(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) **EP 1 876 890 B9**

(12) **CORRECTED EUROPEAN PATENT SPECIFICATION**

(15) Correction information:
Corrected version no 1 (W1 B1)
Corrections, see
Claims EN 1

(48) Corrigendum issued on:
27.03.2013 Bulletin 2013/13

(45) Date of publication and mention of the grant of the patent:
08.08.2012 Bulletin 2012/32

(21) Application number: **06754780.2**

(22) Date of filing: **21.04.2006**

(51) Int Cl.:
A01N 25/10 *(2006.01)* ***A01N 57/16*** *(2006.01)*
A01N 47/40 *(2006.01)* ***A01N 47/18*** *(2006.01)*
A01N 47/02 *(2006.01)*

(86) International application number:
PCT/EP2006/061724

(87) International publication number:
WO 2006/111570 (26.10.2006 Gazette 2006/43)

(54) BIOLOGICALLY ACTIVE FORMULATION BASED ON CYCLODEXTRIN SUPRAMOLECULAR COMPLEXES

BIOLOGISCH WIRKSAME FROMULIERUNG AUF BASIS CYCLODEXTRIN SUPRAMOLEKULARER KOMPLEXE

FORMULATION BIOLOGIQUEMENT ACTIVE A BASE DE COMPLEXES SUPRAMOLECULAIRES DE CYCLODEXTRINE

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

(30) Priority: **22.04.2005 IT MI20050729**

(43) Date of publication of application:
16.01.2008 Bulletin 2008/03

(73) Proprietor: **ENDURA S.p.A.**
I-40121 Bologna (IT)

(72) Inventors:
- **PICCOLO, Oreste**
  I-23896 Sirtori (IT)
- **BORZATTA, Valerio**
  I-40127 Bologna (IT)
- **DELOGU, Giovanna**
  I-07100 Sassari (IT)
- **CAPPARELLA, Elisa**
  I-48100 Ravenna (IT)
- **DE CANDIA, Cristina**
  Sassari, 07100 (IT)
- **GOBBI, Carlotta**
  Ravenna, 48100 (IT)
- **DI BLASI, Giovanna**
  I-40013 Castel Maggiore (IT)

(74) Representative: **Gerli, Paolo et al**
Notarbartolo & Gervisi S.p.A.
Corso di Porta Vittoria, 9
20122 Milano (IT)

(56) References cited:
EP-A- 0 282 706 **WO-A2-2005/039287**
US-A- 4 524 068

- **DATABASE WPI Section Ch, Week 199003 Derwent Publications Ltd., London, GB; Class C01, AN 1990-019276 XP002322687 & JP 01 299203 A (DAINIPPON JOCHUGIKU KK) 4 December 1989 (1989-12-04)**
- **R. BIEBEL ET AL.: "Action of pyrethrum-based formulations against weevils" INTERNATIONAL JOURNAL OF PHARMACEUTICS, vol. 256, 30 April 2003 (2003-04-30), pages 175-181, XP002322686**

Note: Within nine months of the publication of the mention of the grant of the European patent in the European Patent Bulletin, any person may give notice to the European Patent Office of opposition to that patent, in accordance with the Implementing Regulations. Notice of opposition shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Printed by Jouve, 75001 PARIS (FR)

(Cont. next page)

- **LAJOS SZENTE ET AL: "FORMULATION OF INSECT CONTROLLING AGENTS WITH B-CYCLODEXTRIN" PESTICIDE SCIENCE, ELSEVIER APPLIED SCIENCE PUBLISHER. BARKING, GB, vol. 28, no. 1, January 1990 (1990-01), pages 7-16, XP000133136 ISSN: 0031-613X**

Remarks:

The file contains technical information submitted after the application was filed and not included in this specification

Description

FIELD OF THE INVENTION

[0001] The present invention relates to the field of insecticide, acaricide, fungicide, snailcide and vermicide compositions and in particular those in which the active principle is mixed with synergistic substances having various mechanisms of action, for example substances inhibitory to detoxification mechanisms in insects. New formulations are described in which the effect of the insecticide, acaricide, fungicide, snailcide and vermicide and synergistic substance is further enhanced by formation of cyclodextrin based complexes.

PRIOR ART

[0002] The problem of tolerance and resistance to insecticidal, acaricidal, fungicidal, snailcidal and vermicidal activity is particularly serious and of growing importance, leading to the ever more difficult control and eradication of damaging species (insects, mites, moulds, snails, worms) so that protection against their action in agriculture, veterinary medicine, domestic hygiene and in manufactured articles becomes necessary.

[0003] Many damaging species have strengthened their natural defences and immune systems against the toxins with which they come into contact, so that to achieve their eradication, dosages have to be increased or new insecticides, acaricides, fungicides, snailcides or vermicides must be continually used with consequent greater risks and damage to the entire ecosystem and the overall food chain up to man, and with rising costs.

[0004] It is widely reported in the literature that the use of substances such as piperonyl butoxide (PBO) and its analogues, sesamol, verbutin, MGK 264 and DEF (S,S,S-tributyl phosphorotrithioate), can enhance insecticidal, acaricidal, fungicidal, snailcidal and vermicidal activity *in vitro* and/or *in vivo,* either by inhibiting the activity of certain insect metabolic enzymes involved in detoxification and resistance or by other mechanisms of action [see for example Gunning et al., "Piperonyl Butoxide", pages 215-225, Academic Press (1998); Nishiwaki, H. et al., J. Pest. Sci. 2004, 29, 110-116, Ahmad, M. et al., Pest. Manag. Sci. 2004, 60, 465-473, Li A.Y. et al., J. Med. Entomol. 2004, 41, 193-200, Sanchez, S. et al., J. Vet.Pharmacol. Therap., 2003, 26 (suppl1), 197, Uesugi, Y. et al., Agric. Biol. Chem., 1978, 42, 2181-2183 and the following patent applications: WO 94/17798, WO 00/02557, EP 830813].

[0005] In order to better demonstrate the synergistic activities, particularly in cases where the damaging species is most resistant, treatment with the synergistic product at different times prior to the active principle or a repeated treatment with active principle was proposed; pre-treatment with the synergistic compound is particularly beneficial in that subsequent exposure to the active principle occurs on the already sensitised damaging species, thus with weakened capacity to defend themselves, and is therefore more effective. Separate administrations however are not very practical and are economically unfavourable compared with a single application of the two components.

[0006] Also described in the literature and in patent applications are insecticide, acaricide, fungicide, snailcide and vermicide formulations in cyclodextrins (CD) [see for example Szente ,L. et al, "Cyclodextrins in Pesticides", in "Comprehensive Supramolecular Chemistry" , pages 503-514 , Elsevier (1996); Castillo, J.A. et al., Drug Develop. Ind. Pharm. 1999, 25, 1241-1248; Lezcano, M. et al., J. Agric. Food Chem. 2002, 50, 108-112]. The main purposes of said supramolecular complexes are: modification of the physico-chemical properties of active principles without however altering their biological activity once the active principles are released, greater stability, increased wettability and bioavailability of poorly soluble and difficultly absorbable active principles, reduced environmental toxicity and reduced toxicity for operators.

[0007] The α,β,γ cyclodextrins are natural or semi-synthetic cyclic oligosaccharides, being generally non-toxic and biodegradable; β-CD, γ-CD and certain derivatives thereof such as hydroxypropyl-β-cyclodextrin (HP-β-CD) and sulfobutyl ether-β-cyclodextrin (SBE-β-CD) are particularly preferred for applications.

[0008] Although some improvements in the insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity and physico-chemical properties of active principles have been described, when comparing the properties of active principles and their corresponding complexes with CD [see for example Kamiya, M. et al., Chemosphere 1995, 30, 653-660; Shehatta, I., Monatsh. Chem. 2002, 133, 1239-1247; Tanari, F. et al., Inclus. Phenom. Macrocycl. Chem. 2003, 46, 1-13], no formulation that simultaneously contains a synergistic compound has been previously reported to the best of our knowledge.

[0009] PBO has also been prepared in the form of a complex with CD (see US 4524068) and found to be more effective as an insecticide synergist than uncomplexed PBO; again in this case the trials were carried out on mixtures of insecticides and PBO/CD and not on a single formulation as in the present invention. Furthermore, the process used in US 4524068 was found not to be ideal for preparing a supramolecular complex containing the active principle and the synergistic compound simultaneously in CD. To the best of our knowledge complexes of other synergists with CD are not known, with the exception of a study on the formation and the physico-chemical properties of an inclusion complex of MGK 264 in β-CD (Szente, L. et al., Pestic. Sci., 1990, 28, 7-16); this work, however, does not face problems similar to those of

the present invention as said complex was not used in combination with biologically active substances.

[0010] In WO2005/039287, which is an Art.54(3) EPC document, complexes with cyclodextrins of active principles with insecticidal activity of the pyrethroid class or of growth regulators are described

[0011] The previous literature, even when combined, has therefore not provided the expert of the art with any useful information for preparing the innovative formulation of the present invention, nor has it suggested an effectiveness of said formulation surprisingly superior to that of a mixture of the individual components, either free or complexed with CD, on insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity for agricultural applications, for veterinary medicine use, for domestic hygiene or for the protection of manufactured articles. The present invention proposes to overcome the drawbacks of the known art and to significantly improve the performance of commercially known products with insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity.

SUMMARY

[0012] The present invention relates to an innovative formulation, characterised by the formation of a supramolecular complex in cyclodextrins of:

(i) an active principle consisting of a component with insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity
(ii) a component able to synergistically enhance the activity of the active principle selected from piperonyl butoxide (PBO) or its analogues, sesamol, verbutin or MGK264, wherein the active principle with insecticidal activity is selected from neonicotinoids with the proviso that the following complexes are excluded:

β-CD-fenvalerate-PBO.
β-CD-cypermethrin-PBO,
β-CD-bifenthrin-PBO,
β-CD-β-cyfluthrin-PBO
β-CD-λ-cyhalothrin-PBO,
β-CD-deltamethrin-PBO,
β-CD-ketoconazole-PBO, and
β-CD-pyrethrum extracts-PBO.

[0013] The formulation is obtained by jointly subjecting both an active principle and a synergistic compound to treatment with CD, under particular reaction conditions. By "supramolecular" complex it is meant a complex as defined for example in "Cyclodextrin in Pesticides" Comprehensive Supramolecular Chemistry 503-514, Elsevier, 1996). The invention also relates to the preparation of said formulation and to its use for eradicating damaging species in agriculture, in veterinary medicine, in domestic hygiene or in manufactured articles. The formulation is obtained by jointly subjecting both the active principle and the synergistic compound to supramolecular complex formation with CD.

[0014] The aforesaid formulation is also effective in cases where the damaging species demonstrate tolerance and resistance to treatment with the same active substance, and induces, for the same quantity of principle, a substantially higher mortality of the damaging species than that demonstrated by the same components i) and ii) used in a mixture as such or complexed separately with cyclodextrin.

DETAILED DESCRIPTION OF THE INVENTION

[0015] Any cyclodextrin can be used for the purposes of the present invention. For example the cyclodextrin can be α,β,γ cyclodextrin as such or suitably derivatized to increase its hydrophilic or hydrophobic character. Particularly preferred are β-CD, γ-CD and HP-β-CD. Usable active principles in the present invention belong to one of the following classes of chemical products: carbamates, organophosphates, thioureas, pentatomic or hexatomic heterocyles where 1, 2 or 3 nitrogen atoms are present, such as pyridine, pyrrole, imidazole, benzimidazole, thiazole, pyrazole, pyridazine, quinazoline, oxadiazine, triazine. When the invention relates to active principles having insecticidal activity, it relates to neonicotinoids, such as Imidacloprid, Acetamiprid, Thiacloprid, Thiamethoxam and AKD1022, while preferred active principles having acaricidal, fungicidal, snailcidal or vermicidal activity are carbamates such as Pyrimicarb, Aldicarb, Thiodicarb, Carbosulfan, Carbofuran and Propoxur; organophosphates such as Profenofos, Dimethoate, Omethoate, Terbufos, Azinphos-methyl, Pyrimiphos-methyl, Demeton-s-methyl, Fenitrothion, Trichlorfon and Malathion; mitochondrial electron transport inhibitors ("METI") such as Fenazaquin, Tebufenpyrad, Fenpyroximate, Pyridaben and Tolfenpyrad; fungicides such as Fludioxonil, Clotrimazole, Imazalil and Pyrimethanil; vermicides such as Mebendazole, Metronidazole, Fenbendazole, Thiabendazole and Praziquantel; nerve transmission inhibitors such as Indoxacarb and Fipronil and other active principles in which the mechanism of action against damaging species is still uncertain or which have miscellaneous mechanisms, such as Pymetrozine, Chlorfenapyr and Pyridalyl. Even more preferred are: Imidacloprid, Acetamiprid,

Thiacloprid, Thiodicarb, Carbosulfan, Carbofuran, Fenazaquin, Pyridaben, Fludioxonil, Pyrimethanil, Fenbendazole, Clotrimazole, Praziquantel, Fipronil, Pymetrozine and Pyridalyl.

[0016] The aforesaid preferred compounds can be subdivided on the basis of their activity as follows:

Insecticides: Imidacloprid, Acetamiprid, Thiacloprid, Thiamethoxam, AKD 1022.
Acaricides: Dimethoate, Omethoate, Pyrimiphos-methyl, Demeton-S-methyl, Fenithrothion, Malathion, Fenazaquin, Tebufenpyrad, Fenpyroximate, Pyridaben.
Snailcides: Propoxur , Terbufos, Pyrimiphos-methyl, Fenitrothion, Trichlorfon, Malathion, Tolfenpyrad, Fipronil, Chlorphenapyr, Pyridalyl.
Vermicides: Carbosulfan, Carbofuran, Terbufos, Pyrimiphos-methyl, Fenithrotion, Trichlorfon, Malathion, Fipronil, Mebendazole, Metronidazole, Fenbendazole, Thiabendazole, Clotrimazole, Praziquantel.
Fungicides: Fludioxonil, Clotrimazole, Imazalil, Pyrimethanil.

[0017] The quantity of active principle relative to cyclodextrin is preferably between 1% and 50% (weight/weight) and even more preferably between 2% and 30%.

[0018] The components able to synergistically enhance active principle activity (referred to herein in brief as "synergistic compounds") are substances for se known and already in use. Preferred examples of synergistic compounds are piperonyl butoxide and its analogues, sesamol, verbutin and MGK264, piperonyl butoxide and verbutin being particularly preferred. Piperonyl butoxide is most preferred. The synergistic compounds can be used as such or already pre-formulated with additives; an example of a commercially available pre-formulation is marketed as PB80EC-NF, containing 88% PBO and 12% emulsifier (dialkylsulfosuccinate, also known as SOITEM).

[0019] The quantity of synergistic compound relative to cyclodextrin is between 0.1 % and 100% (weight/weight), preferably between 10% and 80% and even more preferably between 20% and 70%. These percentages refer to the quantity of pure synergistic compound, therefore excluding any additives present in the pre-formulation.

[0020] The quantity of active principle relative to the synergistic compound is between 0.5% and 7000% (weight/weight), preferably between 1% and 1500%, more preferably between 2% and 100% and even more preferably between 10% and 70%.

[0021] Emulsifiers, UV stabilizers, antioxidants and other additives can also be present in the aforesaid formulation.

[0022] The quantity of said additives relative to cyclodextrin is preferably between 0% and 30% (weight/weight), more preferably between 1% and 15%. These percentages refer to all the additives present, also including those already present in the pre-formulations of the active principles utilized.

[0023] Usable emulsifiers are for example dodecylbenzenesulfonate, dialkylsulfosuccinate, lignin sulfonates, phospholipids, polyethylene glycols. Usable UV stabilizers are for example 2-hydroxy-4-methoxy-benzophenone, 2-hydroxy-4-octoxy-benzophenone, 4-hydroxy-2,2,6,6-tetramethylpiperidine sebacate.

[0024] A usable antioxidant is for example 2,6-di-tert-butyl-1-hydroxy-toluene.

[0025] A microemulsified synergist can be optionally added to the formulations of the present invention, being the same as or different from that present in the supramolecular complex, in a quantity from 0% to 300% (weight/weight) relative to the cyclodextrin.

[0026] The composition of the invention is preferably formulated as a solid or as a solid/oil composition; said formulations can be utilised as such, or previously dissolved/emulsified in water or in aqueous solutions of water-miscible solvents, such as a C1-4 alcohol; said aqueous solutions contain 0%-99% by weight of organic solvent, preferably from 0-60% by weight of organic solvent.

[0027] The process for preparing the aforedescribed formulations is characterized by the formation of a supramolecular complex in cyclodextrins of the synergistic compound and the active principle having insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity.

[0028] More specifically the preparation process can be performed in accordance with one of the following methods, indicated as procedure A and procedure B respectively.

Procedure A:

[0029]

(a) preparing a solution or suspension, in a suitable solvent, of the synergistic compound and the active principle optionally in the presence of a suitable surfactant, the latter being present in a quantity from 0% to 12%, preferable from 2% to 4% of the synergistic compound; the solvent is preferably an alcoholic solvent, e.g. ethanol or isopropanol;
(b) preparing a solution of cyclodextrin in water or in water/water-miscible organic solvent mixtures; the dissolution of the CD can conveniently be facilitated by heating (e.g. between 50° and 90°C, preferably between 70°C and 80°C, for 30-90 minutes).

(c) adding the solution/suspension obtained in (a) to the solution obtained in (b); preferably the solution/suspension of (a) is added slowly, e.g. over 2-10 hours (more preferably over 4-8 hours), pre-heated to a temperature between 50° and 90°C, preferably between 50° and 75°C;
(d) maintaining the mixture under agitation at a temperature between 40° and 90°C (preferably between 50° and 75°C) for a time period generally between 12 and 36 hours (preferably 18-24 hours).

[0030] The supramolecular complex of the synergistic compound and the active principle in CD is recovered from the reaction mixture by known methods, such as filtration, drying or lyophilization.

Procedure B

[0031]

(a) dissolving the active principle in the synergistic compound, heating to a temperature preferably between 70° and 140°C, possibly in the presence of a suitable surfactant in a quantity up to 12%, preferably from 2% to 4% relative to the synergistic compound;
(b) preparing a suspension of cyclodextrin in water preferably using a percentage (weight/weight) of CD between 30% and 70% and heating the suspension to a temperature between 60° and 80°C;
(c) adding the hot solution obtained in (a) to the hot suspension obtained in (b) over a time period between 10 and 600 minutes;
(d) maintaining the mixture under stirring at a temperature between 50° and 90°C (preferably between 70° and 90°C) for a time period generally comprised between 1 and 12 hours (preferably between 1 and 4 hours).

[0032] The supramolecular complex of the synergistic compound and the active principle in CD is recovered from the reaction mixture by filtration and subsequent drying.
[0033] The complex thus formed can be mixed with the previously indicated possible additional components of said formulations; said optional components also include an additional quantity of synergistic compound in free form, being the same as or different from that present in the supramolecular complex; said components can be mixed with the supramolecular complex as solids or as microemulsions, immediately prior to use.
[0034] A further aspect of the invention is the use of the aforesaid formulations as insecticides, acaricides, fungicides, snailcides or vermicides in agriculture, for use in veterinary medicine, for eradicating household insects and for protecting manufactured articles. Formation of said supramolecular complex of the active principle and synergistic compound in CD has surprisingly led to a significant increase in composition effectiveness compared to the mixture of the two components used as such or complexed individually with cyclodextrin. By means of the invention an enhanced interaction between the active principle and the synergistic compound is achieved; in comparative trials undertaken by the inventors, said enhancement was always found to be greater than 50%.
[0035] Enhancement of activity leads to various advantages of industrial significance: for example for the same active substance used, more active synergistic compositions can be obtained; or compositions with an effectiveness equal to known compositions can be obtained but with lower amount of active substance; the lesser amount of active substance in use leads to reduced product cost, reduced environmental impact of the manufacturing process, as well as reduced volume/weight of the final composition, with further practical advantages for the operator using these formulations.
[0036] Consequently with the present invention insecticide, acaricide, fungicide, snailcide or vermicide formulations are unexpectedly obtained, which are highly effective and less costly than known formulations.
[0037] The following examples illustrate the invention without however in any way limiting it.

EXPERIMENTAL PART

Example 1

General procedure for preparing the formulation according to procedure A

[0038] The suitable CD in distilled water is introduced at 50°-90°C into a 2-neck flask equipped with cooler and nitrogen outlet. The CD aqueous solution, with concentration between 2% and 15% by weight, for example at 10%, is left under stirring at the same temperature for 1 hour. After said period a solution in water soluble solvent containing the active principle and synergistic compound in the required proportions is added in portions over a 6-hour period. The mixture is maintained under stirring at 40°-90°C for a further 12-36 hours, then the mixture is left to cool to ambient temperature under stirring and finally left to decant for 3-5 hours. The mixture is evaporated to dryness under vacuum. The supramolecular complexes thus obtained prove to be stable in the solid phase for at least 30 days at 23°C.

Example 2

Preparation of a formulation based on acetamiprid and PBO

[0039] The βCD (2g) in distilled water (20 ml) is introduced at 75°C into a 2-neck flask, equipped with cooler and nitrogen outlet. The solution is left under stirring for 1 hour at 75°C. After this period a solution of isopropanol (25 ml) containing PBO/SOITEM (98/2, 0.536 g equal to 0.525 g of PBO and 0.011 g of SOITEM in total) and acetamiprid (0.115 g) is added in portions over a 6-hour period. The mixture is maintained under stirring at 75°C for a further 18 hours, then left to cool to ambient temperature under stirring over a 2-hour period and finally left to decant for 3 hours. The solution is evaporated under vacuum to a solid residue to provide 2.6 g of formulated product.

Example 3

Preparation of a formulation based on imidacloprid and PBO

[0040] The βCD (2g) in distilled water (20 ml) is introduced at 75°C into a 2-neck flask, equipped with cooler and nitrogen outlet. The solution is left under stirring for 1 hour at 75°C. After said period a solution of isopropanol (25 ml) containing PBO/SOITEM (98/2, 0.536 g equal to 0.525 g of PBO and 0.011 g of SOITEM in total) and imidacloprid (0.134 g) is added in portions over a 6-hour period. The mixture is maintained under stirring at 75°C for a further 18 hours, then left to cool to ambient temperature under stirring over a 2-hour period and finally left to decant for 3 hours. The solution is evaporated under vacuum to a solid residue to provide 2.4 g of formulated product.

Example 4

Preparation of a formulation based on acetamiprid and PBO

[0041] Using the same method as described in example 2, a solution of isopropanol (22.5 ml) containing PBO/SOITEM (98/2) (0.0018 g equal to 0.0017g of PBO and 0.0001 g of SOITEM) and 0.103 g of acetamiprid is slowly added to a solution of 1.8 g βCD in 18 ml of distilled water.

[0042] By following the aforegiven method, 1.9 g of formulated product are obtained.

Example 5

Preparation of a formulation based on acetamiprid and PBO

[0043] Using the same method as described in example 2, a solution of isopropanol (25 ml) containing PBO/SOITEM (98/2) (0.01 g equal to 0.0098 g of PBO and 0.0002 g of SOITEM) and 0.115 g of acetamiprid is slowly added to a solution of 2.0 g βCD in 20ml of distilled water.

[0044] By following the aforegiven method, 2.1 g of formulated product are obtained.

Example 6

Preparation of a formulation based on imidacloprid and PBO

[0045] Using the same method as described in example 3, a solution of isopropanol (22.5 ml) containing PBO/SOITEM (98/2) (0.0018 g equal to 0.0017g of PBO and 0.0001 g of SOITEM) and 0.12 g of imidacloprid is slowly added to a solution of 1.8 g βCD in 20 ml of distilled water.

[0046] By following the aforegiven method, 1.8 g of formulated product are obtained.

Example 7

Preparation of a formulation based on imidacloprid and PBO

[0047] Using the same method as described in example 3, a solution of isopropanol (45 ml) containing PBO/SOITEM (98/2) (0.018 g equal to 0.017g of PBO and 0.001 g of SOITEM) and 0.241 g of imidacloprid is slowly added to a solution of 3.6 g βCD in 36 ml of distilled water.

[0048] By following the aforegiven method 3.8 g of formulated product are obtained.

Example 8

Preparation of a formulation based on Thiabendazole and PBO.

[0049] Using the same method as described in example 2, a solution of isopropanol (120 ml) containing PBO/SOITEM (98/2, 2.92 g equal to 2.87g of PBO and 0.050 g of SOITEM in total) and thiabendazole (1.7 g) is slowly added to a solution of β-CD (14,4 g) in 120 ml of water. The mixture is maintained under stirring at 75 °C for a further 5 hours, then allowed to cool at about 40°C and maintained at this temperature under stirring for 15 hours. Cooling at ambient temperature is then performed and the solution is dried under vacuum yielding 19.1 g of formulated product.

Example 9

Preparation of a formulation based on Fipronil and PBO.

[0050] Using the same method as described in example 2 a solution of isopropanol (120 ml) containing PBO/SOITEM (98/2, 3.87g equal to 3.79 g of PBO and 0.077 g of SOITEM in total) and fipronil (1.6 g) is slowly added to una solution of β-CD (14.4 g) in 120 ml of water. The mixture is maintained under stirring at 75 °C for a further 5 hours, then it is allowed to cool at about 40°C and maintained at this temperature under stirring for 15 hours. Cooling at ambient temeparature is then performed, and the solution is dried under vacuum, yielding 19.7 of formulated product.

Example 10

General procedure for preparing the formulation according to procedure B

[0051] The suitable CD in distilled water is introduced at a temperature comprised between 20° and 30°C into a 2-neck flask equipped with cooler and nitrogen outlet in weight/weight proportions preferably between 30% and 70%. The suspension is then heated to a temperature comprised between 60° and 80°C and left under stirring at the same temperature for a convenient time period e.g. 10-30 minutes. After said period a preheated mixture of the active principle and synergistic compound in the required proportions are added in portions. The mixture is maintained at a temperature comprised between 70° and 90°C under stirring for a further 1-2 hours then left to cool to ambient temperature under stirring. A solid is obtained by filtration which is then dried under vacuum.

[0052] The supramolecular complexes thus obtained prove to be stable in the solid phase for at least 30 days at 23°C.

Example 11

Preparation of a formulation based on acetamiprid and PBO

[0053] βCD (13.9 g) in water (20 ml) is introduced into a 2-neck flask at 25°C. The mixture, consisting of a suspension, is left under stirring (300 rpm) for 15 minutes at 25°C. After this time the temperature is brought to 70°C, then a mixture of acetamiprid (0.802 g), PBO (3.65 g) and SOITEM (0.07 g) is added over a 2-hour period. The mixture is agitated for 1 hour at a temperature comprised between 70° and 80°C, then left to cool to ambient temperature. By means of filtration a white solid is obtained which is dried for 3 hours under vacuum (25°C/1 mbar) to provide 14.4 g of formulated product.

Example 12

Preparation of a formulation based on imidacloprid and PBO

[0054] βCD (13.9 g) in distilled water (20 ml) is introduced into a 2-neck flask at 25°C. The mixture, consisting of a suspension, is left under stirring (300 rpm) for 15 minutes at 25°C. After this time the temperature is brought to 70°C, then a mixture of imidacloprid (0.933 g), PBO (3.65 g) and SOITEM (0.07 g) is added over a 2-hour period. The mixture is agitated for 1 hour at 90°C, then left to cool to ambient temperature. By means of filtration a white solid is obtained which is dried under vacuum (25°C/1 mbar) for 3 hours to provide 16.4 g of formulated product.

Example 13

Preparation of a formulation based on Diazinon and PBO

[0055] Using the same method as described in example 11, a formulation was prepared starting from β-CD (50 g) in

distilled water (72 ml), diazinon (4 g) in a mixture with PBO (14.1 g) and SOITEM (0.3 g).
[0056] By following the previously reported procedure, 64 g of formulated product are obtained.

Example 14

Preparation of a formulation based on Imazalil and PBO

[0057] Using the same method as described in example 11, a formulation was prepared starting from of β-CD (25 g) in of distilled water (36 ml), imazalil (1,95 g) in a mixture with PBO (7 g) and SOITEM (0.15 g).
[0058] By following the previously reported procedure, 27.5 g of formulated product are obtained.

Example 15

Preparation of a formulation based on Fenazaquin and PBO

[0059] Using the same method as described in example 11, a formulation was prepared starting from β-CD (50 g) in distilled water (72 ml), fenazaquin (4.0 g) in a mixture with PBO (14 g) and SOITEM (0,3 g).
[0060] By following the previously reported procedure 58.2 g of formulated product are obtained.

Example 16

Preparation of a formulation based on Pyrimicarb and PBO

[0061] Using the same method as described in example 11, a formulation was prepared starting from β-CD (50 g) in distilled water (72 ml), pyrimicarb (3.1 g) in a mixture with PBO (13.2 g) and SOITEM (0.27 g).
[0062] By following the previously reported procedure 60.5 g of formulated product are obtained.

Example 17

Preparation of a formulation based on Pyridaben and PBO

[0063] Using the same method as described in example 11, a formulation was prepared starting from β-CD (50 g) in distilled water (72 ml) pyridaben (4.8 g) in a mixture with PBO (14.1 g) and SOITEM (0.3 g).
[0064] By following the previously reported procedure 64.2 g of formulated product are obtained.

Example 18

Preparation of a formulation based on Pyrimethanil and PBO

[0065] Using the same method as described in example 11, a formulation was prepared starting from β-CD (50 g) in distilled water (72 ml), pyrimethanil (2.6 g) in a mixture with PBO (14.1 g) and SOITEM (0.3 g).
[0066] By following the previously reported procedure 57.3 g of formulated product are obtained.

Example 19

Preparation of a formulation based on Imidacloprid and PBO

[0067] Hydroxypropyl β-cyclodextrin (10g) in distilled water (250 ml) is introduced at room temperature into a two-neck flask provided with cooler and nitrogen outlet. Thereafter, a solution of PBO/SOITEM 98/2 p/p (4.4 g) and imidacloprid (1.0 g), in isopropanol (10 ml) is added. The solution is heated to 75°C and is allowed to react at this temperature for 3h, then the mixture is allowed to cool at room temperature under stirring. The mixture is dried under vacuum , yielding 15.3 g of formulated product.

Example 20

Mortality assay (for insecticide compounds)

[0068] The "leaf dip bioassay" used for testing the activity of insecticides against Bemisia tabaci (whitefly) biotype B,

was similar to that described by Cahill, M et al, Bull. Entomol. Res. 85, 181-187, 1995.

[0069] Cotton plants (Gossypium hirsutum L.) were grown without any exposure to the insecticides. The leaves were cut up into disc shapes and immersed in an aqueous solution of insecticide containing 0.01 % of Agral then left to dry at 25°C. Control leaves were immersed in Agral and distilled water only.

[0070] About 20 adult insects were placed onto the small discs of treated cotton leaf. The insects were allowed to feed and maximum mortality was evaluated at 24 and 48 hours.

[0071] By using the formulations prepared as in examples 2 and 3 the results given in table 1 were obtained.

[0072] LC50% a.i. and LC99% a.i indicate the quantity of active ingredient (i.e pure insecticide) able to achieve mortality for 50% and 99% of the insects tested.

[0073] As a comparison, both the data obtained with imidacloprid and acetamiprid in the absence of the synergistic compound (PBO) and the data obtained with imidacloprid and acetamiprid in a mixture with the same quantity of PBO present in the formulation products of examples 2 and 3 are given in the same table.

[0074] The data demonstrate that the formulations of examples 2 and 3 are much more effective than both the corresponding pure insecticides and the mixture of insecticides and synergistic compound.

[0075] The resistance factor to imidacloprid was equal to 2336 times that of non-resistant insects.

[0076] The resistance factor to acetamiprid was equal to 21 times that of non-resistant insects.

Table 1

Product	**LC50% a.i. (*) (ppm)**	**LC99% a.i. (*) (ppm)**
Acetamiprid	0.00038	0.098
Acetamiprid +PBO mix	0.00042	0.013
Formulation ex.2	0.000078	0.00036
Imidacloprid	4.7	-
Imidacloprid+PBO mix.	0.019	9.7
Formulation ex. 3	0.0012	0.043
(*): a.i. = "active ingredient", being the amount of pure insecticide administered.		

Claims

1. Supramolecular complex in cyclodextrins of:

(i) an active principle with insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity
(ii) a component able to synergistically enhance the activity of the active principle(i) selected from piperonyl butoxide (PBO) or its analogues, sesamol, verbutin, or MGK264, wherein the active principle with insecticidal activity is selected from neonicotinoids, with the proviso that the following complexes are excluded:

β-CD-fenvalerate-PBO,
β-CD-cypermethrin-PBO,
β-CD-bifenthrin-PBO,
β-CD-β-cyfluthrin-PBO,
β-CD-λ-cyhalothrin-PBO,
β-CD-deltamethrin-PBO,
β-CD-ketoconazole-PBO, and
β-CD-pyrethrum extracts-PBO.

2. Complex as claimed in claim 1, wherein the cyclodextrin (CD) is chosen from α,β,γ-CD and their derivatives.

3. Complex as claimed in anyone of claims 1 and 2, wherein the cyclodextrin is chosen from β-CD, γ-CD and the hydroxypropyl derivative of β-CD.

4. Complex as claimed in anyone of claims 1-3, wherein the active principle (i) is chosen from the following classes of chemical products: carbamates, organophosphates, thioureas, pentatomic or hexatomic heterocyles where 1, 2 or 3 nitrogen atoms are present, such as pyridine, pyrrole, imidazole, benzimidazole, thiazole, pyrazole, pyridazine,

quinazoline, oxadiazine, triazine.

5. Complex as claimed in anyone of claims 1-4, wherein the neonicotinoid is chosen from Imidacloprid, Acetamiprid, Thiacloprid, Thiamethoxam, AKD1022.

6. Complex as claimed in anyone of claims 1-5, wherein the quantity of active principle (i) relative to cyclodextrin is between 1% and 50% (weight/weight).

7. Complex as claimed in anyone of claims 1-6, wherein the quantity of active principle (i) relative to cyclodextrin is between 2% and 30% (weight/weight).

8. Complex as claimed in anyone of claims 1-7, wherein the quantity of synergistic component (ii) relative to cyclodextrin is between 0.1 % and 100% (weight/weight).

9. Complex as claimed in anyone of claims 1-8, wherein the quantity of synergistic component (ii) relative to cyclodextrin is between 20% and 70% (weight/weight).

10. Complex as claimed in anyone of claims 1-9, wherein the quantity of active principle relative to the synergistic compound is between 0.5% and 7000% (weight/weight).

11. Complex as claimed in anyone of claims 1-10, wherein the quantity of active principle relative to the synergistic compound is between 1% and 1500% (weight/weight).

12. Complex as claimed in anyone of claims 1-11, wherein the quantity of active principle relative to the synergistic compound is between 10% and 70% (weight/weight).

13. Composition with insecticidal, acaricidal, fungicidal, snailcidal or vermicidal activity **characterised by** containing the supramolecular complex described in anyone of claims 1-12, in combination with suitable additives and carriers.

14. Composition as claimed in claim 13, comprising as a suitable additive a synergistic compound in free or microemulsified form, being the same as or different from that present in the supramolecular complex with cyclodextrin.

15. Composition as claimed in claim 14, wherein the quantity of synergistic compound in free or microemulsified form is not higher than 300% (weight/weight).

16. Composition as claimed in anyone of claims 13-15, formulated as a solid or as a solid/oil composition.

17. Process for preparing the supramolecular complex described in anyone of claims 1-12, **characterised by** the following steps:

(a) preparing a solution or suspension, in a suitable solvent, of the synergistic compound and the active principle, optionally in the presence of a suitable surfactant
(b) preparing a solution of cyclodextrin in water or in water/water-miscible organic solvent mixtures
(c) adding the solution/suspension obtained in (a) to the solution obtained in (b)
(d) maintaining the mixture obtained in (c) under stirring at a temperature between 40° and 90°C for a period between 12 and 36 hours.

18. Process as claimed in claim 17, wherein:

- in step (a) the surfactant is utilised in a quantity up to 12% by weight relative to the synergistic compound, and the solvent is an alcoholic solvent
- in step (b), dissolving the CD;
- in step (c) the solution/suspension of (a) is added over 2-10 hours, pre-heated to a temperature between 50° and 90°C;
- in step (d) the mixture is maintained under stirring, at a temperature between 50° and 75°C for a period between 18 and 24 hours.

19. Process as claimed in anyone of claims 17 and 18, wherein the surfactant is utilized in a quantity between 2% and

4% by weight relative to the synergistic compound, and the solution or suspension prepared in (a) is prepared in ethanol or isopropanol.

20. Process for preparing the supramolecular complex described in anyone of claims 1-12, **characterised by** the following steps:

(a) dissolving the active principle in the synergistic compound, heating the mixture;
(b) preparing a suspension of cyclodextrin in water and heating the suspension to a temperature between 60° and 80°C;
(c) adding the hot solution obtained in (a) to the hot suspension obtained in (b)
(d) maintaining the mixture obtained in (c) under stirring at a temperature between 50° and 90°C for a period between 1 and 12 hours.

21. Process as claimed in claim 20 wherein:

- in step (a) the active principle is dissolved in the synergistic compound at a temperature between 70° and 140°C in the presence of a suitable surfactant in a quantity up to 12% by weight relative to the synergistic compound;
- in step (b) the weight/weight percentage of cyclodextrin in water is between 30% and 70%;
- in step (c) the solution of (a) is added over a period between 10 and 600 minutes;
- in step (d) the mixture is maintained under stirring at a temperature between 70° and 90°C for a period between 1 and 4 hours.

22. Non-medical use of a supramolecular complex of anyone of claims 13-16 as a insecticide, acaricide, fungicide, snailcide or vermicide.

23. A supramolecular complex of anyone of claims 1-12 or a composition of anyone of claims 13-16 for use in veterinary medicine.

Patentansprüche

1. Supramolekularer Komplex in Cyclodextrinen aus:

(i) einem aktiven Hauptbestandteil mit insektizider, akarizider, fungizider, molluskizider oder vermizider Wirkung,
(ii) einem Bestandteil, welcher synergistisch die Aktivität des aktiven Hauptbestandteils (i) verstärken kann, ausgewählt aus Piperonylbutoxid (PBO) oder dessen Analoga, Sesamöl, Verbutin oder MGK264, wobei der aktive Hauptbestandteil mit insektizider Aktivität aus Neonicotinoiden ausgewählt ist,
mit der Maßgabe, dass die nachfolgenden Komplexe ausgeschlossen sind:

β-CD-Fenvalerat-PBO,
β-CD-Cypermethrin-PBO,
β-CD-Bifenthrin-PBO,
β-CD-β-Cyfluthrin-PBO,
β-CD-λ-Cyhalothrin-PBO,
β-CD-Deltamethrin-PBO,
β-CD-Ketoconazol-PBO und
β-CD-Pyrethrumextrakt-PBO.

2. Komplex nach Anspruch 1, wobei das Cyclodextrin (CD) aus α,β,γ-CD und deren Derivaten ausgewählt ist.

3. Komplex nach einem der Ansprüche 1 oder 2, wobei das Cyclodextrin aus β-CD, γ-CD und dem Hydroxypropylderivat von β-CD ausgewählt ist.

4. Komplex nach einem der Ansprüche 1 bis 3, wobei der aktive Hauptbestandteil (i) aus den nachfolgenden Klassen von chemischen Produkten ausgewählt ist: Carbamaten, Organophosphaten, Thioharnstoffen, fünfgliedrigen oder sechsgliedrigen Heterocyclen, in denen 1, 2 oder 3 Stickstoffatome vorliegen, wie beispielsweise Pyridin, Pyrrol, Imidazol, Benzimidazol, Thiazol, Pyrazol, Pyridazin, Chinazolin, Oxadiazin, Triazin.

5. Komplex nach einem der Ansprüche 1 bis 4, wobei das Neonicotinoid aus Imidacloprid, Acetamiprid, Thiacloprid, Thiamethoxam, AKD 1022 ausgewählt ist.

6. Komplex nach einem der Ansprüche 1 bis 5, wobei die Menge des aktiven Hauptbestandteils (i) relativ zu Cyclodextrin zwischen 1 % und 50 % (Gewicht/Gewicht) beträgt.

7. Komplex nach einem der Ansprüche 1 bis 6, wobei die Menge des aktiven Hauptbestandteils (i) relativ zu Cyclodextrin zwischen 2 % und 30 % (Gewicht/Gewicht) beträgt.

8. Komplex nach einem der Ansprüche 1 bis 7, wobei die Menge des synergistischen Bestandteils (ii) relativ zu Cyclodextrin zwischen 0,1 % und 100 % (Gewicht/Gewicht) beträgt.

9. Komplex nach einem der Ansprüche 1 bis 8, wobei die Menge des synergistischen Bestandteils (ii) relativ zu Cyclodextrin zwischen 20 % und 70 % (Gewicht/Gewicht) beträgt.

10. Komplex nach einem der Ansprüche 1 bis 9, wobei die Menge des aktiven Hauptbestandteils relativ zu dem synergistischen Bestandteil zwischen 0,5 % und 7000 % (Gewicht/Gewicht) beträgt.

11. Komplex nach einem der Ansprüche 1 bis 10, wobei die Menge des aktiven Hauptbestandteils relativ zu dem synergistischen Bestandteil zwischen 1 % und 1500 % (Gewicht/Gewicht) beträgt.

12. Komplex nach einem der Ansprüche 1 bis 11, wobei die Menge des aktiven Hauptbestandteils relativ zu dem synergistischen Bestandteil zwischen 10 % und 70 % (Gewicht/Gewicht) beträgt.

13. Zusammensetzung mit insektizider, akarizider, fungizider, molluskizider oder vermizider Wirkung, **dadurch gekennzeichnet, dass** diese einen supramolekularen Komplex nach einem der Ansprüche 1 bis 12 in Mischung mit geeigneten Additiven und Trägern enthält.

14. Zusammensetzung nach Anspruch 13, welche als ein geeignetes Additiv eine synergistische Verbindung in freier oder mikroemulgierter Form enthält, welche gleich oder verschieden von der, welche in dem supramolekularen Komplex mit Cyclodextrin vorliegt, ist.

15. Zusammensetzung nach Anspruch 14, wobei die Menge der synergistischen Verbindung in freier oder mikroemulgierter Form nicht mehr als 300 % (Gewicht/Gewicht) beträgt.

16. Zusammensetzung nach einem der Ansprüche 13 bis 15, welche als ein Feststoff oder als eine Feststoff/Öl-Zusammensetzung formuliert ist.

17. Verfahren zum Herstellen eines supramolekularen Komplexes nach einem der Ansprüche 1 bis 12, welches durch die nachfolgenden Schritte gekennzeichnet ist:

(a) Herstellen, in einem geeigneten Lösungsmittel, einer Lösung oder Suspension des synergistischen Bestandteils und des aktiven Hauptbestandteils, optional in der Gegenwart eines geeigneten Tensids,
(b) Herstellen einer Lösung von Cyclodextrin in Wasser oder in Wasser/Wasser-mischbaren organischen Lösungsmittelmischungen,
(c) Zugabe der in dem Schritt (a) erhaltenen Lösung/Suspension zu der in dem Schritt (b) erhaltenen Lösung,
(d) Halten der in dem Schritt (c) erhaltenen Mischung unter Rühren bei einer Temperatur zwischen 40°C und 90°C für eine Zeitspanne zwischen 12 und 36 Stunden.

18. Verfahren nach Anspruch 17, wobei:

- in dem Schritt (a) das Tensid in einer Menge von bis zu 12 Gew.-% bezogen auf den synergistischen Bestandteil eingesetzt wird und das Lösungsmittel ein alkoholisches Lösungsmittel ist,
- in dem Schritt (b) Lösen von CD,
- in dem Schritt (c) die Lösung/Suspension aus dem Schritt (a) über 2 bis 10 Stunden zugegeben wird, und zwar vorerhitzt auf eine Temperatur zwischen 50°C und 90°C,
- in dem Schritt (d) die Mischung unter Rühren für eine Zeitspanne zwischen 18 und 24 Stunden bei einer Temperatur zwischen 50°C und 75°C gehalten wird.

19. Verfahren nach einem der Ansprüche 17 oder 18, wobei das Tensid in einer Menge zwischen 2 % und 4 Gew.-% bezogen auf den synergistischen Bestandteil verwendet wird und die in dem Schritt (a) hergestellte Lösung oder Suspension in Ethanol oder Isopropanol hergestellt wird.

20. Verfahren zum Herstellen eines supramolekularen Komplexes nach einem der Ansprüche 1 bis 12, welches durch die nachfolgenden Schritte gekennzeichnet ist:

(a) Lösen des aktiven Hauptbestandteils in der synergistischen Verbindung, Erhitzen der Mischung,
(b) Herstellen einer Suspension von Cyclodextrin in Wasser und Erhitzen der Lösung auf eine Temperatur zwischen 60°C und 80°C,
(c) Zugabe der in dem Schritt (a) erhaltenen heißen Lösung zu der in dem Schritt (b) erhaltenen heißen Suspension,
(d) Halten der in dem Schritt (c) erhaltenen Mischung unter Rühren bei einer Temperatur zwischen 50°C und 90°C für eine Zeitspanne zwischen 1 und 12 Stunden.

21. Verfahren nach Anspruch 20, wobei:

- in dem Schritt (a) der aktive Bestandteil in der synergistischen Verbindung bei einer Temperatur zwischen 70°C und 140°C in der Gegenwart eines geeigneten Tensids in einer Menge von bis zu 12 Gew.-% bezogen auf die synergistische Verbindung gelöst wird,
- in dem Schritt (b) das Gewicht/ Gewicht-Verhältnis von Cyclodextrin in Wasser zwischen 30 % und 70 % beträgt,
- in dem Schritt (c) die Lösung aus dem Schritt (a) über eine Zeitspanne zwischen 10 und 600 Minuten zugegeben wird,
- in dem Schritt (d) die Mischung für eine Zeitspanne zwischen 1 und 4 Stunden bei einer Temperatur zwischen 70°C und 90°C gehalten wird.

22. Nichtmedizinische Verwendung eines supramolekularen Komplexes nach einem der Ansprüche 13 bis 16 als ein Insektizid, Akarizid, Fungizid, Molluskizid oder Vermizid.

23. Supramolekularer Komplex nach einem der Ansprüche 1 bis 12 oder eine Zusammensetzung nach einem der Ansprüche 13 bis 16 zur Verwendung in der Veterinärmedizin.

Revendications

1. Complexe supramoléculaire dans des cyclodextrines, comprenant :

(i) un principe actif ayant une activité insecticide, acaricide, fongicide, mollusquicide ou vermicide
(ii) un composant capable d'améliorer de manière synergique l'activité du principe actif (i) choisi parmi le butoxyde de pipéronyle (PBO) ou ses analogues, le sésamol, la verbutine, ou MGK264, dans lequel le principe actif ayant une activité insecticide est choisi parmi les néonicotinoïdes,
à condition que les complexes suivants soient exclus :

β-CD-fenvalérate-PBO,
β-CD-cyperméthrine-PBO,
β-CD-bifenthrine-PBO,
β-CD-β-cyfluthrine-PBO,
β-CD-λ-cyhalothrine-PBO,
β-CD-deltaméthrine-PBO,
β-CD-kétoconazole-PBO, et
β-CD-extraits de pyréthrum-PBO.

2. Complexe selon la revendication 1, dans lequel la cyclodextrine (CD) est choisie parmi les α,β,γ-CD et leurs dérivés.

3. Complexe selon l'une quelconque des revendications 1 et 2, dans lequel la cyclodextrine est choisie parmi la β-CD, la γ-CD et le dérivé hydroxypropyle de β-CD.

4. Complexe selon l'une quelconque des revendications 1 à 3, dans lequel le principe actif (i) est choisi parmi les

classes suivantes de produits chimiques : carbamates, organophosphates, thiourées, hétérocycles pentatomiques ou hexatomiques où 1, 2 ou 3 atomes d'azote sont présents, tels que la pyridine, le pyrrole, l'imidazole, le benzimidazole, le thiazole, le pyrazole, la pyridazine, la quinazoline, l'oxadiazine, la triazine.

5. Complexe selon l'une quelconque des revendications 1 à 4, dans lequel le néonicotinoïde est choisi parmi l'imidacloprid, l'acétamiprid, le thiacloprid, le thiaméthoxam, et AKD1022.

6. Complexe selon l'une quelconque des revendications 1 à 5, dans lequel la quantité de principe actif (i) par rapport à la cyclodextrine est de 1% à 50 % (poids/poids).

7. Complexe selon l'une quelconque des revendications 1 à 6, dans lequel la quantité de principe actif (i) par rapport à la cyclodextrine est de 2 % à 30 % (poids/poids).

8. Complexe selon l'une quelconque des revendications 1 à 7, dans lequel la quantité de composant synergique (ii) par rapport à la cyclodextrine est de 0,1 % à 100 % (poids/poids).

9. Complexe selon l'une quelconque des revendications 1 à 8, dans lequel la quantité de composant synergique (ii) par rapport à la cyclodextrine est de 20 % à 70 % (poids/poids).

10. Complexe selon l'une quelconque des revendications 1 à 9, dans lequel la quantité de principe actif par rapport au composé synergique est de 0,5 % à 7 000 % (poids/poids).

11. Complexe selon l'une quelconque des revendications 1 à 10, dans lequel la quantité de principe actif par rapport au composé synergique est de 1% à 1 500 % (poids/poids).

12. Complexe selon l'une quelconque des revendications 1 à 11, dans lequel la quantité de principe actif par rapport au composé synergique est de 10 % à 70 % (poids/poids).

13. Composition ayant une activité insecticide, acaricide, fongicide, mollusquicide ou vermicide **caractérisée en ce qu'**elle contient le complexe supramoléculaire selon l'une quelconque des revendications 1 à 12, en une combinaison optimale avec des additifs et vecteurs adaptés.

14. Composition selon la revendication 13, comprenant en tant qu'additif adapté un composé synergique sous une forme libre ou micro-émulsifiée, étant identique à ou différente de celle présente dans le complexe supramoléculaire avec la cyclodextrine.

15. Composition selon la revendication 14, dans laquelle la quantité de composé synergique sous une forme libre ou microémulsifiée n'est pas supérieure à 300 % (poids/poids).

16. Composition selon l'une quelconque des revendications 13 à 15, formulée sous la forme d'un solide ou d'une composition solide/huileuse.

17. Procédé de préparation du complexe supramoléculaire selon l'une quelconque des revendications 1 à 12, **caractérisé par** les étapes suivantes :

(a) la préparation d'une solution ou suspension, dans un solvant adapté, du composé synergique et du principe actif, facultativement en présence d'un surfactant adapté
(b) la préparation d'une solution de cyclodextrine dans l'eau ou dans des mélanges de solvants organiques aqueux/miscibles à l'eau
(c) l'ajout de la solution/suspension obtenue à l'étape (a) à la solution obtenue à l'étape (b)
(d) le maintien du mélange obtenu à l'étape (c) sous agitation à une température de 40°C à 90°C pendant une période de 12 à 36 heures.

18. Procédé selon la revendication 17, dans lequel :

- à l'étape (a), le surfactant est utilisé en une quantité pouvant atteindre jusqu'à 12 % en poids par rapport au composé synergique, et le solvant est un solvant alcoolique ;
- à l'étape (b), la CD est dissoute ;

- à l'étape (c), la solution/suspension de l'étape (a) est ajoutée pendant 2 à 10 heures, préchauffée à une température de 50°C à 90°C ;
- à l'étape (d), le mélange est maintenu sous agitation, à une température de 50°C à 75°C pendant une période de 18 à 24 heures.

19. Procédé selon l'une quelconque des revendications 17 et 18, dans lequel le surfactant est utilisé en une quantité de 2 % à 4 % en poids par rapport au composé synergique, et la solution ou suspension préparée à l'étape (a) est préparée dans l'éthanol ou l'isopropanol.

20. Procédé de préparation du complexe supramoléculaire selon l'une quelconque des revendications 1 à 12, **caractérisé par** les étapes suivantes, consistant à :

(a) dissoudre le principe actif dans le composé synergique, chauffer le mélange ;
(b) préparer une suspension de cyclodextrine dans l'eau et chauffer la suspension à une température de 60°C à 80°C ;
(c) ajouter la solution chaude obtenue à l'étape (a) à la suspension chaude obtenue à l'étape (b)
(d) maintenir le mélange obtenu à l'étape (c) sous agitation à une température de 50°C à 90°C pendant une période de 1 à 12 heures.

21. Procédé selon la revendication 20, dans lequel :

- à l'étape (a), le principe actif est dissous dans le composé synergique à une température de 70°C à 140°C en présence d'un surfactant adapté en une quantité pouvant atteindre jusqu'à 12 % en poids par rapport au composé synergique ;
- à l'étape (b), le pourcentage poids/poids de cyclodextrine dans l'eau est de 30 % à 70 % ;
- à l'étape (c), la solution de l'étape (a) est ajoutée pendant une période de 10 à 600 minutes ;
- à l'étape (d), le mélange est maintenu sous agitation à une température de 70°C à 90°C pendant une période de 1 à 4 heures.

22. Utilisation non médicale d'un complexe supramoléculaire selon l'une quelconque des revendications 13 à 16 en tant qu'insecticide, acaricide, fongicide, mollusquicide ou vermicide.

23. Complexe supramoléculaire selon l'une quelconque des revendications 1 à 12 ou une composition selon l'une quelconque des revendications 13 à 16, pour une utilisation en médecine vétérinaire.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- WO 9417798 A **[0004]**
- WO 0002557 A **[0004]**
- EP 830813 A **[0004]**
- US 4524068 A **[0009]**
- WO 2005039287 A **[0010]**

Non-patent literature cited in the description

- **GUNNING et al.** Piperonyl Butoxide. Academic Press, 1998, 215-225 **[0004]**
- **NISHIWAKI, H. et al.** *J. Pest. Sci.,* 2004, vol. 29, 110-116 **[0004]**
- **AHMAD, M. et al.** *Pest. Manag. Sci.,* 2004, vol. 60, 465-473 **[0004]**
- **LI A.Y. et al.** *J. Med. Entomol.,* 2004, vol. 41, 193-200 **[0004]**
- **SANCHEZ, S. et al.** *J. Vet.Pharmacol. Therap.,* 2003, vol. 26 (1), 197 **[0004]**
- **UESUGI, Y. et al.** *Agric. Biol. Chem.,* 1978, vol. 42, 2181-2183 **[0004]**
- Cyclodextrins in Pesticides. **SZENTE ,L. et al.** Comprehensive Supramolecular Chemistry. Elsevier, 1996, 503-514 **[0006]**
- **CASTILLO, J.A. et al.** *Drug Develop. Ind. Pharm.,* 1999, vol. 25, 1241-1248 **[0006]**
- **LEZCANO, M. et al.** *J. Agric. Food Chem.,* 2002, vol. 50, 108-112 **[0006]**
- **KAMIYA, M. et al.** *Chemosphere,* 1995, vol. 30, 653-660 **[0008]**
- **SHEHATTA, I.** *Monatsh. Chem.,* 2002, vol. 133, 1239-1247 **[0008]**
- **TANARI, F. et al.** *Inclus. Phenom. Macrocycl. Chem.,* 2008, vol. 46, 1-13 **[0008]**
- **SZENTE, L. et al.** *Pestic. Sci.,* 1990, vol. 28, 7-16 **[0009]**
- Cyclodextrin in Pesticides. Comprehensive Supramolecular Chemistry. Elsevier, 1996, 503-514 **[0013]**
- **CAHILL, M et al.** *Bull. Entomol. Res.,* 1995, vol. 85, 181-187 **[0068]**