

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
31 March 2005 (31.03.2005)

PCT

(10) International Publication Number
WO 2005/027636 A2

(51) International Patent Classification⁷: **A01N 37/12**,
37/02, A61K 31/25, 31/08, 31/22

(21) International Application Number:
PCT/GB2004/004037

(22) International Filing Date:
22 September 2004 (22.09.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0322117.3 22 September 2003 (22.09.2003) GB
0322118.1 22 September 2003 (22.09.2003) GB

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMPROVED TOPICAL TREATMENT FOR THE ERADICATION AND/OR CONTROL OF ECTOPARASITES

(57) Abstract: The use is described of a fluid comprising one or more fatty acid esters of a mono-, di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol as, a topical treatment for the eradication and/or control of ectoparasites and arthropods. Preferably the fluid is free from an active amount of any other ectoparasite killing compound. Preferred fatty acids are aliphatic carboxylic acids having from 8 to 14 carbon atoms. The mono-, di-, tri-hydric alcohol is an aliphatic alcohol having from three to eight carbon atoms may be an nor iso-alcohol having from three to four carbon atoms. The fluid may comprise a mixture of caprylcaproyl macrogol-8 glycerides and/or diethylene glycol monomethyl ether. The fluid may be applied in the form of a foam or a gel. The ectoparasites may be body lice, crab lice, scabies mites or ticks. The host species may be a mammal such as Homo sapiens and the ectoparasites are head lice or companion animals, such as dogs or cats and the ectoparasites are fleas or ticks. The fluids may also applied to plants and wood.



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IMPROVED TOPICAL TREATMENT FOR THE ERADICATION AND/OR CONTROL OF ECTOPARASITES.

This invention relates to an improved topical treatment for the eradication and/or control of ectoparasites, and particularly arthropods, and to compositions for use in such treatment.

Ectoparasites are widely present on many animal species. The infestations can spread easily in groups of animals. This may occur through direct transfer of ectoparasites from animal to animal when in close proximity. Alternatively the ectoparasite may drop from a host animal to the ground or other object until picked up by a passing animal. In the case of mammals ectoparasites usually dwell in portions of the body which carry hair which provides protection for them.

Compounds have been suggested and used to eliminate ectoparasites whose toxic action has deleterious effects on the host animal. In some cases ectoparasites evolve resistance to the compounds which cease to be effective.

A similar problem exists with parasites which attack vegetable matter including arthropods such as thrips, white fly, aphids and wood boring and burrowing insects.

The present invention provides a topical treatment for the eradication and/or control of ectoparasites and other arthropods which has minimal deleterious effect on the subject being treated.

According to the present invention there is provided the use of a fluid comprising one or more fatty acid esters of a mono-, di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol as a topical treatment for the eradication and/or control of ectoparasites and arthropods.

There is further provided the use of a fluid comprising one or more fatty acid esters of a di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol as a topical treatment for the eradication and/or control of ectoparasites and arthropods.

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The fluid may be free from an active amount of any other ectoparasite killing compound or may contain such a compound. The preferred fatty acids are aliphatic carboxylic acids having from 8 to 14 carbon atoms. Acids having an even number of carbon atoms, such as caprylic, capric, lauric and myristic acids, are particularly preferred. When the ester is formed from a mono-, di- or tri-hydric alcohol it is preferably an aliphatic alcohol having from three to eight carbon atoms. The most preferred alcohols have three or four carbon atoms such as n-propyl-, iso-propyl-, n-butyl- or iso-butyl alcohol and provide most effective compounds for treatment such as iso-propyl myristate. Other esters that may be used in the invention include a mixture of caprylcaproyl macrogol-8 glycerides. A further effective ester is diethylene glycol monoethyl ether. The esters used in the treatment of the present invention are lipophilic.

The treatment is particularly effective on mammals. These may include companion animals such as dogs, cats, ferrets, rabbits, gerbils and guinea pigs. Farm animals such as bovine, porcine, ovine and equine species. The treatment may be safely used on Homo sapiens. Many ectoparasites are host specific however the treatment according to the invention is effective against most of them. The treatment may also be used to eradicate and control arthropods such as thrips, white fly, aphids and wood boring and burrowing insects.

Topical application on a mammal may comprise direct manual application, painting, spraying or application as a foam or gel.

In order that the invention may be clearly understood it will now be described in the following examples.

Example 1.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES

A fluid composition was prepared consisting of 30% by weight caprylcaproyl macrogol-8 glycerides mixed with isopropanol. As a control 60% aqueous isopropanol was used.

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The tests were performed with one replicate each and with an overnight exposure to the fluid. The ectoparasites were human head lice, *Pediculus humanus*, obtained from the culture colony of Insect R&D Limited.

Adult male and female lice, in approximately equal numbers, were used in each test. The lice were fed on the morning of the test and allowed a minimum of four hours to recover. During this period they were able to excrete excess water that had been imbibed with their blood meal. The lice were then counted into batches and placed on squares of open mesh nylon gauze (tulle) as a substrate on which to stand. Each batch was allocated to a marked 50 mm plastic Petri dish. For the test procedure each specimen of gauze carrying lice was immersed in the test formulation for 10 seconds during which time the gauze was turned at least once to eliminate any air bubbles. After removal from the test formulation each sample was lightly blotted to remove excess fluid and returned to its allocated Petri dish. The samples in the dishes were incubated under normal maintenance conditions for the remainder of the test period. The conditions were $30\text{ C} \pm 2\text{ C}$ and $50\% \pm 15\% \text{ RH}$. At the end of the test period the lice were washed for 30 seconds using a 1:9 mixture of "Boots" frequent wash shampoo with tap water, rinsed three times with tap water at 35 C poured over and through the gauze. Finally the sample was blotted with medical wipe tissue. The samples with lice were then incubated under normal maintenance conditions until the results were recorded. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 1 as a percentage.

TABLE 1

Test liquid	Total	Dead	Morbid	Alive	%
caprylcaproyl macrogol-8 glycerides	20	20	0	0	100
control	20	1	0	19	5

Example 2

USE OF DIETHYLENE GLYCOL MONOETHYL ETHER

A fluid composition was prepared consisting of 30% by weight diethylene glycol monoethyl ether mixed with isopropanol. As a control 60% aqueous isopropanol was used.

The tests were performed with one replicate each and with an overnight exposure to the fluid. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 2 as a percentage.

TABLE 2

Test liquid	Total	Dead	Morbid	Alive	%
diethylene glycol monoethyl ether	20	20	0	0	100
control	20	1	0	19	5

Example 3

USE OF CAPRYL/CAPRIC TRIGLYCERIDES

Fluid compositions were prepared consisting of 30% by weight capryl/capric triglyceride blended esters mixed with isopropanol. The ratios of the acid moieties of the esters were 70/30, 55/45 and 65/35. As a control 60% aqueous isopropanol was used.

The tests were performed with one replicate each and with an overnight exposure to the fluid. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 3 as a percentage.

TABLE 3

Test liquid	Total	Dead	Morbid	Alive	%
caprylic/capric triglyceride blend 70:30	18	18	0	0	100

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TABLE 3 (cont.)

Test liquid	Total	Dead	Morbid	Alive	%
55:45	18	18	0	0	100
65:35	20	20	0	0	100
control	20	1	0	19	5

Example 4

USE OF ISOPROPYL MYRISTATE

A fluid composition was prepared consisting of 30% by weight isopropyl myristate mixed with isopropanol. As a control 60% aqueous isopropanol was used.

The tests were performed with one replicate each and with an overnight exposure to the fluid. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 4 as a percentage.

Table 4

Test liquid	Total	Dead	Morbid	Alive	%
isopropyl myristate	19	19	0	0	100
control	20	1	0	19	5

Example 5.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES AS A FOAM

A fluid composition was prepared as described in Example 1 with the addition of 0.5% by weight of a preservative and the balance of the fluid being water. The composition was converted to a foam by means of a mechanical foaming device. As a control 60% aqueous isopropyl alcohol was used.

Tests were performed with one replicate each and with an overnight exposure to the foam. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 5 as a percentage.

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Table 5

Test liquid	Total	Dead	Morbid	Alive	%
foamed liquid	21	21	0	0	100
control	20	2	0	18	10

Example 6.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES AS A FOAM

A fluid composition was prepared as described in Example 5 with the addition of 0.5% by weight of d-phenothrin as well as the preservative. The balance of the fluid was water. The composition was converted to a foam by means of a mechanical foaming device. As a control 60% aqueous isopropanol was used.

Tests were performed with one replicate each and with an overnight exposure to the foam. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were recorded after 24 hours and are shown in Table 6 as a percentage.

Table 6

Test liquid	Total	Dead	Morbid	Alive	%
foamed liquid	20	20	0	0	100
control	20	3	0	17	12.5

Example 7.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES AS A FOAM

A fluid composition was prepared as described in Example 6 but with the addition of 0.5% by weight of permethrin in place of the d-phenothrin. The composition was converted to a foam by means of a mechanical foaming device. As a control 60% aqueous isopropanol was used.

Tests were performed with one replicate each and with an overnight exposure to the foam. The ectoparasites were human head lice and the procedure followed was the same as that for Example 1. Observations on the mortality of the lice were

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recorded after 24 hours and are shown in Table 7 as a percentage.

Table 7

Test liquid	Total	Dead	Morbid	Alive	%
foamed liquid	20	20	0	0	100
control	20	2	0	18	10

Example 8.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES AS A GEL

An effective gelled fluid for topical application to eliminate ectoparasites was created using the following composition.

caprylcaproyl macrogol-8 glycerides	20%
d-phenothrin	0.5%
diethylene glycol monoethyl ether	20%
natrosol	2%

water to make up 100%.

Example 9.

USE OF CAPRYLCAPROYL MACROGOL-8 GLYCERIDES AND DIETHYLENE MONOETHYL ETHER AS A GEL

A very effective gelled fluid for topical application to eliminate ectoparasites was created using the following composition.

caprylcaproyl macrogol-8 glycerides	10%
diethylene glycol monoethyl ether	20%
natrosol	2%

water to make up 100%.

It will be seen from the examples that the use of the fluid compositions in accordance with the invention, whether free flowing, as a foam or as a gel, provide a very effective method of eliminating head lice. Similarly the method may be used to eliminate body lice, crab lice and scabies mites all of which seek human hosts. The method can also eradicate ticks and fleas from companion animals. The compositions may also be used to eradicate or control arthropods such as thrips, white fly, aphids and wood boring and burrowing

insects by application in the various manners described.

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CLAIMS

1. The use of a fluid comprising one or more fatty acid esters of a mono-, di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol as a topical treatment for the eradication and/or control of ectoparasites and arthropods.
2. The use of a fluid comprising one or more fatty acid esters of a di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol as a topical treatment for the eradication and/or control of ectoparasites and arthropods.
3. The use as claimed in claim 1 or claim 2, wherein the fluid is free from an active amount of any other ectoparasite killing compound.
4. The use as claimed in claim 1 or claim 2, wherein the fluid contains an active amount of an ectoparasite killing compound as well as the fatty acid ester.
5. The use as claimed in any of the preceding claims, wherein the fatty acid is an aliphatic carboxylic acid having from 8 to 14 carbon atoms.
6. The use as claimed in any of the preceding claims, wherein the mono-, di-, tri-hydric alcohol is an aliphatic alcohol having from three to eight carbon atoms.
7. The use as claimed in claim 5, wherein the alcohol is an n- or iso-alcohol having from three to four carbon atoms.
8. The use as claimed in any of the preceding claims 1 to 4, wherein the fluid comprises a mixture of caprylcaproyl macrogol-8 glycerides.
9. The use as claimed in any of the preceding claims 1 to 4, wherein the fluid comprises diethylene glycol monomethyl ether.
10. The use as claimed in any of the preceding claims wherein the fluid is applied in the form of a foam or a gel.
11. The use as claimed in any of the preceding claims, wherein the ectoparasite is selected from the group consisting of body lice, crab lice, scabies mites and ticks.

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12. The use as claimed in any of the preceding claims, wherein the topical treatment is applied to the surface of a mammal.

13. The use as claimed in claim 12, wherein the mammal is Homo sapiens and the ectoparasites are head lice.

14. The use as claimed in claim 12, wherein the topical treatment is applied to a dog or a cat and the ectoparasites are fleas or ticks.

15. The use as claimed in any of the preceding claims, wherein the topical treatment is applied to the surface of a plant or wood.

16. A fluid composition for use in the eradication or control of ectoparasites in accordance with claim 1 comprising one or more fatty acid esters of a mono-, di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol.

17. A fluid composition for use in the eradication or control of ectoparasites in accordance with claim 1 comprising one or more fatty acid esters of a di-, tri- or polyhydric alcohol or a lower alkyl ether of a glycol.