR on a 500 MHz machine at least. Make sure to do a prediction of the active compound and other compound and identify the signals.

Example 5. Mosquito method

The following mosquito method is performed to prove that an active compound is still active in the formulation for insect repellent compounds.

In lack of official standard methodology, the procedure was based upon the "Guidelines for efficacy testing of spatial repellent" from the World Health Organization (Guidelines for efficacy testing of spatial repellent, World Health Organization, 2013, ISBN 978 92 4 150 502 4).

For the preparation of the test samples, aliquots of the IRLs (Insect Repellent Liquids) were applied (3.0 mL) evenly to a 20.0 x 27.5 cm (550 cm2) paper (type: Whatman No 1.) with a micro pipette. The samples were dried at ambient conditions (20-25 °C) without any forced heating. All IRLs were stored in their original packaging at 15 – 25 °C until the start of the test.

Female mosquitoes of the genera *Anopheles Arabiensis KGB* were reared according to a standard protocol. The mosquitoes were reared at a temperature of 27 ± 2 °C, a relative humidity of 80 ± 10%, and a photoperiod of 11.5 h light: 45 min dusk : 11.15 h dark : 45 min dusk. Pupae were collected and transferred to a screen cage where they were enclosed as adults. Adults were maintained in screen cages with a 10% sucrose solution as an energy source. Five to eight-day old non-blood-fed female nulliparous mosquitoes were starved (provided only with water) for 24 h before testing. Actively host-seeking females were selected from general colony groups to ensure a maximum behavioural response. This was done with an aspirator or an appropriate airflow apparatus while holding a hand close to (but not touching) the cage and collecting those mosquitoes that actively probe. All repellency tests were observed in female mosquitoes starved for preceding 12 h. The mosquitoes were transferred to holding containers with care to avoid physically damaging them.

A modular test system was used based on the WHO Guidelines (Guidelines for efficacy testing of spatial repellent, World Health Organization, 2013, ISBN 978 92 4 150 502 4). The spatial repellency assay allowing examination of both spatial repellent and contact irritant responses. The main components of the modular system are illustrated and numbered in Figure 17. The actual used modular test system is depicted in Figure 18. The total length of the test system use was 80 cm.

Each treatment cylinder (Figure 17) was constructed of Plexiglas tubing (9.0 cm outside diameter, 0.3 cm thick, 28.5 cm long, 25 cm long trapping area) and had a butterfly valve installed at one side and an end cap on the other side. The end cap was constructed of a Plexiglas cylinder (9.8 cm outside diameter, 0.4 cm thick, 2.6 cm long), and covered with a membrane that allows air

coming in and out of the modular system. The clear middle cylinder (Figure 18) was constructed of Plexiglas tubing with the same outside diameter and thickness as the treatment cylinders (both ends have an outside diameter 9.8 cm, 0.4 cm thick and length of 3.4 cm) but with a length of 25.8 cm and a trapping area of 16.4 cm. Midway along the length of the clear cylinders, a hole covered with cork provided for transferring mosquitoes.

Treatment filter paper (Whatman No. 1 or similar) was cut to 10 x 27.5 cm to fit (two pieces) inside the treatment cylinder trapping area and are held in place by scotch tape. The room in which all repellency tests were performed were kept at a temperature of 27 ± 2 °C and a relative humidity of 80 ± 10%.

The spatial repellency assay was performed in a closed temperature and humidity-controlled room, without windows and with light. Groups of 20 female mosquitoes were introduced from holding tubes into the clear cylinder (with an aspirator) and were allowed to acclimatize to the test environment for 30 seconds. The number of mosquitoes that were physically damaged and were incapable of flying or walking were recorded to correct for the total mosquito sample size available to respond to the test sample in that replicate. All butterfly valves were simultaneously opened for 4 min to allow chemical vapours to flow through the test unit and also to allow free movement of the mosquitoes throughout the unit, as indicated by the grey arrows in Figure 17. The butterfly valves were closed after 4 min, and the number of mosquitoes in each cylinder were recorded. The number of knock-down mosquitoes in each cylinder were also recorded.

The treatment cylinders were disconnected from the centre clear cylinder and the end cap was removed from both treatment cylinders and the mosquitoes were blown out into a mosquito collection cage. Also, the mosquitoes from the centre clear cylinder were blown to the mosquito collection cage. Between the replicates, all treated substrates remained in place. Successive replicates were carried out without delay.

Replicates were performed for each test sample. At the conclusion of testing, the proportion of mosquitoes repelled by the treatment was determined. Spatial repellency was expressed as the proportion of mosquitoes prevented from entering the treatment space in relation to all mosquitoes moving within the system and is calculated from a 'spatial activity index':

$$SAI = \left[\frac{(Nc - Nt)}{(Nc + Nt)}\right] \times \left(\frac{Nm}{N}\right)$$

where SAI is the spatial activity index, Nc is the number of mosquitoes in the control metal chamber, Nt is the number of mosquitoes in the treatment metal chamber, Nm is the total number of mosquitoes in the two metal chambers, and N is the total number of mosquitoes in the test unit.

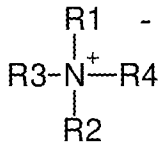
The spatial activity index varies from –1 to 1: zero indicates no response; –1 indicates that all mosquitoes moved into the treatment chamber, resulting in an attractant response; and 1 indicates that all the mosquitoes moved into the control chamber (away from the treatment source), resulting in a spatial repellent response. If no movement is recorded within the system (i.e. $N_t = 0$, $Nc = 0$), the test is valid but the spatial activity index is 0.

The spatial activity index as calculated for each replicate. The number of replicates, the total number of mosquitoes and the spatial activity index for each test sample was reported.

CONCLUSIES

1. Gebruik van een samenstelling voor het oplossen van een in water onoplosbare actieve verbinding, omvattende:

- een alcohol gekozen uit de groep bestaande uit: methanol, ethanol, propanol, propanolderivaten, butanol en butanolderivaten,
- een oppervlakte-actieve stof, welke een quaternair ammoniumzout volgens Formule I is en
- water



Formule I

waarbij R3 een C1-C18 alkyl of alkeen is.

2. Gebruik volgens conclusie 1, waarbij de samenstelling verder een effectieve hoeveelheid van een in water onoplosbare actieve verbinding, bij voorkeur een olieachtige actieve verbinding omvat.

3. Gebruik volgens conclusie 1 of 2, waarbij de actieve verbinding is gekozen uit de groep bestaande uit icaridin, DEET, N,N-Diethyl-meta-toluamide, citronellal, citronellol, eucalyptol, nepetalacton, azadirachtine, A-terpineol, carvacrol, thymol, kaneelaldehyde, Rozemarijnolie, Cederhoutolie, myrceen, citral, geranylacetaat, nerol, geraniol, limoneen, permethrine, zinkpyrithion of derivaten daarvan, bij voorkeur icaridine of derivaten daarvan.

4. Gebruik volgens één der conclusies 1-3, waarbij R4 van Formule I een methylgroep, een alkyl korter dan de alkyls in R1, R2 en R3 of R4 één tot drie koolstoffen met een carbonzuur-, hydroxy-, sulfonaat- of fenylgroep is.

5. Gebruik volgens één der conclusies 1-3, waarbij R1, R2 en R3 hetzelfde zijn.

6. Gebruik volgens één der conclusies 1-3, waarbij R1 en R2 een methylgroep en R3 C_nH_{2n+1} met n=1-18 is en R4 een alkyl korter dan de alkyls in R1, R2 en R3 of R4 één tot drie koolstoffen met een carbonzuur-, hydroxy-, sulfonaat- of fenylgroep is.

7. Gebruik volgens één der conclusies 1-3, waarbij R1, R2, R3 en R4 hetzelfde zijn.

8. Gebruik volgens één der conclusies 1-7, waarbij het tegenion van het quaternair ammoniumzout een halide-ion is, bij voorkeur een chloride-ion of een bromide-ion.

9. Gebruik volgens één der conclusies 1-8, waarbij de oppervlakte-actieve stof een verbinding uit de lijst is, bestaande uit trimethyloctadecylammoniumchloride (SQ), stearyltrimethylammoniumchloride, hexadecyltrimethylammoniumchloride, cetyltrimethylammoniumchloride, tetradecyltrimethylammoniumbromide, myristyltrimethylammoniumbromide, tetradecyltrimethylammoniumchloride, dodecyltrimethylammoniumbromide, dodecyltrimethylammoniumchloride, trimethylactylammoniumchloride, tetramethylammoniumchloride, dimethyloctadecyl[3-(trimethoxysilyl)propyl]ammoniumchloride, cetyldimethylbetaïne, benzalkoniumchloride, 3-(dimethyl(octadecyl)ammonio)propaan-1-sulfonaat, N-dodecyl-N,N-(dimethylammonio)butyraat (DDMAB), bezyldimethyldodecylammoniumchloride, zefirol, N-dodecyl-N,N-dimethyl-3-ammonio-1-propaansulfonaat, domiohenbromide, (lauryldimethylammonio)acetaat, didecyldimethylammoniumbromide, didodecyldimethylammoniumbromide, methyltrioctylammoniumchloride, tridodecylmethylammoniumchloride, tetraoctylammoniumbromide, tetradodecylammoniumbromide.

10. Gebruik volgens één der conclusies 1-9, waarbij de oppervlakte-actieve stof trimethyloctadecylammoniumchloride (SQ) is.

11. Gebruik volgens één der conclusies 1-10, waarbij de alcohol propanol, propanolderivaten, butanol of butanolderivaten zijn.

12. Gebruik volgens conclusie 11, waarbij het propanolderivaat 2-propanol of isopropylether-ethylacohol is.

13. Gebruik volgens conclusie 11, waarbij het butanolderivaat is gekozen uit de lijst bestaande uit tert-butanol, isobutanol, 2-methoxy-3-methyl-1-butanol (MMB), 3-ethoxy-3-methyl-1-butanol, 3-benzyloxy-3-methyl-1-butanol, 3-methyl-3-methyl-1-butanol, 3-methyl-1,3-butaandiol, bij voorkeur 2-methoxy-3-methyl-1-butanol (MMB).

14. Gebruik volgens één der conclusies 2-13, waarbij de in water onoplosbare actieve verbinding aanwezig is in de samenstelling in ongeveer 0,01 gew.% tot ongeveer 44,9 gew.%, bij voorkeur in ongeveer 0,1 gew.% tot ongeveer 20 gew.%, meer bij voorkeur in ongeveer 0,1 gew.% tot ongeveer 10 gew.%, nog meer bij voorkeur in ongeveer 0,5 gew.% tot ongeveer 7 gew.%, zelfs nog meer bij voorkeur in ongeveer 1 gew.% tot ongeveer 5 gew.%, meest bij voorkeur in ongeveer 2 gew.% tot ongeveer 3 gew.% in verhouding tot het totale gewicht van de samenstelling.

15. Gebruik volgens één der conclusies 1-14, waarbij de oppervlakte actieve stof aanwezig is in de samenstelling in ongeveer 0,1 gew.% tot ongeveer 6 gew.%, bij voorkeur ongeveer 0,5 gew.% tot ongeveer 4 gew.%, meer bij voorkeur in ongeveer 0,75 gew.% tot ongeveer 3 gew.%, meest bij voorkeur in ongeveer 1 gew.% tot ongeveer 2 gew.% in verhouding tot het totale gewicht van de samenstelling.

16. Gebruik volgens één der conclusies 1-15, waarbij de alcohol aanwezig is in de samenstelling in ongeveer 5 gew.% tot 49,9 gew.%, bij voorkeur in ongeveer 7 gew.% tot 40 gew.%, bij meer voorkeur in ongeveer 9 gew.% tot 30 gew.%, bij nog meer voorkeur in ongeveer 10 gew.% to 25 gew.%, voor bij voorkeur in ongeveer 12,5 gew.% in verhouding tot het totale gewicht van de samenstelling, met de voorwaarde dat water aanwezig is in de samenstelling in een hoger gew.% dan elk andere component van de samenstelling afzonderlijk.

17. Gebruik volgens één der conclusies 1-16, waarbij het water aanwezig is in de samenstelling in een hoger gew.% dan elk andere component in de samenstelling afzonderlijk.

18. Gebruik volgens één der conclusies 1-17, waarbij het water gedeïoniseerd water is.

19. Gebruik volgens één der conclusies 1-18, waarbij het water aanwezig is in de samenstelling in een hoger gew.% dan de andere componenten van de samenstelling gezamenlijk.

20. Gebruik volgens één der conclusies 1-19, waarbij water aanwezig is in de samenstelling in meer dan 50 gew.%, bij voorkeur meer dan 60 gew.%, meer bij voorkeur in meer dan 70 gew.%, meest bij voorkeur in meer dan 80 gew.% in verhouding tot het totale gewicht van de samenstelling, of waarbij het water aanwezig is in de samenstelling in meer dan ongeveer 80 gew.% in verhouding tot het totale gewicht van de samenstelling.

21. Gebruik volgens één der conclusies 2-20, waarbij de samenstelling 2-methoxy-3-methyl-1-butanol, trimethyloctadecylammoniumchloride, icaridine en water omvat.

22. Gebruik volgens conclusie 21, waarbij de samenstelling ten minste 12,5 gew.% 2-methoxy-3-methyl-1-butanol en ten minste 1 gew.% trimethyloctadecylammoniumchloride, in verhouding tot het totale gewicht van de samenstelling omvat.

23. Gebruik volgens conclusie 1, waarbij alcohol aanwezig is in de samenstelling in ten minste 12,5 gew.% bij voorkeur tussen 12,5 gew.% en 50 gew.%, meer bij voorkeur tussen 15 gew.% en 40 gew.%, zelfs meer bij voorkeur tussen 15 gew.% en 25 gew.%, meest bij voorkeur in ongeveer 20 gew.% in verhouding tot het totale gewicht van de samenstelling.

24. Gebruik volgens conclusie 1, waarbij alcohol aanwezig is in de samenstelling in ten minste 12,5 gew.% bij voorkeur tussen 12,5 gew.% en 50 gew.%, meer bij voorkeur tussen 15 gew.% en 40 gew.%, zelfs meer bij voorkeur tussen 15 gew.% en 25 gew.%, meest bij voorkeur in ongeveer 20 gew.% in verhouding tot het totale gewicht van de samenstelling.

25. Gebruik volgens één der conclusies 2-22, voor gebruik als insectenwerend middel, insecticide, antimicrobiële samenstelling, antibacteriële samenstelling, geurmiddel of fungicide.

26. Gebruik volgens één der conclusies 2-22, voor gebruik in een gebouw, gedeelte van een gebouw, bouwmateriaal zoals beton, plastic, steen, schuim of polyester.

27. Gebruik volgens één der conclusies 2-22, voor gebruik in coating, verf, epoxy, hout, steen, vezels, composietmateriaal of textiel.

28. Gebruik volgens één der conclusies 2-22, voor gebruik op menselijke of dierlijke huid.

29. Gebruik volgens één der conclusies 2-22, voor gebruik als topische huid- of cosmetische lotion, spray of crème of als deel van een topische huid- of cosmetische lotion, spray of crème.

30. Werkwijze voor het weren van insecten, omvattende:

- het toepassen van de samenstelling volgens één der conclusies 2-22 op een oppervlak, waarbij het oppervlak bij voorkeur een menselijke of dierlijke huid of het oppervlak van een gebouw, gedeelte van een gebouw, bouwmateriaal of een coating is.

31. Werkwijze voor vervaardigen van de samenstelling volgens één der conclusies 1-24, omvattende:

- het oplossen van de alcohol en de oppervlakte-actieve stof zoals gedefinieerd in één der conclusies 1-24 in water zodat een oplossing wordt verkregen.

32. Werkwijze voor het vervaardigen van de samenstelling volgens één der conclusies 2-22, omvattende:

- het oplossen van de alcohol en de oppervlakte-actieve stof zoals gedefinieerd in één der conclusies 1-24 in water zodat een oplossing wordt verkregen,
- het toevoegen van de in water onoplosbare actieve verbinding zoals gedefinieerd in één der conclusies 2-22 aan de oplossing.

33. Gebruik van een samenstelling zoals gedefinieerd in één der conclusies 2-22 voor het opslaan van een actieve verbinding in extreme omstandigheden, waarbij de extreme omstandigheden een temperatuur tussen -20 °C en 20 °C, in het bijzonder tussen -20 °C en 4 °C, meer in het bijzonder tussen -20 °C en 0°C.

34. Gebruik van een samenstelling zoals gedefinieerd in één der conclusies 2-22 voor het opslaan van een actieve verbinding in extreme omstandigheden, waarbij de extreme omstandigheden een temperatuur tussen 20 °C en 60 °C, in het bijzonder tussen 30 °C en 55 °C, meer in het bijzonder tussen 40 °C en 50°C.

35. Gebruik van een samenstelling zoals gedefinieerd in één der conclusies 2-22 voor het opslaan van een actieve verbinding voor ten minste 1 week, in het bijzonder ten minste 1 maand, meer in het bijzonder ten minste 2 maanden, het meest in het bijzonder ten minste 3,5 maanden.

Figure 1

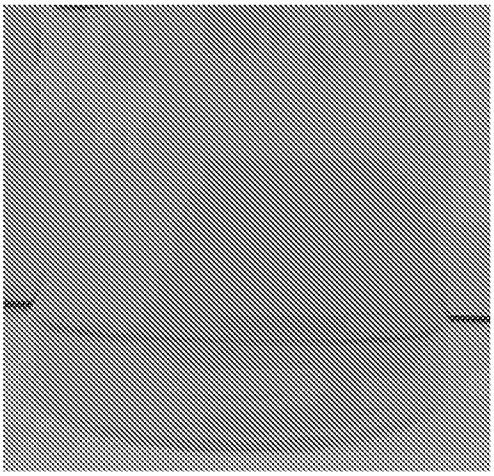


Figure 2

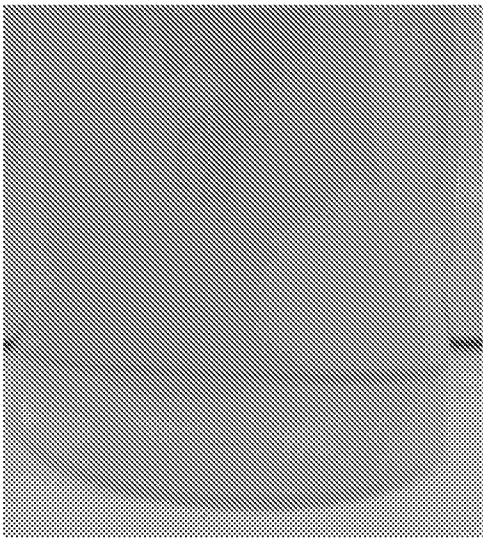


Figure 3

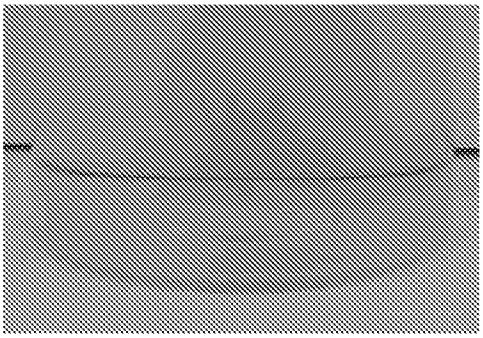


Figure 4

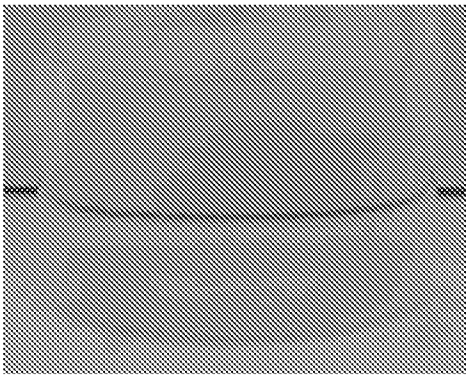


Figure 5

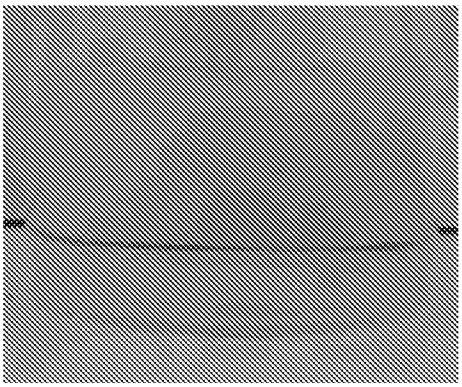


Figure 6

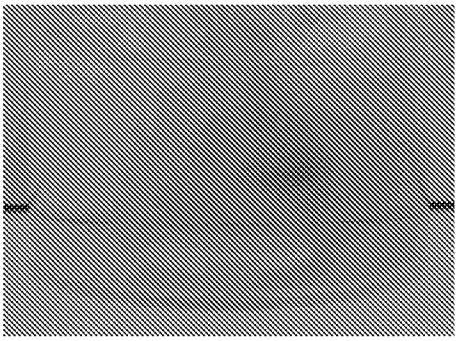


Figure 7

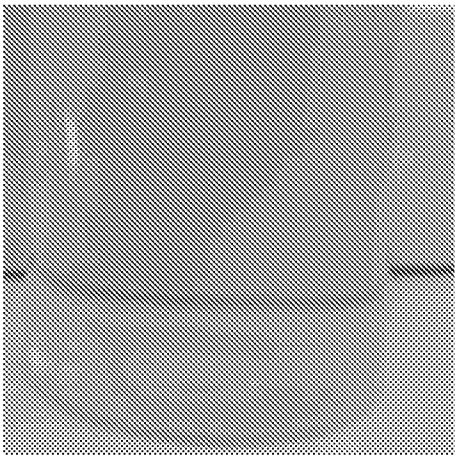


Figure 8

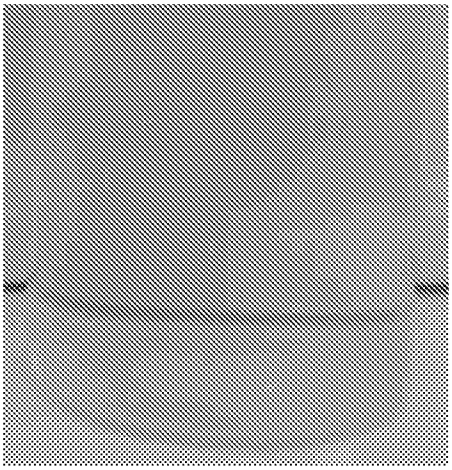


Figure 9

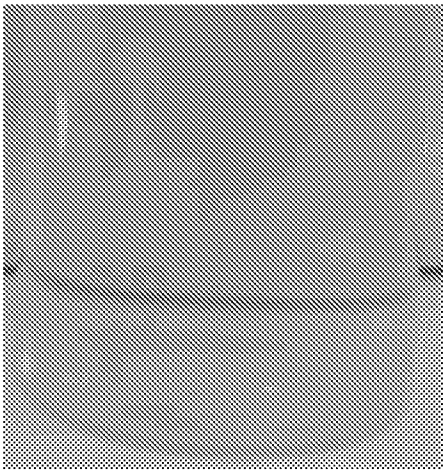


Figure 10

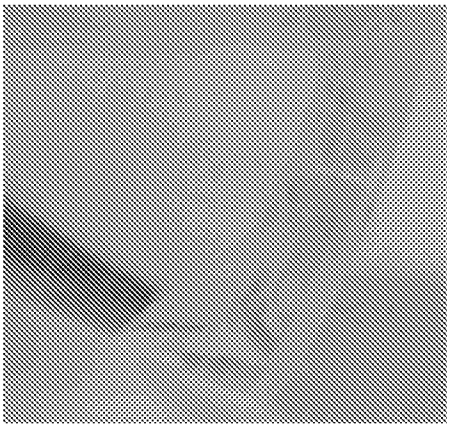


Figure 11

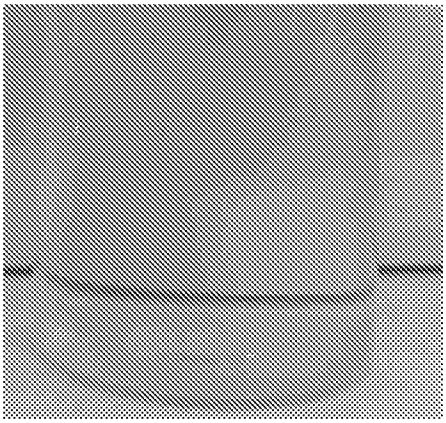


Figure 12

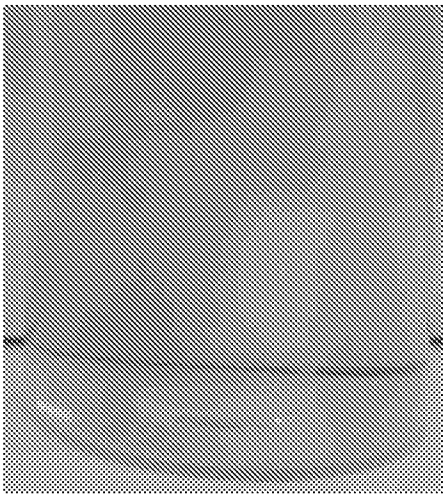


Figure 13

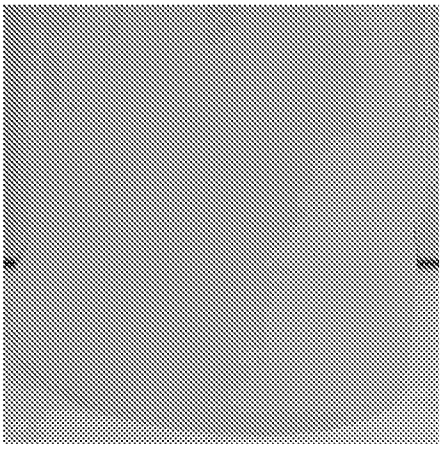


Figure 14

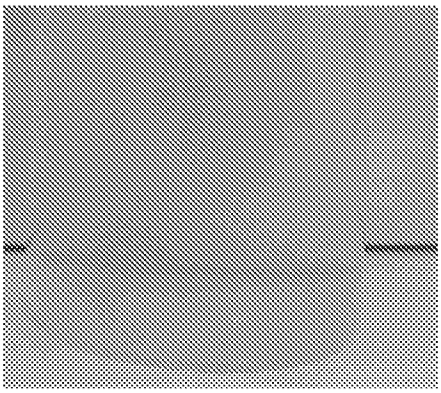


Figure 15

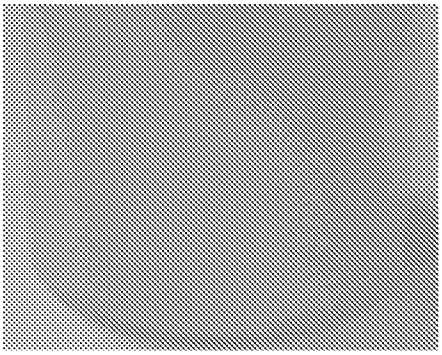


Figure 16

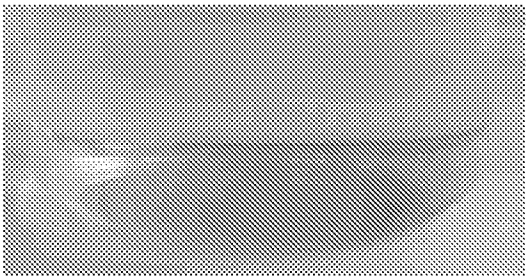


Figure 17

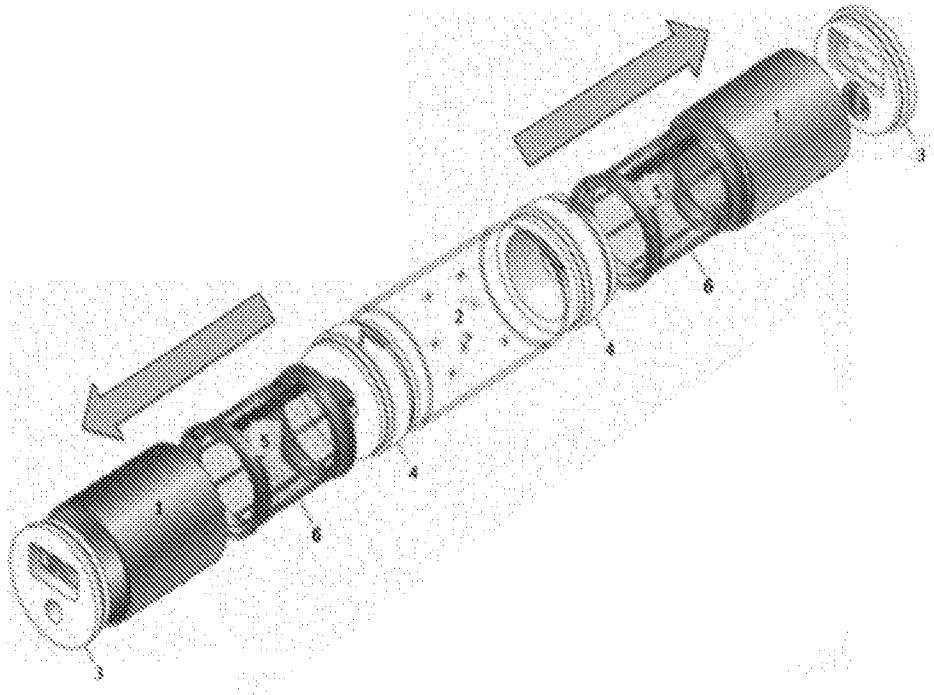
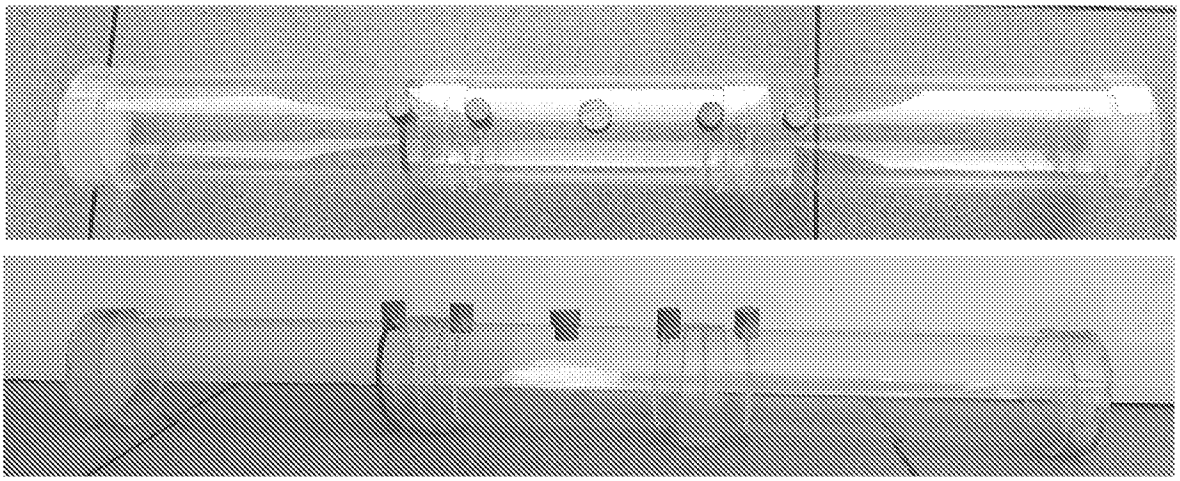


Figure 18.



SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE
Nederlands aanvraag nr. **2032600**	Indieningsdatum **26-07-2022**
	Ingeroepen voorrangsdatum
Aanvrager (Naam) **AFFIX Labs Oy**	
Datum van het verzoek voor een onderzoek van internationaal type **10-01-2023**	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. **SN82896**

I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)

Volgens de internationale classificatie (IPC)

Zie onderzoeksrapport

II. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimumdocumentatie

Classificatiesysteem	Classificatiesymbolen
IPC	**Zie onderzoeksrapport**

Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

III.	☐	**GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES**	(opmerkingen op aanvullingsblad)
IV.	☐	**GEBREK AAN EENHEID VAN UITVINDING**	(opmerkingen op aanvullingsblad)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2032600

A. CLASSIFICATIE VAN HET ONDERWERP

INV. A01N25/02 A01N25/30 A01N37/18 A01N47/16 A01P17/00
ADD.

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte miminum documentatie (classificatie gevolgd door classificatiesymbolen)
A01N A01P

Onderzochte andere documentatie dan de mimimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)

EPO-Internal, CHEM ABS Data, WPI Data

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	DATABASE GNPD [Online] MINTEL; 19 december 2017 (2017-12-19), anonymous: "Insect Repellent Body Spray for Kids", XP093032050, Database accession no. 5316223	1-4,6, 11,25-30
Y	* samenvatting * * Ingredients; bladzijde 2 *	1-32

-/--

[X] Verdere documenten worden vermeld in het vervolg van vak C.

[ ] Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

"A" niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft

"D" in de octrooiaanvrage vermeld

"E" eerdere octrooi(aanvrage), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven

"L" om andere redenen vermelde literatuur

"O" niet-schriftelijke stand van de techniek

"P" tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur

"T" na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvrage, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding

"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur

"Y" de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht

"&" lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid	Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type
16 maart 2023	

Naam en adres van de instantie	De bevoegde ambtenaar
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	**Galley, Carl**

1

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2032600

C.(Vervolg). VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
X	ZHAO JIANXI ET AL: "Spherical micelle formation by mixed quaternary ammonium surfactants with long, and short, tails in ethanol/water solvent and micellar freezing upon solubilising styrene polymerisation", COLLOIDS AND SURFACES A : PHYSIOCHEMICAL AND ENGINEERINGS ASPECTS, ELSEVIER, AMSTERDAM, NL, deel 513, 28 oktober 2016 (2016-10-28), bladzijden 274-279, XP029836799, ISSN: 0927-7757, DOI: 10.1016/J.COLSURFA.2016.10.054	1-32
Y	* samenvatting * * figuur 1 * * figuur 3 * * Materials; bladzijde 275, rechter kolom *	1-32

Y	LI DONG MEI ET AL: "Interfacial properties and micellization of octadecyltrimethylammonium bromide in aqueous solution containing short chain alcohol and effect of chain length of alcohol", JOURNAL OF DISPERSION SCIENCE AND TECHNOLOGY., deel 41, nr. 6, 14 mei 2019 (2019-05-14), bladzijden 856-862, XP093031988, NEW YORK, NY, US ISSN: 0193-2691, DOI: 10.1080/01932691.2019.1614027 * het gehele document *	1-32

Y	MEDOS ZIGA ET AL: "Insight into the Hydration of Cationic Surfactants: A Thermodynamic and Dielectric Study of Functionalized Quaternary Ammonium Chlorides", LANGMUIR, deel 35, nr. 10, 12 februari 2019 (2019-02-12), bladzijden 3759-3772, XP093032250, US ISSN: 0743-7463, DOI: 10.1021/acs.langmuir.8b03993 Gevonden op het Internet: URL:http://pubs.acs.org/doi/pdf/10.1021/acs.langmuir.8b03993> * het gehele document * * bladzijde 3767, rechter kolom, alinea 2nd *	1-32

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1

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

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C.(Vervolg). VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
Y	Gani Rafiqul: "Chemical Product (Formulation) Design Lecture 2", Workshop on Product Design, NTUA; CAPEC 13th Year, 1 maart 2011 (2011-03-01), bladzijden 1-34, XP093032090, Lyngby, Denmark Gevonden op het Internet: URL:https://www.chemeng.ntua.gr/seminars/download/seminar_2011-3-17_partB.pdf [gevonden op 2023-03-15] * bladzijden 18-19 * -----	1-32

1

WRITTEN OPINION

File No.	Filing date *(day/month/year)*	Priority date *(day/month/year)*	Application No.
SN82896	26.07.2022		NL2032600

International Patent Classification (IPC)
INV. A01N25/02 A01N25/30 A01N37/18 A01N47/16 A01P17/00

Applicant
AFFIX Labs Oy

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the application
- ☐ Box No. VIII Certain observations on the application

	Examiner
	Galley, Carl

Application number

WRITTEN OPINION

NL2032600

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the application as filed.

   b. ☐ furnished subsequent to the filing date for the purposes of search,

      ☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the application as filed.

3. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.

4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes:	Claims	7, 10, 12, 13, 21, 22
	No:	Claims	1-6, 8, 9, 11, 14-20, 23-32
Inventive step	Yes:	Claims	
	No:	Claims	1-32
Industrial applicability	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 DATABASE GNPD [Online]; MINTEL; 19 december 2017, anonymous: "Insect Repellent Body Spray for Kids", XP093032050, Database accession no. 5316223

D2 ZHAO JIANXI ET AL: "Spherical micelle formation by mixed quaternary ammonium surfactants with long, and short, tails in ethanol/water solvent and micellar freezing upon solubilising styrene polymerisation", COLLOIDS AND SURFACES A : PHYSIOCHEMICAL AND ENGINEERINGS ASPECTS, deel 513, 28 oktober 2016, bladzijden 274-279, XP029836799

D3 Li Dong Mei ET AL: "Interfacial properties and micellization of octadecyltrimethyl-ammonium bromide in aqueous solution containing short chain alcohol and effect of chain length of alcohol", JOURNAL OF DISPERSION SCIENCE AND TECHNOLOGY, deel 41, nr. 6, 14 mei 2019, bladzijden 856-862, XP093031988

D4 Medos Ziga ET AL: "Insight into the Hydration of Cationic Surfactants: A Thermodynamic and Dielectric Study of Functionalized Quaternary Ammonium Chlorides", Langmuir, deel 35, nr. 10, 12 februari 2019, bladzijden 3759-3772, XP093032250

D5 Gani Rafiqul: "Chemical Product (Formulation) Design Lecture 2", Workshop on Product Design, NTUA; CAPEC 13th Year, 1 maart 2011, bladzijden 1-34, XP093032090, Lyngby, Denmark; Gevonden op het Internet: URL:https://www.chemeng.ntua.gr/seminars/download/seminar_2011-3-17_partB.pdf [gevonden op 2023-03-15]

1 Claims 1–29 relate to compositions for dissolving a water-insoluble compound. However, the term "for" in composition claims is interpreted as merely meaning that the composition is suitable for such a purpose. A known product which prima facie is the same as the composition defined in the claim and is in a form suitable for the stated use, even though it has never been described for that use, would deprive the claim of novelty. In this regard, compositions comprising an alcohol and a quaternary ammonium compound of formula (I) are extremely well known, including hand sanitisers, cosmetics, etc...

2 In addition to the above comment, the feature "alcohol" of claim 1 encompasses any from the vast number of organic compounds that comprise a hydroxyl group, including phenols, fatty alcohols, compounds such as carvacrol, terpineol, nerol, geranoil, and even icaridin, all listed in claim 3 as the water-insoluble compound. Thus, not only is there a possible overlap of features, leading to a severe lack of clarity, but also it appears the invention cannot be carried out over the entire scope of at least claim 1. Furthermore, the R1, R2 and R4 groups of the quaternary ammonium compound in claim 1 have not been defined, leading to another severe lack of clarity.

3 The intended use of a product in a product claim does not constitute a technical feature in claims 25–29 and are not considered to limit the compositions of claims 2–22. Thus, there is a lack of conciseness.

4 In light of the above lack of clarity, many documents were found that disclose a composition comprising an alcohol, a quaternary ammonium compound of Formula I and water, and falling within these documents, even those that comprise the preferred icaridin were found: D1 teaches an insect repellent spray comprising hydroxyethyl isobutyl piperidine carboxylate (icaridin), water, alcohol and denatonium benzoate (page 2, Ingredients). Thus, D1 is considered to anticipate the subject-matter of at least claims 1–4, 6, 11 and 25–30.

5 Quaternary ammonium compounds are surface-active agents, well known to the skilled person and used to solubilize oily components by the formation of micelles: For example, D2 discloses a study into the formulation of micelles by a mixture of quaternary ammonium surfactants, octadecyltrimethylammonium bromide (C18) and docosyltrimethylammonium bromide (C22), in ethanol/water solvent mixtures (20:80 and 15:85) and the solubilisation of styrene (i.e. a water-insoluble active; abstract). Concentrations of the surfactants range from 28 mmol/L to 33.3 mmol/L (Figure 1) and of styrene from 0.2 to 0.8 mmol/L (Figure 3). The amounts of components appear to fall within those required in claims 14–16, 23 and 24, and the use of deionised water is also taught (page 275, right-hand column, Materials). Therefore, D2 is considered to anticipate the subject-matter at least claims 1–6, 8, 9, 11, 14–20, 23–29, 31 and 32.

6 As the subject-matter of claims 1–6, 8, 9, 11, 14–20 and 23–32 does not appear to be novel, inventive step for said subject-matter cannot be acknowledged. As a general comment on inventive step, in the absence of any prejudice to the

contrary, the use of a well known group of surfactants to solubilise oily components in aqueous formulations does not appear to involve an inventive step, even with the additional presence of an alcohol (with the understanding that it is miscible with the aqueous phase), which is well reported to reduce the surface tension of water and lower the critical micelle concentration (CMC), helping the solubilization of the oily components. For example, D3 relates to a study into the micellisation of octadecyltrimethylammonium bromide in aqueous solutions comprising short-chain alcohols (whole document). Indeed, this well-known effect appears the only teaching of present Table 2 of the examples.

7 In this regard, even if D1 or D5 were taken as the closest prior art, where solutions of icaridin in alcohol-water mixtures are disclosed (D1: page 2, Ingredients; D5: pages 18–19), the addition of a known surfactant is standard practice for the skilled person using general knowledge and so does not appear to involve an inventive step. The selection of a particular surfactant with a certain HLB value is also standard practice in the art. Thus, the use of a quaternary ammonium surfactant with all R groups identical (claim 7), which are known to encompass surfactants (see for example D4: page 3767, right-hand column, second paragraph), or the chloride in place of bromide (claim 10), or the specific alcohol (claims 12, 13), or a combination thereof (claims 21, 22) is not considered to contribute to any surprising and/or unexpected effect. Therefore, the entire claimed subject-matter appears to lack inventive step.

8 The industrial applicability of the claimed invention is evident from the application.