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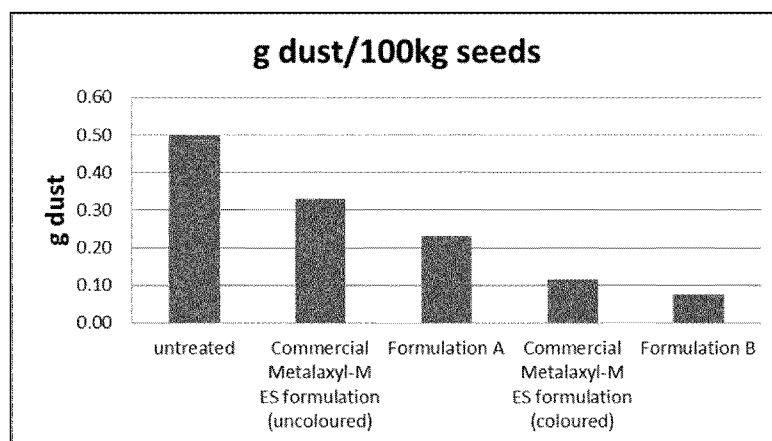
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(54) Title: NEW METALAXYL EMULSION COMPOSITIONS

Figure 4:



(57) Abstract: The present invention relates to a new metalaxyl emulsion composition. Such compositions are useful in agriculture for combating, preventing or controlling phytopathogenic diseases.



Title

New Metalaxyl Emulsion Compositions

Technical field

- 5 The present invention relates to a new metalaxyl emulsion composition. Such compositions are useful in agriculture in combating, preventing or controlling phytopathogenic diseases.

Background

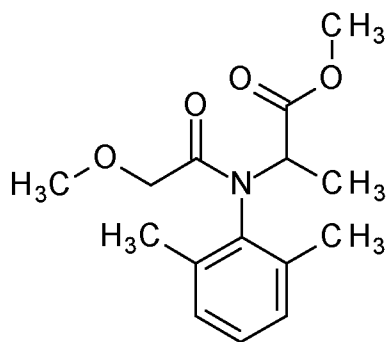
- 10 Metalaxyl has been known for many years as a fungicide with protective and curative action, taken up by leaves, stems and roots. It is known to control fungi of the species plasmopara, phytophthora, peronospora and phytium. Seed treatment has been a particularly important application method for metalaxyl.

WO 2005/044004 discloses fungicidal microemulsions comprising metalaxyl-M.

- 15 There are drawbacks to current commercial seed treatment formulations of metalaxyl, e.g. excessive dusting, issues with long term storage stability and in particular with the stability upon dilution with water. There is thus a need for an improved seed treatment formulation of metalaxyl. The current invention provides a new emulsion composition of metalaxyl with improved storage stability, improved
20 dusting properties and improved stability upon dilution with water.

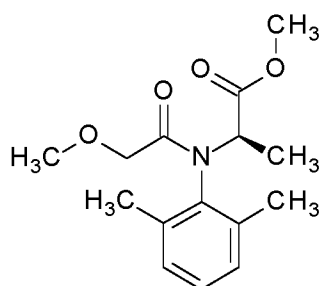
Description of the invention

Metalaxyl may be employed both in its racemic and enantiomerically enriched form due its asymmetric carbon atom:



25

In the emulsion compositions according to the current invention, the use of metalaxyl-M is preferred which is the (R)-stereoisomer:



Metalaxyl-M is also known as mefenoxam or R-metalaxyl. The stereoisomeric purity of the R-stereoisomer may vary but generally the R-stereoisomer makes up at least 90%, more preferably 94%.

- 5 Thus, in a first aspect of the invention, as embodiment 1, there is provided an emulsion composition comprising
- 300 to 400 gram / liter metalaxyl;
- 25 to 100 gram / liter of an anionic surfactant selected from linear or branched alkyl sulfates, sulfonates or phosphonates, linear or branched alkenyl sulfates, sulfonates or phosphonates and linear or
- 10 branched alkylaryl sulfates, sulfonates or phosphonates;
- 50 to 150 gram / liter of a polyalkylene oxide block copolymer;
- wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 75 and 250 gram / liter;
- 150 to 250 gram / liter of a water-miscible solvent; and
- 15 water.

One of the crucial properties of a formulation with a high concentration of active ingredient such as the composition according to embodiment 1 is its long term stability. The temperatures during transportation of said concentrated formulations may vary dramatically, e.g. from -20°C to 50°C. Any form of instability

20 within the formulation may have a severe impact on the active ingredient present in the formulation and the applications and treatments possible. It has been found that surprisingly only very specific combinations of metalaxyl, emulsifiers and water allow to obtain a physically stable formulation over time and a wide temperature range. The amount of anionic and polyalkylene oxide block copolymer within the formulation needs to be tightly controlled, otherwise the emulsion is not stable at low

25 temperatures and upon dilution with water.

The stability of a concentrated emulsion upon dilution is of particular importance as such concentrates are first diluted with many times the amount of water before use. Emulsions according to embodiment 1 are in fact microemulsions. It has been surprisingly found that microemulsions according to embodiment

30 1 retain their properties as microemulsions even upon dilution with many times the amount of water.

As embodiment 2, there is provided an emulsion composition according to embodiment 1 wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 120 and 175 gram / liter.

- 5 As embodiment 3, there is provided an emulsion composition according to embodiment 1 or 2 wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 125 and 150 gram / liter.

- 10 As embodiment 4, there is provided an emulsion composition according to any one of embodiments 1 to 3 wherein the amount of anionic surfactant is between 30 and 100 gram / liter.

- As embodiment 5, there is provided an emulsion composition according to any one of embodiments 1 to 4 wherein the amount of anionic surfactant is between 40 and 80 gram / liter, preferably 40 and 60 gram / liter.

- 15 As embodiment 6, there is provided an emulsion composition according to any one of embodiments 1 to 5 wherein the amount of polyalkylene oxide block copolymer is between 75 and 125 gram / liter.

- 20 As embodiment 7, there is provided an emulsion composition according to any one of embodiments 1 to 6, wherein the ratio of anionic surfactant to polyalkylene oxide block copolymer is from 4 : 1 to 1 : 4.

As embodiment 8, there is provided an emulsion composition according to any one of embodiments 1 to 7, wherein the ratio of anionic surfactant to polyalkylene oxide block copolymer is from 2 : 1 to 1 : 2.

- 25 In particular, as embodiment 9, there is provided an emulsion composition according to any one of embodiments 1 to 8 wherein the anionic surfactant is alkylarylsulfonate, in particular a n-C₁₀-C₁₃-alkylbenzene sulfonate salt, more particularly a n-C₁₀-C₁₃-alkylbenzene sulfonate triethanolamine salt.

- 30 In particular, as embodiment 10, there is provided an emulsion composition according to any one of embodiments 1 to 9 wherein the polyalkylene oxide block copolymer is a block copolymer of ethylene oxide and propylene oxide, more particularly a butyl poly(propylene oxide) poly(ethylene oxide) block copolymer.

- 35 Block copolymers of ethylene oxide and propylene oxide can be di- and tri-block copolymers, such as ABA or BAB block copolymer or BA block copolymers. Examples include the GENAPOL® PF series (CLARIANT), the PLURONIC® series (BASF), the SYNPERONIC® PE series (CRODA), or the TOXIMUL® series (STEPAN). A preferred group of ethylene oxide/propylene oxide block copolymers for use in the compositions of this invention are butyl poly(propylene oxide) poly(ethylene oxide) block

copolymers having an average molecular weight in a range of 2,400 to 3,500. Suitable examples include Pluronic® L10, Pluronic® L44, Pluronic® L63, Pluronic® L64, Pluronic® P84, Pluronic® P104, Pluronic® P105, Step-Flow® 26, Toximul® 8323 and Toximul® 8320.

5 The term “water-miscible” solvent as used herein refers to solvents which are miscible with water, i.e. they do not separate into different layers. Suitable examples are glycol, such as propylene glycol, ethylene glycol, diethylene glycol, 1,2-propylene glycol, tripropylene glycol, alcohol, such as methanol, ethanol, isopropanol, n-propanol. Preferably, the water-miscible solvent is a glycol, more preferably a 1,2-propylene glycol.

10 The emulsion compositions according to any one of embodiment 1 to 10 are useful in combating, preventing or controlling phytopathogenic diseases which comprises applying to a phytopathogen, to the locus of a phytopathogen, or to a plant susceptible to attack by a phytopathogen, or to propagation material thereof, a composition according to any one of embodiments 1 to 10. In particular, the emulsion
15 compositions are suitable in treating propagation material, more particularly propagation material of sunflower, tomato, sugar beet, cotton and vegetables.

Current commercial emulsions for seed treatment comprising metalaxyl develop a milky appearance upon dilution with a lot of water, e.g. with 90% water which is a typical amount before applying the
20 emulsions to propagation material. This milky appearance is a sign of instability of the emulsion, in particular it is a sign of increasing droplet size within the emulsion and leads with time to further increases of the droplet size until the droplets can be visible by naked eye. It is one of the goals of the emulsions of the invention to overcome these instability issues upon dilution with water (water dilutability).

25 Furthermore, it has also surprisingly been found that the emulsion of the inventions exhibit improved adherence / less dusting when applied on propagation material than the commercial emulsion with the same content of active ingredient. This has been tested on a so-called Heubach Dustmeter and the results are disclosed under the “Experimental” section.

30 Another important drawback of many emulsions is the long term storage stability at high and low temperatures. Often emulsions start to show phase separation, streaks/smears or droplet building when storing long term. This can have a detrimental impact on the properties of the emulsion at the final application stage, i.e. when treating the propagation material (seeds). The emulsions of the invention
35 have shown to have good long term stability, in particular at low temperature of -18°C.

Description of the drawings

Figure 1: The results of the water dilutability test are shown. An x indicates when a particular formulation has passed the test whereas a circle o indicates when a formulation has failed the test.

Figure 2: The results of the storage stability test at -18°C for two weeks are shown. An x indicates when a particular formulation has passed this test and a circle o indicates when a formulation has failed this test.

Figure 3: The results of the water dilutability test and storage stability test at -18°C have been combined in one Figure. An x indicates when a particular formulation has passed both the water dilutability and storage stability test at -18°C and a circle o indicates when a formulation has failed one or both tests.

Figure 4: The results of the Heubach dust test are shown in Figure 4.

Experimental:

Preparation of formulations according to the invention:

(i) Colourless formulation:

Colourless emulsions for seed treatment were prepared as follows:

Metalaxyl-M and polyalkylene oxide block copolymer were heated to 50°C.

1. The whole amount of water-miscible solvent was put into the vessel.
2. Metalaxyl-M was added into the vessel and the whole stirred until homogenous.
3. The anionic surfactant was added and then the polyalkylene oxide block copolymer.
4. The total amount of water was added slowly.
5. Antifoam and antibacterial agents were added.
6. The formulation was stirred until homogenous.

(ii) Coloured formulation:

Coloured emulsions for seed treatment were prepared as follows:

Metalaxyl-M and polyalkylene oxide block copolymer were heated to 50°C.

1. The whole amount of water-miscible solvent was put into the vessel.
2. Metalaxyl-M was added into the vessel and the whole stirred until homogenous.
3. The anionic surfactant was added and then the polyalkylene oxide block copolymer.
4. The total amount of water was added slowly.
5. The dye was added into the vessel.
6. Antifoam and antibacterial agents were added.

7. The formulation was stirred until homogenous.

The following exemplary emulsions were prepared using the methods described above:

Component	Formulation A (gram / liter)	Formulation B (gram / liter)	Commercial Metalaxyl-M ES formulation; gram / liter)
Metalaxyl-M	350	350	350
Water-miscible solvent	200	200	200
Anionic surfactant (n-C10-C13- alkylbenzene sulfonate triethanolamine salt)	25 to 150	25 to 150	5
Polyalkylene oxide block copolymer	50 to 150	50 to 150	40
Non-ionic surfactant (Polyoxyalkylene tristyrylphenyl ether)	-	-	50
Antifoam	0.3	0.3	0.3
Antibacterial agents	3	3	1
Dye	0	60	0/60 (coloured)
Water	up to 1 liter	up to 1 liter	up to 1 liter
TOTAL	1 liter	1 liter	1 liter

5

Comparative data:

Formulations similar to Formulation A above were prepared but the amount of anionic and polyalkylene oxide block copolymer was varied and the amount of water adjusted accordingly. These formulations were then compared against each other for different technical criteria.

10

(i) Water dilutability at 90%:

Emulsions for seed treatment are diluted with water before they are applied to seeds. These emulsions for seed treatment are clear and translucent before the dilution with water. The best emulsions stay stable upon dilution, i.e. the droplet sizes in the emulsion stay constant upon dilution with water.

15

Emulsions which are not stable upon dilution change their appearance, i.e. with increasing particle sizes, the emulsion first becomes blue opalescent, then milky and finally the droplets are visible with the naked eye. Dilution with 90% water, i.e. 9 times water and 1 time formulation, has been carried out for the different formulations and the formulations have then been marked whether they are stable or not. Any formulation exhibiting some sort of cloudiness upon dilution was regarded as having failed this test.

Test conditions. A dilution of tap water and formulated product was prepared as 90% dilution in a 10ml glass testing tube and closed with a glass plug. The liquid was inverted 10 times and then visually observed on opacity, cloudiness or transparency.

5

Figure 1 shows the results of the water dilutability test. An x indicates when a particular formulation has passed the test whereas a circle o indicates when a formulation has failed the test. One can see that most formulations did not pass this crucial test.

10 (ii) Storage stability at -18°C for two weeks:

One important criterion for the stability of an emulsion for seed treatment is the storage stability at different temperatures, in particular at high and low temperature. Hence, one such important test is storing emulsions at -18°C for two weeks. Any formulation which exhibits a phase separation or streaks/smears within the solution or droplet building was regarded as having failed this test.

15

The formulated product was stored in 2 ml vials at -18°C for 2 weeks. The samples were allowed to thaw and were then judged: Phase separation or streaks/smears within the solution or droplet building was regarded as having failed the test.

20 Figure 2 shows the results of the storage stability test at -18°C for two weeks. An x indicates when a particular formulation has passed this test and a circle o indicates when a formulation has failed this test. One can see that only very few formulations have passed this test which means that only specific combinations of co-formulants are technically suitable.

25 Figure 3 shows the combination of the water dilutability (i) and storage stability test at -18°C (ii). One can see that only very few formulations are acceptable.

(iii) Heubach dust measurement on sunflower seeds:

30 The Heubach Dustmeter is a monitoring/feedback device designed to help control the dust properties of bulks, powders, granules and fibers, with the unique ability to simulate an array of mechanical handling scenarios, which makes it the only device of its kind on the market.

It functions by the method of the rotating drum and performs according to the German industry standardisation for dust measurement, the DIN55992. It can also be used with customised measuring criteria, like the ESA (European Seed Association) does for the so called "Heubach value".

35

The formulated product was treated on sunflower seeds using a common rotary seed coater machine using a 70% dilution in water (300 ml formulated product / 100 kg of sunflower seed). The treated seed

was dried at room temperature conditions and the Heubach dust-off test was done after 2 days drying time.

The results of the Heubach test are shown in Figure 4. One can see from Figure 4 that the dust levels are significantly lower for the formulations according to the invention compared to the current commercial Metalaxyl-M ES formulation. The composition of the commercial Metalaxyl-M ES formulation has been given above. This is an important parameter as dust development during seed treatment with a formulation is a health risk for the operator and it also makes accurate dosing of the active ingredient difficult.

10

Claims

1. An emulsion composition comprising
300 to 400 gram / liter metalaxyl;
5 25 to 100 gram / liter of an anionic surfactant selected from linear or branched alkyl sulfates, sulfonates or phosphonates, linear or branched alkenyl sulfates, sulfonates or phosphonates and linear or branched alkylaryl sulfates, sulfonates or phosphonates;
50 to 150 gram / liter of a polyalkylene oxide block copolymer;
wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 75
10 and 250 gram / liter;
150 to 250 gram / liter of a water-miscible solvent; and
water.
2. The emulsion composition according to claim 1,
15 wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 120 and 175 gram / liter.
3. The emulsion composition according to claim 1 or 2,
wherein the total amount of anionic surfactant and polyalkylene oxide block copolymer is between 125
20 and 150 gram / liter.
4. The emulsion composition according to any one of claims 1 to 3,
wherein the amount of anionic surfactant is between 30 and 100 gram / liter.
- 25 5. The emulsion composition according to any one of claims 1 to 4,
wherein the amount of polyalkylene oxide block copolymer is between 75 and 125 gram / liter.
6. The emulsion composition according to any one of claims 1 to 6,
wherein the ratio of anionic surfactant to polyalkylene oxide block copolymer is from 2 : 1 to 1 : 2.
30
7. The emulsion composition according to any one of claims 1 to 6,
wherein the anionic surfactant is alkylarylsulfonate.
8. The emulsion composition according to claim 8,
35 wherein the anionic surfactant is an n-C₁₀-C₁₃-alkylbenzene sulfonate triethanolamine salt.
9. The emulsion composition according to any one of claims 1 to 8, wherein

the polyalkylene oxide block copolymer is a butyl poly(propylene oxide) poly(ethylene oxide) block copolymer.

10. The emulsion composition according to any one of claims 1 to 9, wherein
5 the metalaxyl active ingredient is Metalaxyl-M.
11. The emulsion composition according to any one of claims 1 to 10, wherein
the water-miscible solvent is propylene glycol.
- 10 12. A method of combating, preventing or controlling phytopathogenic diseases which comprises
applying to a phytopathogen, to the locus of a phytopathogen, or to a plant susceptible to attack by a
phytopathogen, a composition according to any one of claims 1 to 11.
13. A method of combating, preventing or controlling phytopathogenic diseases which comprises
15 applying a composition according to any one of claims 1 to 11 to propagation material.
14. The method according to claim 13, wherein the propagation material is selected from sunflower,
tomato, sugar beet, cotton and vegetables.

Figure 1:

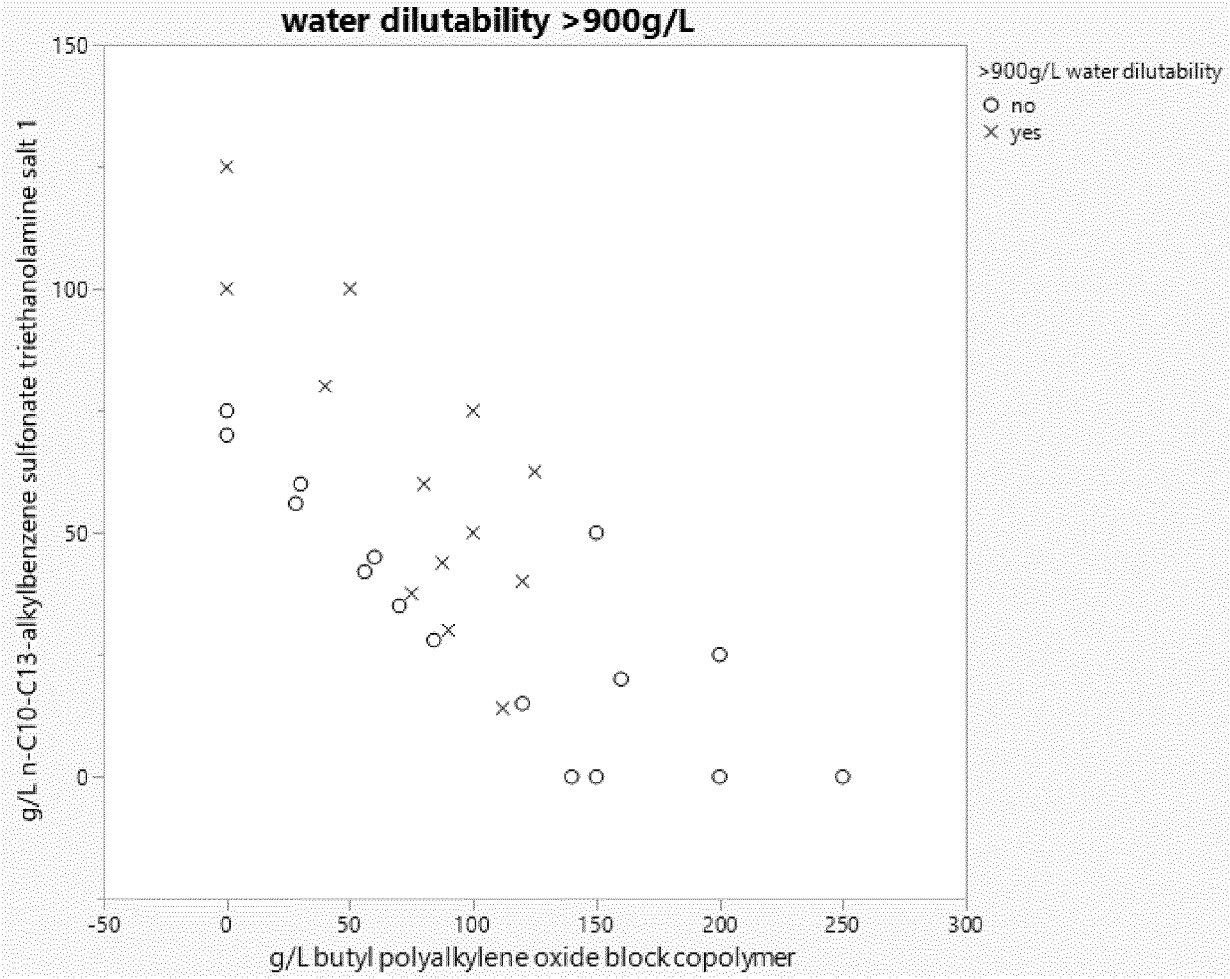


Figure 2:

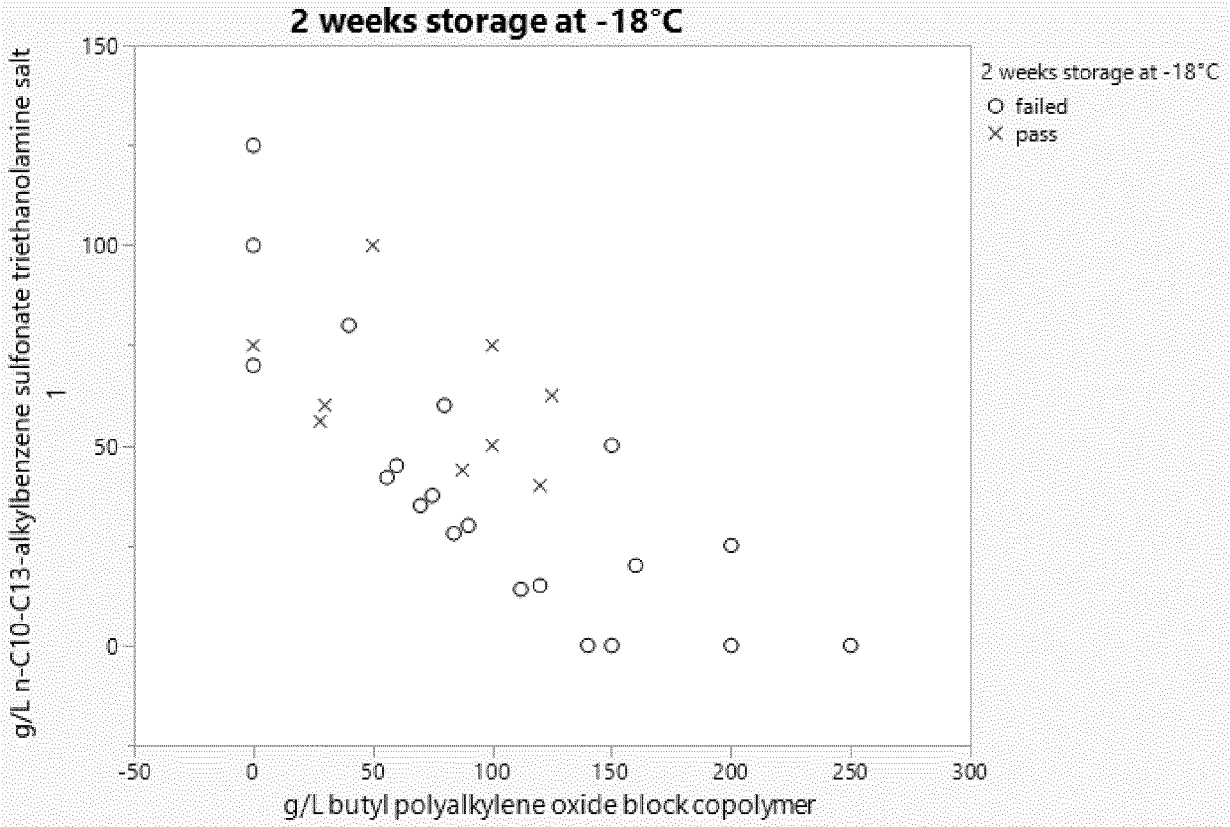


Figure 3:

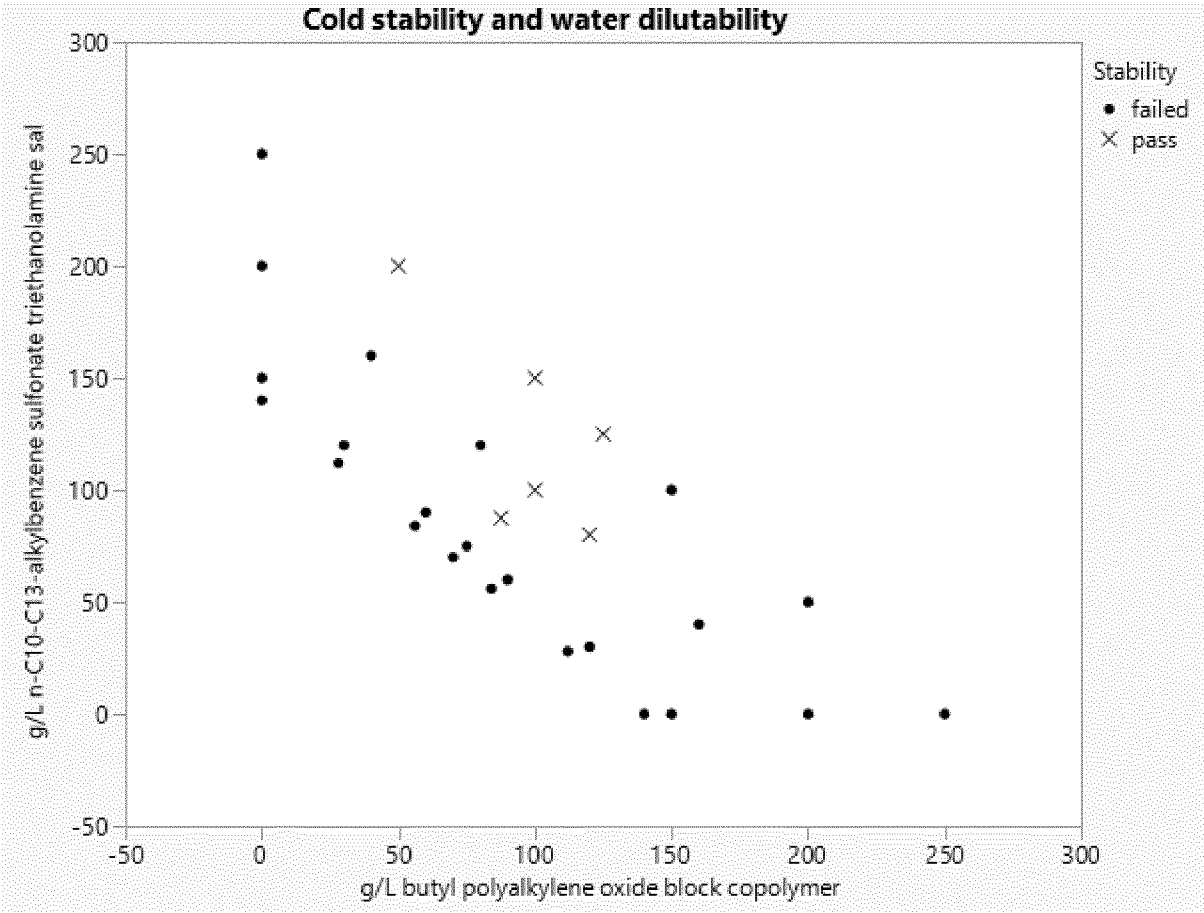
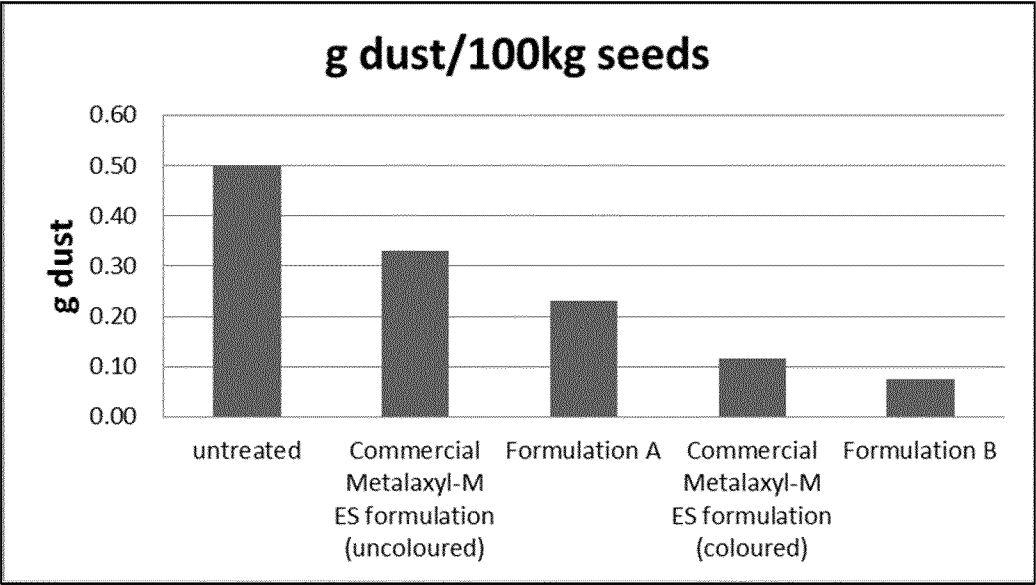


Figure 4:



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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/054675

A. CLASSIFICATION OF SUBJECT MATTER
INV. A01N25/04 A01N25/30 A01N37/46
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 7 199 081 B2 (SYNGENTA CROP PROT INC [US]) 3 April 2007 (2007-04-03) column 2, line 7 - line 21 column 2, line 25 - line 58 column 4, line 12 - line 58 column 5, line 2 - line 15 column 6, line 39 - line 59 column 7, line 55 - line 60 column 10, line 35 - line 65 table 4 column 17, line 25 - line 66 ----- -/-	1-14



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

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Date of the actual completion of the international search

16 April 2020

Date of mailing of the international search report

28/04/2020

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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Zanobini, Alessandra

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2020/054675

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2015/124661 A1 (BASF SE [DE]) 27 August 2015 (2015-08-27) page 1, line 33 - page 2, line 4 page 2, line 35 - page 4, line 32 page 5, line 1 - line 6 page 6, line 5 - line 14 page 9, line 34 - page 10, line 14 page 18, line 12 - line 32 page 20, line 15 - line 25 -----	1-14
A	WO 2015/124662 A1 (BASF SE [DE]) 27 August 2015 (2015-08-27) page 3, line 5 - line 19 page 3, line 30 - page 4, line 38 page 6, line 5 - line 26 page 9, line 36 - page 11, line 34 page 29, line 22 - page 31, line 3 table 6 -----	1-14
X	WO 2005/044004 A1 (LG LIFE SCIENCES LTD [KR]; KANG KYUNG-GOO [KR] ET AL.) 19 May 2005 (2005-05-19) paragraphs [0004], [0014], [0024] - [0033], [0038], [0040] tables 1,2 paragraphs [0059] - [0082] -----	1-7, 10-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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