



(11) **EP 2 681 998 B9**

(12) **CORRECTED EUROPEAN PATENT SPECIFICATION**

(15) Correction information:
Corrected version no 1 (W1 B1)
Corrections, see
Description Paragraph(s) 3, 10
Claims EN 1

(51) Int Cl.:
A01N 57/34 ^(2006.01) **A01P 1/00** ^(2006.01)
C09D 5/14 ^(2006.01) **C10L 10/00** ^(2006.01)
A01N 43/68 ^(2006.01) **A01N 35/02** ^(2006.01)

(48) Corrigendum issued on:
17.06.2015 Bulletin 2015/25

(45) Date of publication and mention
of the grant of the patent:
04.03.2015 Bulletin 2015/10

(21) Application number: **13172706.7**

(22) Date of filing: **08.10.2010**

(54) **Synergistic antimicrobial composition**

Synergistische antimikrobielle Zusammensetzung

Composition antimicrobienne synergique

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR

(30) Priority: **20.10.2009 US 279397 P**

(43) Date of publication of application:
08.01.2014 Bulletin 2014/02

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
10766196.9 / 2 485 588

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- **S. B. SELVARAJU ET AL: 'Biocidal Activity of Formaldehyde and Nonformaldehyde Biocides toward Mycobacterium immunogenum and Pseudomonas fluorescens in Pure and Mixed Suspensions in Synthetic Metalworking Fluid and Saline' APPLIED AND ENVIRONMENTAL MICROBIOLOGY vol. 71, no. 1, 01 January 2005, pages 542 - 546, XP055117123 DOI: 10.1128/AEM.71.1.542-546.2005 ISSN: 0099-2240**

Remarks:

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

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Description

[0001] This invention relates to combinations of biocides, the combinations having greater activity than would be observed for the individual antimicrobial compounds.

[0002] Use of combinations of at least two antimicrobial compounds can broaden potential markets, reduce use concentrations and costs, and reduce waste. In some cases, commercial antimicrobial compounds cannot provide effective control of microorganisms, even at high use concentrations, due to weak activity against certain types of microorganisms, or relatively slow antimicrobial action, or instability under certain conditions such as high temperature and high pH. Combinations of different antimicrobial compounds are sometimes used to provide overall control of microorganisms or to provide the same level of microbial control at lower use rates in a particular end use environment. For example, U.S. Pat. No. 5,385,896 discloses combinations of phosphonium salts and aldehydes, but this reference does not suggest any of the combinations claimed herein. Moreover, there is a need for additional combinations of antimicrobial compounds having enhanced activity to provide effective control of the microorganisms. The problem addressed by this invention is to provide such additional combinations of antimicrobial compounds.

STATEMENT OF THE INVENTION

[0003] The present invention is directed to a synergistic antimicrobial composition comprising: (a) a hydroxymethyl-substituted phosphorus compound selected from the group consisting of tetrakis(hydroxymethyl) phosphonium salts and tris(hydroxymethyl)phosphine; and (b) hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (HHT); wherein a weight ratio of the hydroxymethyl-substituted phosphorus compound to hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine is from 15:1 to 1: 15.

DETAILED DESCRIPTION OF THE INVENTION

[0004] As used herein, the following terms have the designated definitions, unless the context clearly indicates otherwise. The term "antimicrobial compound" refers to a compound capable of inhibiting the growth or propagation of microorganisms, and/or killing microorganisms; antimicrobial compounds include bactericides, bacteristats, fungicides, fungistats, algacides and algistats, depending on the dose level applied, system conditions and the level of microbial control desired. The term "microorganism" includes, for example, fungi (such as yeast and mold), bacteria and algae. The following abbreviations are used throughout the specification: ppm = parts per million by weight (weight/weight), mL = milliliter, Unless otherwise specified, temperatures are in degrees centigrade (°C), and references to percentages are by weight (wt%). Percentages of antimicrobial compounds in the composition of this invention are based on the total weight of active ingredients in the composition, i.e., the antimicrobial compounds themselves, exclusive of any amounts of solvents, carriers, dispersants, stabilizers or other materials which may be present. The hydroxymethyl-substituted phosphorus compound is selected from the group consisting of tetrakis(hydroxymethyl)phosphonium salts (e.g., tetrakis(hydroxymethyl)phosphonium sulfate (THPS) and tetrakis(hydroxymethyl)phosphonium chloride) and tris(hydroxymethyl)phosphine. More than one hydroxymethyl-substituted phosphorus compound may be present, in which case the biocide ratio is calculated from the total content of such compounds.

[0005] HHT is a known formaldehyde-releasing biocide (see US Environmental Agency Reregistration Eligibility Decision (RED) on Grotan (HHT) from 27 June 2008).

[0006] In some embodiments of the invention, the antimicrobial composition is substantially free of oxazolidine compounds, i.e. it has less than 5% oxazolidine compounds relative to total biocide active ingredient content, alternatively less than 2%, alternatively less than 1%, alternatively less than 0.5%, alternatively less than 0.1%.

[0007] In some embodiments of the invention, the antimicrobial combination of this invention is useful in oil and gas field injection, produced fluids, fracturing fluids and other functional fluids, oil and gas wells, oil and gas operation, separation, storage, and transportation systems, oil and gas pipelines, oil and gas vessels, and fuel. The combination is especially useful in aqueous fluids added to or produced by oil and gas well. The composition also is useful for controlling microorganisms in other industrial water and water containing/contaminated matrixes, such as cooling water, air washer, heat exchangers, boiler water, pulp and paper mill water, other industrial process water, ballast water, wastewater, metalworking fluids, latex, paint, coatings, adhesives, inks, tape joint compounds, pigment, water-based slurries, personal care and household products such as detergent, filtration systems (including reverse osmosis and ultrafiltration systems), toilet bowl, textiles, leather and leather production system, or a system used therewith.

[0008] Typically, the amount of the biocide combinations of the present invention to control the growth of microorganisms is from 10 ppm to 5,000 ppm active ingredient. In some embodiments of the invention, the active ingredients of the composition are present in an amount of at least 20 ppm, alternatively at least 50 ppm, alternatively at least 100 ppm, alternatively at least 150 ppm, alternatively at least 200 ppm. In some embodiments, the active ingredients of the composition are present in an amount of no more than 2,000 ppm, alternatively no more than 1,000 ppm, alternatively

no more than 500 ppm, alternatively no more than 400 ppm, alternatively no more than 300 ppm, alternatively no more than 250 ppm, alternatively no more than 200 ppm, alternatively no more than 100 ppm, alternatively no more than 50 ppm. Concentrations mentioned above are in a liquid composition containing the biocide combinations. Biocide concentrations in a high-sulfide and high-temperature environment typically will be higher than in other environments. In some embodiments of the invention, active ingredient concentrations downhole in an oil well are from 30 to 500 ppm, alternatively from 50 to 250 ppm. In some embodiments of the invention, active ingredient concentrations for top side treatment at an oil well are from 10 to 300 ppm, alternatively from 30 to 100 ppm.

[0009] The present invention also encompasses a method for preventing microbial growth in the use areas described above, especially in oil or natural gas production operations, by incorporating the claimed biocide combination into the materials.

EXAMPLES

Example 1. Synergistic effect of THPS and HHT against sulfate reducing bacteria (SRB)

[0010] Inside an anaerobic chamber (Bactron anaerobic chamber), a deaerated sterile salt solution (3.1183 g of NaCl, 1.3082 mg of NaHCO₃, 47.70 mg of KCl, 72.00 mg of CaCl₂, 54.49 mg of MgSO₄, 172.28 mg of Na₂SO₄, 43.92 mg of Na₂CO₃ in 1 L water) was contaminated with an oil field isolated anaerobic consortium, mainly SRB, at final bacterial concentrations of 10⁶ to 10⁷ CFU/mL. The aliquots of this contaminated water were then treated with THPS and hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (HHT), or the THPS /HHT combination at different active concentration levels. After the mixtures were incubated at 40°C for 24 hour, the biocidal efficacy was determined by minimum tested biocide concentration for a complete bacteria kill in the aliquots (MBC). Table 1 summarizes the efficacy of each biocide and their blend, and the Synergy Index*¹ of each combination.

Table 1. Biocidal efficacy of THPS, hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine (HHT), THPS /HHT combination, and Synergy Index

Ratio of THPS to HHT (active w/w)	Average MBC (active ppm)		Average Synergy Index	p value in Z test* ²
	THPS	HHT		
1:0	6.1	0.0		
9:1	5.2	0.6	0.88	0.00
3:1	5.0	1.7	0.87	0.00
1:1	7.0	7.0	1.26	0.00
1:3	3.3	10.0	0.69	0.00
1:9	2.4	21.5	0.69	0.00
0:1	0.0	79.0		

*1 Synergy Index = Ca /CA + Cb/CB
 Ca: Concentration of biocide A required to achieve a complete bacterial kill when used in combination with Biocide B
 CA: Concentration of biocide A required to achieve a complete bacterial kill when used alone
 Cb: Concentration of biocide B required to achieve a complete bacterial kill when used in combination with Biocide A
 CB: Concentration of biocide B required to achieve a complete bacterial kill when used alone
 A Synergy Index less than 1 indicates synergy.
 *2 P value < 0.05 means that there is significant difference between the average Synergy Index and 1.00

Example 2. Evaluation of biocidal efficacy of THPS /HHT combinations, against anaerobic bacteria for a high temperature and sulfide-rich environment.

[0011] Inside an anaerobic chamber (BACTRON IV), biocides solutions were challenged with 10⁴ to 10⁵ CFU/mL of an oilfield SRB consortium and 10 ppm sulfide ion (added in the form of sodium sulfide). The biocide solutions were then incubated at 80°C under anaerobic condition for 7 days, with daily challenge of the SRB consortium (10⁴ to 10⁵ CFU/mL) and sulfide ion (10 ppm). The biocidal efficacy was determined by selecting the lowest testing biocide dosage required for 99.999% or complete bacterial kill after both 2 hours and 7 days of heat, SRB and sulfide exposure. Synergy Index was then calculated. Table 2 summarizes the efficacy of each biocide and their blend, and the Synergy Index of each combination.

Table 2. Biocidal efficacy evaluation of THPS, HHT, and THPS / HHT combination for a high temperature and sulfide-rich environment, and Synergy Index

Ratio of THPS to HHT(active w/w)	Dosage (active ppm) required for 99.999% or complete bacterial kill of both 2h and 7day heat, SRB, and sulfide exposure		Synergy Index*3
	THPS	HHT	
1:0	88.9	0.0	
5.1:1	59.3	11.7	0.75
2.3:1	59.3	26.3	0.86
1:1	39.5	39.5	0.74
1:2.3	17.6	39.5	0.49
1:5.1	11.7	59.3	0.58
0:1	0.0	133.3	

*3 Synergy Index = $C_a / CA + C_b / CB$

Ca: Concentration of biocide A required to achieve a 99.999% bacterial kill when used in combination with Biocide B

CA: Concentration of biocide A required to achieve a 99.999% bacterial kill when used alone

Cb: Concentration of biocide B required to achieve a 99.999% bacterial kill when used in combination with Biocide A

CB: Concentration of biocide B required to achieve a 99.999% bacterial kill when used alone

A Synergy Index less than 1 indicates synergy.

[0012] The data above show that the THPS and HHT combination was synergistic for a high temperature and sulfide-rich environment.

Claims

1. A synergistic antimicrobial composition comprising: (a) a hydroxymethyl-substituted phosphorus compound selected from the group consisting of tetrakis(hydroxymethyl)phosphonium salts and tris(hydroxymethyl)phosphine; and (b) hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine; wherein a weight ratio of the hydroxymethyl-substituted phosphorus compound to hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazine is from 15:1 to 1:15.
2. The composition of claim 1 in which the weight ratio is from 12:1 to 1:12.

Patentansprüche

1. Eine synergistische antimikrobielle Zusammensetzung, die Folgendes beinhaltet: (a) eine Hydroxymethyl-substituierte Phosphorverbindung, ausgewählt aus der Gruppe, bestehend aus Tetrakis(hydroxymethyl)phosphoniumsalzen und Tris(hydroxymethyl)phosphin; und (b) Hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazin; wobei ein Gewichtsverhältnis der Hydroxymethyl-substituierten Phosphorverbindung zu Hexahydro-1,3,5-tris(2-hydroxyethyl)-s-triazin von 15 : 1 bis 1 : 15 beträgt.
2. Zusammensetzung gemäß Anspruch 1, wobei das Gewichtsverhältnis von 12 : 1 bis 1 : 12 beträgt.

Revendications

1. Une composition antimicrobienne synergique comprenant : (a) un composé phosphoré substitué par un hydroxyméthyle sélectionné dans le groupe constitué de sels de tétrakis(hydroxyméthyl)phosphonium et de tris(hydroxyméthyl)phosphine ; et (b) de l'hexahydro-1,3,5-tris(2-hydroxyéthyl)-s-triazine ; dans laquelle un rapport en poids du composé phosphoré substitué par un hydroxyméthyle à l'hexahydro-1,3,5-tris(2-hydroxyéthyl)-s-triazine va de 15/1 à 1/15.

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2. La composition de la revendication 1 dans laquelle le rapport en poids va de 12/1 à 1/12.

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REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US 5385896 A [0002]

Non-patent literature cited in the description

- *US Environmental Agency Reregistration Eligibility Decision (RED) on Grotan (HHT), 27 June 2008*
[0005]