

SPECIFICATION

Compositions containing esters of (S) allethrolone and (R) allethrolone

The invention concerns new pesticidal compositions containing synergistic mixtures of (S) allethrolone and (R) allethrolone esters.

- 5 According to the present invention there are provided compositions endowed with activity against arthropods, comprising as active material from 90% to 60% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and from 10 to 40% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and particularly such compositions wherein the active material contains from 80% to 70% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and from 20% to 30% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.

- 10 The invention also provides a method of combating arthropods which comprises administering to a site infested with or susceptible to infestation by arthropods an effective amount of a composition according to the invention.

- 15 Particularly preferred compositions according to the invention are those wherein the active material contains about 75% of (S) 1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and about 25% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.

The compositions according to the invention are active against arthropods and particularly against insects and arachnids. Among the arachnids, the compositions according to the invention are particularly useful against ixodides and sarcoptides.

- 20 Thus according to one feature of the invention the compositions may be in a form suitable for use as an insecticide. Advantageously the compositions will be in the form of fumigating compositions, e.g. in the form of a combustible insecticide coil (serpentine). Alternatively the fumigating compositions may be in the form of an incombustible fibrous substrate, having the active material incorporated therein, which in use is placed on a heating device such as an electric mosquito destroyer.

- 25 In the case of an insecticide coil the active material is incorporated into an inert support which may, for example, be composed of pyrethrum marc, Tabu powder, (or powder from the leaves of *Machilus Thunbergii*), powered pyrethrum stem, cedar-leaf powder, wood powder (such as e.g. pine saw-dust), starch or powdered coconut shell. The amount of active material can then be, for example, from 0.03 to 1% in weight.

- 30 In the case where an incombustible fibrous support is used, the amount of active material can then be, for example, from 0.03 to 95% by weight.

- The insecticidal compositions according to the invention can also be in the form of an atomizable oil, i.e. an oil based on the active material, which oil may be used to feed the wick of e.g. a lamp and thus be submitted to combustion. The concentration of active material incorporated in such an oil is preferably from 0.03 to 95% in weight. According to a further alternative the insecticidal compositions according to the invention can be formulated as aerosols.

These various examples of insecticidal compositions according to the invention are in no way limitative and the compositions according to the invention may be used in any form allowing the active material to be diffused.

- 40 In addition to conventional carriers and/or excipients the compositions according to the invention may include other additives for example stabilizers, such as e.g. phenols or arylamines; conventional synergistic agents for the pyrethrinoids such as e.g. 1-(2,5,8-trioxa-dodecyl-2-propyl-4,5-methylenedioxy)-benzene [piperonyl butoxide], N-(2-ethyl-heptyl)-bicyclo[2,2-1]-5-hepten-2,3-dicarboximide and piperonyl-bis-2-(2'-n-butoxyethoxy)ethyl acetal [Tropital]; antioxidizing agents such as e.g. tocopherol acetate; and emulsifying agents.

The compositions according to the invention may be used domestically to destroy insects such as e.g. flies and mosquitoes and also in industrial areas to destroy, for example, insects harmful to crops such as cereals and insects harmful to horticulture.

- 50 The compositions of the invention may also be used as medicaments for veterinary use, e.g. to combat sarcoptides and ixodides such as for example manges and ticks.

Thus according to a further feature of the invention there are provided compositions as hereinbefore defined in the form of veterinary compositions.

- 55 The veterinary compositions according to the invention can be prepared according to conventional techniques. They may for example contain synergistic agents, stabilizers, antioxidants and/or emulsifiers as exemplified above.

Conveniently the active material, together with any additives, is dissolved in an alcohol or in a mixture of alcohols.

- 60 The synergistic compositions according to the invention can be prepared by mixing the two active ingredients in the desired proportions optionally together with other non-active material. These two active esters can, for example, be prepared by conventional esterification of S-allethrolone or R-allethrolone with d-trans-chrysanthemic acid. S-allethrolone and R-allethrolone themselves, can, for example, be prepared according to the process of French Patent Specifications Nos. 2,355,815 or 2,362,830.

A study of the insecticidal activity of the compositions according to the invention has been carried out on flies and on *Culex* and *Aedes*.

As used herein, the term "bioallethrine" denotes RS-allethrolone d-trans-chrysanthemate, the term "S-bioallethrine" denotes S-allethrolone d-trans-chrysanthemate, the term "R-bioallethrine" denotes R-allethrolone d-trans-chrysanthemate and the term "esbiothrine" denotes a mixture of about 75% of (S) allethrolone d-trans-chrysanthemate and about 25% of (R) allethrolone d-trans-chrysanthemate.

Further, by "relative power" of a component A in relation to a component B is intended the ratio:

$$RP = \frac{\text{Activity of A}}{\text{Activity of B.}}$$

The compositions according to the invention, which are mixtures of S-bioallethrine and R-bioallethrine in defined proportions, exhibit a marked synergistic effect. Surprisingly the experimentally determined insecticidal activity of these compositions has been found to be clearly superior to the sum of the activities of the constituents of the mixtures. It is known that R-bioallethrine is endowed with a negligible insecticidal activity.

Thus, for example, whilst an esbiothrine mixture of about 75% of S-bioallethrine and about 25% of R-bioallethrine should theoretically possess a relative power of $75/50 = 1.5$ referred to bioallethrine, in reality a relative power of 2 to 2.5 is found experimentally.

Study of the activity of an insectical mixture according to the invention. (Esbiothrine). Demonstration of synergic effect.

A) Tests on flies.

b) Operating procedure

Neutral coils are impregnated with the insecticide to be tested, in solution in acetone, by depositing the solution on both faces of the coils at a rate of 1.5 to 2 ml per gram of coil.

The tests are carried out in an enclosure of transparent glass of cubic form, measuring 70 mm along the edge, using 20 female domestic flies for each test. The flies are 4 to 5 days old.

After a few minutes, a piece of coil weighing about 2 grams and lit at both ends is introduced through a central trap-door provided for this purpose in the lower face of the enclosure. The coil burns for the whole period of the test or until 95% of the flies are in a Knock-Down (K.D.) state. The tests are repeated 3 times for each dose.

The K.D. checks are carried out every minute.

Five minutes after the burning is complete, the enclosure is ventilated and the insects are gathered together in small cylindrical cages (O.M.S. model) provided with a piece of moistened cotton so as to ensure the survival of the individuals which might eventually recover. The insects are then stored in a room maintained at $22^{\circ} \pm 1^{\circ}\text{C}$ and at $65 \pm 5\%$ relative humidity. At the end of 24 hours a check is made of the number of apparent deaths (Killing Time or KT).

b) Experimental results:Table 1 : Insecticidal activity of the coils on
Musca Domestica

PRODUCTS	Dose (%)	Averages of KT 50	Averages of KT 90	Rate of burning of coil (mg/mn)
Bioallethrine (50 % R + 50 % S)	0.15	19.3	25.3	68.4
	0.30	15.3	19.8	73.8
	0.45	14.2	18.5	71.3
	0.60	12.9	16.7	69.9
S-Bioallethrine (100 % S)	0.075	23.7	33.7	69.7
	0.15	16.8	21.8	69.5
	0.30	12.6	15.7	72.6
	0.45	11.0	14.8	71.5
Esbiothrine (75 % S + 25 % R)	0.075	21.8	31.3	68.6
	0.15	14.8	19.5	73.1
	0.30	12.1	16.8	72.8
	0.45	10.8	14.7	71.5

The results from table 1 have allowed tables 2 and 3 which follow to be prepared.

Table 2 : Relative powers at KT 50 for the products studies on Musca Domestica.

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 50 of:					
	11.5 mn		13 mn		14.5 mn	
	C	R.P.	C.	R.P.	C.	R.P.
Bioallethrine	-	-	0.600	1	0.390	1
S-Bioallethrine	0.395	1	0.295	2.03	0.220	1.77
Esbiothrine	0.365	1.08	0.240	2.50	0.160	2.44
				1.23		1.38

Table 3 : Relative powers at KT 90 for the products studied on Musca Domestica

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 90 of:					
	17 mn		18 mn		19 mn	
	C	R.P.	C	R.P.	C	R.P.
Bioallethrine	0.580	1	0.48	1	0.37	1
S-Bioallethrine	0.275	2.11	0.24	1.96	0.205	1.81
Esbiothrine	0.275	2.11	0.22	2.14	0.175	2.11
				1.09		1.17

B) Tests on Culex

a) Operating procedure

This is similar to that used for flies. The individuals used are aged from 2 to 3 days. The piece of coil introduced by the trap-door weighs about 1 gram and it is lit at the two ends. The K.D. checks are carried out every 30 seconds.

b) Experimental results:Table 4: Insecticidal activity of the coils on
Culex Pipiens

PRODUCTS	Dose (%)	Averages of KT 50	Averages of KT 90	Rate of burning of coil (mg/mn)
Bioallethrine	0.15	<u>7.8</u>	<u>9.3</u>	72.5
	0.30	<u>6.2</u>	<u>7.4</u>	75.3
	0.45	<u>5.3</u>	<u>6.6</u>	75.7
S-Bioallethrine	0.075	<u>7.6</u>	<u>9.5</u>	75.8
	0.15	<u>6.2</u>	<u>8.1</u>	76.7
	0.30	<u>4.7</u>	<u>6.1</u>	72.5
Esbiothrine	0.075	<u>7.3</u>	<u>8.7</u>	76.6
	0.15	<u>6.1</u>	<u>7.6</u>	73.8
	0.30	<u>4.8</u>	<u>6.3</u>	74.7

The results of table 4 have allowed tables 5 and 6 which follow to be prepared.

Table 5. Relative powers at KT 50 for the products studied on Culex Pipiens.

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 50 of :								
	5.5 mn			6.25 mn			7.0 mn		
	C	R.P.		C	R.P.		C	R.P.	
Bioallethrine	0.410	1		0.295	1		0.210	1	
S-Bioallethrine	0.205	2.00	1	0.145	2.03	1	0.102	2.06	1
Esbiothrine	0.205	2.00	1.00	0.135	2.19	1.07	0.088	2.39	1.16

Table 6: Relative powers at KT 90 for the products studied on Culex Pipiens.

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 90 of:								
	7 mn			7.75 mn			8.5 mn		
	C	R.P.		C	R.P.		C	R.P.	
Bioallethrine	0.37	1		0.27	1		0.20	1	
S-Bioallethrine	0.22	1.68	1	0.16	1.69	1	0.118	1.70	1
Esbiothrine	0.205	1.81	1.07	0.135	2.0	1.19	0.086	2.33	1.37

C) Tests on *Aedes*:

a) Operating procedure:

This is similar to that used for *Culex*. The piece of coil weighs about 1 gram and is lit at one end only.

b) Experimental results:

Table 7: Insecticidal activity of the coils of *Aedes Aegypti*.

PRODUCTS	Dose (%)	Averages of KT 50	Averages of KT 90	Rate of burning of coil (mg/mn)
Bioallethrine	0.0375	18.3	21.7	35.4
	0.075	9.0	11.2	38.5
	0.150	7.6	9.7	38.3
S-Bioallethrine	0.0375	12.5	15.8	35.6
	0.075	7.4	9.0	40.0
	0.150	6.0	7.7	43.5
Esbiothrine	0.0375	12.3	15.3	36.9
	0.075	6.7	8.8	42.0
	0.150	5.0	6.3	41.5

The results of table 7 have allowed tables 8 and 9 which follow to be prepared.

Table 8: Relative powers at KT 50 for the products studied on *Aedes Aegypti*.

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 50 of:					
	5.5 mn		6.5 mn		7.5 mn	
	C	R.P.	C	R.P.	C	R.P.
Bioallethrine	—	—	—	—	0.155	1
S-Bioallethrine	0.190	1	0.115	1	0.070	2.21
Esbiothrine	0.120	1.58	0.080	1.44		

Table 9: Relative powers at KT 90 for the product studied on *Aedes Aegypti*.

PRODUCTS	Concentrations (C) and Relative Powers (RP) at KT 90 of:						
	8.0 mn		8.5 mn		9.0 mn		
	C	R.P.	C	R.P.	C		R.P.
Bioallethrine	—	—	—	—	0.20	1	
S-Bioallethrine	0.125	1	0.097	1	0.075	2.67	1
Esbiothrine	0.092	1.36	0.080	1.21			

D) General Conclusions:

If the insectical activity was strictly proportional to the content of isomer S, i.e. there was no synergistic effect, by calculating the relative powers of bioallethrine, S-bioallethrine and esbiothrine as a function of the proportion of s-bioallethrine which these three products contain, the following results would be found:

— S-bioallethrine/bioallethrine	RP $\approx$ 2
— esbiothrine/bioallethrine	RP $\approx$ 1.5
— esbiothrine/S-bioallethrine	Rp $\approx$ 0.75

Now, the experimental results given previously can be summarized thus:

- 10 — S-bioallethrine/bioallethrine: at KT 50, RP $\approx$ 2 for flies, Culex and Aedes. Also at KT 90, RP $\approx$ 2 for flies, Aedes and Culex. 10
- esbiothrine/bioallethrine, at KT 50, RP from 2.3 to 2.50 for flies and near to 2 for Culex. Also at KT 90 esbiothrine/bioallethrine RP $\approx$ 2 for flies and Culex.
- 15 — esbiothrine/S-bioallethrine, at KT 50, RP $\approx$ 1 for flies and Culex and RP $\approx$ 1.5 for Aedes. At KT 90, RP slightly greater than 1 for flies and Culex and RP = 1.30 for Aedes. 15

This data shows that whilst the relative power values obtained experimentally agree in general with the expected values for S-bioallethrine/bioallethrine (RP $\approx$ 2), they differ from esbiothrine/S-bioallethrine (RP between 1 and 1.38 instead of the 0.75 calculated) and for esbiothrine/bioallethrine (ratio between 1.81 and 2.50 instead of the 1.5 calculated) whatever the insect studied and the KT taken as reference (KT 50 or KT 90). 20

Consequently this study points to the existence of an interesting phenomenon of synergy in insectical activity in a mixture of approximately 75% of S-bioallethrine and about 25% of R-bioallethrine (esbiothrine), which has been shown by determining the relative powers of esbiothrine and bioallethrine or of esbiothrine and S-bioallethrine.

25 EXAMPLE 1 25

Fumigating coil

Tabu powder	: 40 g
Coconut flour	: 35 g
Pine-wood powder	: 10 g
30 Starch	: 12.4 g 30
Perfume	: 0.5 g
Salicyl anilide	: 1.3 g
Esbiothrine	: 0.8 g

35 EXAMPLE 2 35

Aerosol

Esbiothrine	: 0.2%
Emulsifier	: 19.8%
Freon (registered Trade Mark)	: 80%

40 EXAMPLE 3 40

Preparation of a composition intended to be heated electrically.

A solution of 0.6 g of esbiothrine in 5 cm³ of toluene is adsorbed on the surface of a piece of inert fibrous material of parallelepipedal shape and dimensions 2 x 2 x 0.8 cm. On this piece of fibrous material a second piece of the same dimensions is fixed. In this way a fumigating composition is obtained which in use may be heated on a plate provided with an electric resistance. 45

EXAMPLE 4
Veterinary composition

Esbiothrine	: 5 g
Piperonyl butoxide	: 25 g
Polysorbate 80	: 10 g
"Triton" X 100	: 25 g
Tocopherol acetate	: 1 g
Ethanol	q.s. : 100 cm ³

("Triton" is a registered Trade Mark)

- 10 CLAIMS**
1. Compositions endowed with activity against arthropods comprising, as active material, from 90% to 60% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans chrysanthemate and from 10 to 40% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.
 2. Compositions as claimed in claim 1 wherein the active material contains from 80% to 70% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and from 20% to 30% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.
 3. Compositions as claimed in claim 2 wherein the active material contains about 75% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and about 25% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.
 4. Compositions as claimed in any one of claims 1 to 3 in a form suitable for use as an insecticide.
 5. Compositions as claimed in claim 4 in the form of fumigating compositions.
 6. Compositions as claimed in claim 5 in the form of a combustible insecticidal coil.
 7. Compositions as claimed in claim 6 containing from 0.03 to 1% by weight of active material.
 8. Compositions as claimed in claim 5 in the form of a fibrous incombustible substrate having the active material incorporated therein.
 9. Compositions as claimed in claim 8 containing from 0.03 to 95% by weight of active material.
 10. Compositions as claimed in claim 5 in the form of an atomizable oil.
 11. Compositions as claimed in claim 10 containing from 0.03 to 95% by weight of active material.
 12. Compositions as claimed in claim 4 in the form of aerosols.
 13. Compositions as claimed in any one of claims 1 to 3 in the form of veterinary compositions.
 14. Compositions as claimed in any one of claims 1 to 13 further including a synergistic agent for the pyrethrins.
 15. A process for the preparation of compositions as defined in any one of claims 1 to 14 which comprises mixing (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate in the desired proportions optionally together with other non-active material.
 16. A composition as claimed in claim 1 for use in combating arthropods.
 17. A composition as claimed in claim 1 for use in combating insects.
 18. A composition as claimed in claim 1 for use in combating sarcoptides and/or ixodides.
 19. A composition as claimed in claim 1 for use in combating manges and/or ticks.
 20. A method of combating arthropods which comprises administering to a site infested with or susceptible to infestation by arthropods an effective amount of a composition as claimed in any one of claims 1 to 14.
 21. Compositions endowed with activity against arthropods substantially as described in the Examples.
 22. Methods of combating arthropods, employing compositions as claimed in claim 1, substantially as herein described.

EXAMPLE 4
Veterinary composition

Esbiothrine	:	5 g
Piperonyl butoxide	:	25 g
Polysorbate 80	:	10 g
"Triton" X 100	:	25 g
Tocopherol acetate	:	1 g
Ethanol	q.s. :	100 cm ³

("Triton" is a registered Trade Mark)

10 CLAIMS

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2. Compositions as claimed in claim 1 wherein the active material contains from 80% to 70% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and from 20% to 30% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.
3. Compositions as claimed in claim 2 wherein the active material contains about 75% of (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and about 25% of (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate.
4. Compositions as claimed in any one of claims 1 to 3 in a form suitable for use as an insecticide.
5. Compositions as claimed in claim 4 in the form of fumigating compositions.
6. Compositions as claimed in claim 5 in the form of a combustible insecticidal coil.
7. Compositions as claimed in claim 6 containing from 0.03 to 1% by weight of active material.
8. Compositions as claimed in claim 5 in the form of a fibrous incombustible substrate having the active material incorporated therein.
9. Compositions as claimed in claim 8 containing from 0.03 to 95% by weight of active material.
10. Compositions as claimed in claim 5 in the form of an atomizable oil.
11. Compositions as claimed in claim 10 containing from 0.03 to 95% by weight of active material.
12. Compositions as claimed in claim 4 in the form of aerosols.
13. Compositions as claimed in any one of claims 1 to 3 in the form of veterinary compositions.
14. Compositions as claimed in any one of claims 1 to 13 further including a synergistic agent for the pyrethrinoids.
15. A process for the preparation of compositions as defined in any one of claims 1 to 14 which comprises mixing (S)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate and (R)-1-oxo-2-allyl-3-methyl-cyclopent-2-en-4-yl d-trans-chrysanthemate in the desired proportions optionally together with other non-active material.
16. A composition as claimed in claim 1 for use in combating arthropods.
17. A composition as claimed in claim 1 for use in combating insects.
18. A composition as claimed in claim 1 for use in combating sarcoptides and/or ixodides.
19. A composition as claimed in claim 1 for use in combating manges and/or ticks.
20. A method of combating arthropods which comprises administering to a site infested with or susceptible to infestation by arthropods an effective amount of a composition as claimed in any one of claims 1 to 14.
21. Compositions endowed with activity against arthropods substantially as described in the Examples.
22. Methods of combating arthropods, employing compositions as claimed in claim 1, substantially as herein described.

