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Schering-Plough Animal Health 'SeaLice, Technical Monograph, SLICE

DESCRIPTION

[0001] This invention relates to an organophosphate or carbamate, or alternatively a pyrethroid or pyrethrin, for use in a method of topical treatment of living fish to combat multicellular ectoparasites with exoskeletons, especially ectoparasites of the crustacean order copepod, more particularly of the genera *Lepeophtheirus* (especially the salmon louse, *Lepeoptheirus salmonis*) and *Caligus* (especially *Caligus elongates*).

[0002] Strange though it may seem, in aquaculture there is a major problem with the infestation of the cultured fish, for example salmon, with sea lice. Generally, the fish are treated with organophosphates, for example azamethiphos or dichlorvos, or pyrethroids, for example deltamethrin or cypermethrin which are known chemical sea lice treatments.

[0003] Chemical sea lice treatments which are currently available generally fall into three classes: organophosphates (e.g. malathion), carbamates (e.g. carbaryl), and pyrethroids (e.g. permethrin).

[0004] Various sea lice treatments have been discussed in "Sea Lice, Technical Monograph, SLICE" published by Schering-Plough Animal Health. Carbaryls in particular have been discussed by Bruno et al. in Aquasci, as documented by STN-INTERNATIONAL, database accession No. 89:18918.

[0005] These sea lice treatment chemicals however have toxic effects. Concerns have long been expressed about organophosphate toxicity in particular, for example in relation to farm workers. Organophosphate poisoning does not require ingestion - cutaneous absorption can lead to signs of poisoning. Symptoms of organophosphate poisoning may include excessive excessive salivation, sweating, rhinorrhea, muscle twitching, weakness, tremor, incoordination, headache, dizziness, nausea, vomiting, abdominal cramps, diarrhoea, respiratory depression, wheezing, blurred vision and more. Carbamates can cause adverse reactions such as sweating, vision blurring, incoordination and convulsions. Pyrethroids similarly can cause adverse reactions even on dermal exposure, such as excitory neurotoxicity, altered dopamine uptake, and dermatitis.

[0006] This is of particular concern not only in relation to the health of workers in the aquaculture industry and, obviously the health of the cultured fish, but also in relation to the release into the environment which almost inevitably occurs when non-juvenile fish, which are generally held in cages rather than tanks, are treated. We have found however that exposure to these chemical agents may be reduced by application of an organophosphate or carbamate and of a pyrethroid, staggered in that order. Thus, the administration according to the invention is more concerned with reducing exposure to potentially toxic chemicals than with overcoming ectoparasite resistance to sea lice treatments.

[0007] Viewed from one aspect the invention provides a pyrethroid or pyrethrin for use in a

method of treatment of farmed fish to combat infestation by multicellular ectoparasites with exoskeletons which method comprises topically exposing farmed fish, especially fish in cages, to a first and a second sea lice treatment agent sequentially, said first sea lice treatment agent being a carbamate or organophosphate and said second sea lice treatment agent being a pyrethroid or pyrethrin, wherein exposure to the first sea lice treatment agent is effected 10 minutes to 12 hours before exposure to the second sea lice treatment agent. Viewed from another aspect the invention provides an organophosphate or carbamate for use in a method of treatment of farmed fish to combat infestation by multicellular ectoparasites with exoskeletons which method comprises topically exposing farmed fish, especially fish in cages, to a first and a second sea lice treatment agent sequentially, said first sea lice treatment agent being a carbamate or organophosphate and said second sea lice treatment agent being a pyrethroid or pyrethrin, wherein exposure to the first sea lice treatment agent is effected 10 minutes to 12 hours before exposure to the second sea lice treatment agent.

[0008] Viewed from a still further aspect the invention provides the use of a carbamate or organophosphate and a pyrethroid or pyrethrin for the preparation of topical sea lice treatment agent compositions for use in a method of treatment of farmed fish to combat infestation by multicellular ectoparasites with exoskeletons which method comprises topically exposing farmed fish, especially fish in cages, to a first and a second sea lice treatment agent sequentially, said first sea lice treatment agent being a carbamate or organophosphate and said second sea lice treatment agent being a pyrethroid or pyrethrin, wherein exposure to the first sea lice treatment agent is effected 10 minutes to 12 hours before exposure to the second sea lice treatment agent.

[0009] The farmed fish treated according to the invention may be any fish susceptible of ectoparasite infestation. The fish however is especially preferably carp, tilapia, cod, halibut, or, most preferably a salmonid, such as trout or salmon, especially salmon.

[0010] Treatment of the farmed fish is topical in that the fish are introduced into an aqueous environment containing the sea lice treatment agent or caused to transit such an environment, or have the sea lice treatment agent introduced into the aqueous environment containing the fish. Thus for example, fish may be transferred into a tank for treatment or caused to pass from one holding zone, e.g. a tank or cage, into another through a conduit, e.g. a pipe or channel, containing the sea lice treatment agent. Alternatively, the sea lice treatment agent may be released into the cage, tank or pond containing the fish, optionally after surrounding the cage with an impervious barrier, e.g. a tarpaulin, to cause at least temporary retention of the sea lice treatment agent within the water in the cage. Particularly preferably, the sea lice treatment agent is released into the water within a cage, e.g. a sea cage, over an extended period so as to ensure exposure of the fish to the sea lice treatment agent before the agent is flushed out of the cage by the flow of surrounding water. Where the agent is to be released into a sea-cage, the sea-cage net will typically be raised to a depth of 2-2.5 metres and then surrounded by impervious tarpaulins to isolate the cage to be treated.

[0011] Typically, the depth of enclosed water may be about 3 metres such that there will be

some space (e.g. about 0.5-1 m) between the net bottom and the tarpaulin. The sea lice treatment agents may then be added to the prepared sea-cage at several locations to ensure maximum dispersion. Sequential treatment may be effected by sequential addition of different sea lice treatment agents or by sequential transfer through conduits or between tanks as discussed above.

[0012] The exposure to the sea lice treatment agents is desirably for a period of 10 to 100 minutes per agent, especially 15 to 60 minutes, especially about 20 to 40 minutes. The treatment is desirably staggered by an intervening period of 10 minutes to 12 hours, especially at least 15 minutes, e.g. 15 minutes to 4 hours, more preferably 30 minutes to 3 hours, especially about 2 hours.

[0013] Particularly preferably, the fish are also treated (preferably pre-treated) with a monooxygenase inhibitor as a synergist for the pyrethroid/pyrethrin, e.g. piperonyl butoxide. This may be presented with the pyrethroid/pyrethrin treatment (e.g. in a mixture with the pyrethroid/pyrethrin), or prior to the pyrethroid/pyrethrin treatment. For example, this may be administered with the fish food, e.g. 12 hours to 60 hours, especially 24 to 48 hours, before exposure to the pyrethroid/pyrethrin.

[0014] The two sea lice treatment agent compositions may take any convenient topical application form, e.g. solution, dispersion, powder, etc. Since they will be diluted within the water in which the fish are present, their concentrations and formulations are not critical. Commercially available compositions may be used.

[0015] The first-applied composition is an organophosphate-containing solution, or a physiologically tolerable carbamate formulation, and the later applied composition is a pyrethroid-containing composition.

[0016] The organophosphate used according to the invention may be any organophosphate with ectoparasite killing effect (preferably with sea lice killing effect) which is physiologically tolerable on dermal application. Examples of such compounds include malathion, parathion, dichlorvos, azamethiphos, chlorpyrifos, chlorthion, trichlorphon, methyl parathion, and fenchlorphos. The use of azamethiphos or dichlorvos however is preferred. Where a carbamate is used, this may be any carbamate with ectoparasite killing effect (preferably with sea lice killing effect) which is physiologically tolerable on dermal application. One example of such a compound is carbaryl. The use of an organophosphate however is preferred.

[0017] For treatment of sea lice in particular, the organophosphate or carbamate is preferably present in the water to which the fish are exposed at a concentration of 5 to 1,000 ppb by wt., especially 10 to 500 ppb, particularly 20 to 300 ppb. For azamethiphos, the preferred concentration is 40 ppb, while for dichlorvos it is 200 ppb.

[0018] The pyrethroid or pyrethrin used according to the invention may be any pyrethroid or pyrethrin with ectoparasite killing effect (preferably with sea lice killing effect) which is

physiologically tolerable on dermal application. Examples of such pyrethroid compounds, which are generally preferred relative to the pyrethrins, include permethrin, phenothrin, cypermethrin, pyrethrin and deltamethrin. The use of deltamethrin or cypermethrin however is preferred. The pyrethrins, if used, may for example be derived from natural sources such as the chrysanthemum plant. However, where pyrethrins are used, it is preferred also to use a synergist (as discussed above).

[0019] For treatment of sea lice in particular, the pyrethroid or pyrethrin is preferably present in the water to which the fish is exposed at a concentration of 0.5 to 50 ppb wt., especially 1 to 25 ppb, particularly 2 to 20 ppb. The preferred concentration for deltamethrin is 1 to 2 ppb, while that for cypermethrin is 5 to 10 ppb.

[0020] For treatment of other ectoparasites, the sea lice treatment agent concentrations may be adjusted appropriately.

[0021] The method of the invention may if necessary be repeated, e.g. after 7 to 10 days, but for a single case of infestation a single performance of the method will generally be sufficient.

[0022] One or both of the sea lice treatment agent compositions may advantageously contain a further sea lice treatment agent, e.g. selected from the chloronicotinyl (e.g. imidacloprid), phenylpyrazole (e.g. fipronil), oxadiazine (e.g. indoxacarb), pyrazole (eg chlorfenapyr), or organochlorine (e.g. lindane) classes.

REFERENCES CITED IN THE DESCRIPTION

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Non-patent literature cited in the description

- Sea Lice, Technical Monograph, SLICESchering-Plough Animal Health [0004]
- database accession89:18918 [0004]

Patentkrav

1. Organophosphat eller carbamat til anvendelse i en fremgangsmåde til behandling af fiskeopdræt til at bekæmpe angreb af multicellulære ectoparasitter med ydre skelet, hvilken fremgangsmåde omfatter topisk at eksponere fiskeopdrædet med et første og et andet fiskelus-behandlingsmiddel sekventielt, hvilket første fiskelus-behandlingsmiddel er carbamat eller organophosphat og det andet fiskelus-behandlingsmiddel er pyrethroid eller pyrethrin,
hvor eksponering med det første fiskelus-behandlingsmiddel foretages 10 minutter til 12 timer før eksponering med det andet fiskelusbehandlingsmiddel.

2. Pyrethroid eller pyrethrin til anvendelse i en fremgangsmåde til behandling af fiskeopdræt til at bekæmpe angreb af multicellulære ectoparasitter med ydre skelet, hvilken fremgangsmåde omfatter topisk at eksponere fiskeopdræt med et første og et andet fiskelus-behandlingsmiddel sekventielt, hvilket første fiskelus-behandlingsmiddel er carbamat eller organophosphat og det andet fiskelus-behandlingsmiddel er pyrethroid eller pyrethrin,
hvor eksponering med det første fiskelus-behandlingsmiddel foretages 10 minutter til 12 timer før eksponering med det andet fiskelusbehandlingsmiddel.

3. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge krav 1 eller krav 2 hvor ectoparasitterne er fiskelus.

4. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge et hvilket som helst af kravene 1 til 3, hvor fiskeopdrætten er salmonidae.

5. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge krav 4, hvor fiskeopdrætten er laks.

6. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge et hvilket som helst af kravene 1 til 5, hvor fiskeopdrætten er i bure.

7. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge et hvilket som helst af kravene 1 til 6, hvor det første fiskelus-behandlingsmiddel er valgt fra

azamethiphos og dichlorvos og det andet fiskelus-behandlingsmiddel er valgt fra deltamethrin og cypermethrin.

8. Organophosphat, carbamat, pyrethroid eller pyrethrin ifølge et hvilket som helst af kravene 1 til 7, hvor eksponering med fiskelusbehandlingsmidlet er for en periode på 10 til 100 minutter pr. middel, og det første og andet fiskelusbehandlingsmiddel er forskudt af en mellemliggende periode på 15 minutter til 4 timer.

9. Anvendelsen af pyrethroid eller pyrethrin og organophosphat eller carbamat til fremstillingen af topiske fiskelus-behandlingsmiddel-sammensætninger til anvendelse i en fremgangsmåde til behandling af fiskeopdræt til at bekæmpe angreb af multicellulære ectoparasitter med ydre skelet, hvilken fremgangsmåde omfatter topisk behandling af fiskeopdræt med et første og et andet fiskelus-behandlingsmiddel sekventielt, hvilket første fiskelus-behandlingsmiddel er carbamat, eller organophosphat og det andet fiskelus-behandlingsmiddel er pyrethroid eller pyrethrin,
hvor eksponering med det første fiskelus-behandlingsmiddel foretages 10 minutter til 12 timer før eksponering med det andet fiskelusbehandlingsmiddel.