

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(10) International Publication Number
WO 2017/135976 A1

(43) International Publication Date
10 August 2017 (10.08.2017)

- (51) **International Patent Classification:**
A01N 25/30 (2006.01) *A01N 35/02* (2006.01)
- (21) **International Application Number:**
PCT/US2016/019270
- (22) **International Filing Date:**
24 February 2016 (24.02.2016)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
15/016,686 5 February 2016 (05.02.2016) US
- (71) **Applicant:** DOW GLOBAL TECHNOLOGIES LLC
[US/US]; 2040 Dow Center, Midland, MI 48674 (US).
- (72) **Inventor:** YIN, Bei; 400 Arcola Road, RC2162, Collegeville, PA 19426 (US).
- (74) **Agent:** EDWARDS, Tifani; Dow Global Technologies LLC, 2040 Dow Center, Midland, Michigan 48674 (US).
- (81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*



WO 2017/135976 A1

(54) **Title:** MICROBICIDAL COMPOSITION

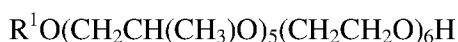
(57) **Abstract:** A synergistic microbicidal composition comprising a non-ionic surfactant and glutaraldehyde and a method for inhibiting the growth of microorganisms in an aqueous medium.

MICROBICIDAL COMPOSITION

This invention relates to microbicidal compositions containing glutaraldehyde and a surfactant.

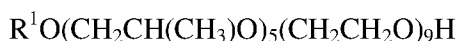
5 A composition containing 5-chloro-2-methylisothiazolin-3-one, 2-methylisothiazolin-3-one and a nonionic dispersant is disclosed in U.S. Patent No. 4,295,932. The composition contains a 3:1 mixture of 5-chloro-2-methylisothiazolin-3-one and 2-methylisothiazolin-3-one, and a copolymer of ethylene oxide and propylene oxide. However, there is a need for combinations of microbicides having synergistic activity against various strains of
10 microorganisms to provide effective control of the microorganisms. Moreover, there is a need for such combinations containing lower levels of individual microbicides for environmental and economic benefit. The problem addressed by this invention is to provide such synergistic combinations of microbicides.

The present invention is directed to a synergistic microbicidal composition
15 comprising: (a) a nonionic surfactant with structure:



where R^1 is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:1.

The present invention is further directed to a synergistic microbicidal composition
20 comprising: (a) a nonionic surfactant with structure:



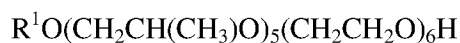
where R^1 is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:4.

The present invention is further directed to methods for controlling the growth of
25 microorganisms in aqueous media by adding to an aqueous medium a nonionic surfactant as described herein and glutaraldehyde in the ratios described herein.

As used herein, the following terms have the designated definitions, unless the context clearly indicates otherwise. The term "glutaraldehyde" refers to glutaraldehyde, (1,5-pentanedial) CAS No. 111-30-8. The term "microbicide" refers to a compound capable of
30 inhibiting the growth of or controlling the growth of microorganisms; microbicides include bactericides, fungicides, viricides, archaeacides and algacides. The term "microorganism" includes, for example, fungi (such as yeast and mold), bacteria, virus, archaea 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

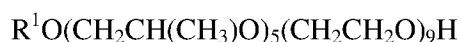
degrees centigrade (°C), references to percentages are percentages by weight (wt%) and amounts and ratios are on an active ingredient basis, i.e., total weight of glutaraldehyde and the nonionic surfactant. Numbers of polymerized units of propylene oxide or ethylene oxide are number averages.

5 The synergistic microbicidal composition of the present invention comprises a) a nonionic surfactant with structure:



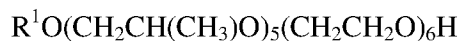
where R¹ is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:1.

10 The invention further comprises: a) a nonionic surfactant with structure:



where R¹ is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:4, alternatively 7.6:1 to 1:3.4.

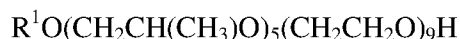
15 The present invention is further directed to a method for inhibiting the growth of bacteria, preferably anaerobic sulfate-reducing bacteria, in an aqueous medium by adding: (a) a nonionic surfactant with structure:



where R¹ is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:1

20

The present invention is further directed to a method for inhibiting the growth of bacteria, preferably anaerobic sulfate-reducing bacteria, in an aqueous medium by adding: a) a nonionic surfactant with structure:



25 where R¹ is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:4, alternatively 7.6:1 to 1:3.4.

30 Preferably, each of the compositions is substantially free of microbicides other than the nonionic surfactant and glutaraldehyde, i.e., it has less than 1 wt% of microbicides other than the nonionic surfactant and glutaraldehyde based on total weight of active ingredients, preferably less than 0.5 wt%, preferably less than 0.2 wt%, preferably less than 0.1 wt%. Preferably, when the nonionic surfactant and glutaraldehyde are added to an aqueous medium, the medium is substantially free of other microbicides, i.e., it has less than 1 wt% of microbicides other than the nonionic surfactant and glutaraldehyde based on total weight of

active ingredients, preferably less than 0.5 wt%, preferably less than 0.2 wt%, preferably less than 0.1 wt%.

The compositions of this invention may contain other ingredients, e.g., defoamers and emulsifiers. The microbicidal compositions of the present invention can be used to inhibit
5 the growth of microorganisms or higher forms of aquatic life (such as protozoans, invertebrates, bryozoans, dinoflagellates, crustaceans, mollusks, etc) by introducing a microbicidally effective amount of the compositions into an aqueous medium subject to microbial attack. Suitable aqueous media are found in, for example: petroleum processing fluids; fuel; oil and gas field functional fluids, such as injection fluids, hydraulic fracturing
10 fluids, produced fluids, drilling mud, completion and workover fluids; oil and gas pipelines, separation, refining, transportation, and storage system; industrial process water; electrocoat deposition systems; cooling towers; air washers; gas scrubbers; mineral slurries; wastewater treatment; ornamental fountains; reverse osmosis filtration; ultrafiltration; ballast water; evaporative condensers; heat exchangers; pulp and paper processing fluids and additives;
15 starch; plastics; emulsions; dispersions; paints; latices; coatings, such as varnishes; construction products, such as mastics, caulks, and sealants; construction adhesives, such as ceramic adhesives, carpet backing adhesives, and laminating adhesives; industrial or consumer adhesives; photographic chemicals; printing fluids; household products, such as bathroom and kitchen cleaners; cosmetics; toiletries; shampoos; soaps; personal care products
20 such as wipes, lotions, sunscreen, conditioners, creams, and other leave-on applications; detergents; industrial cleaners; floor polishes; laundry rinse water; metalworking fluids; conveyor lubricants; hydraulic fluids; leather and leather products; textiles; textile products; wood and wood products, such as plywood, chipboard, flakeboard, laminated beams, oriented strandboard, hardboard, and particleboard; agriculture adjuvant preservation; surfactant
25 preservation; medical devices; diagnostic reagent preservation; food preservation, such as plastic or paper food wrap; food, beverage, and industrial process pasteurizers; toilet bowls; recreational water; pools; and spas.

The specific amount of the microbicidal compositions of this invention necessary to inhibit or control the growth of microorganisms in an application will vary. Typically, the
30 amount of the composition of the present invention is sufficient to control the growth of microorganisms if it provides from 1 to 5000 ppm (parts per million) active ingredients of the composition. It is preferred that the active ingredients (i.e., nonionic surfactant and glutaraldehyde) of the composition be present in the medium to be treated in an amount of at least 10 ppm, preferably at least 100 ppm, preferably at least 200 ppm. It is preferred that the

active ingredients of the composition be present in the locus in an amount of no more than 5000 ppm, preferably no more than 2000 ppm, preferably no more than 1000 ppm, preferably no more than 500 ppm, preferably no more than 300 ppm, preferably no more than 200 ppm. In a method of this invention, a composition is treated to control microbial growth by adding,
5 together or separately, the nonionic surfactant and glutaraldehyde, in amounts that would produce the concentrations indicated above.

EXAMPLE

Surfactants and biocides were evaluated for synergy by determining the synergy index
10 (S.I.) of the combination. Synergy index was calculated based on the concentration required to achieve a certain level of bacterial kill when the two antimicrobial compounds (A and B) alone and in combinations. The test organism was anaerobic sulfate-reducing bacteria
Desulfovibrio longus ATCC #51456.

Surf. A $R^1O(CH_2CH(CH_3)O)_5(CH_2CH_2O)_6H$

15 **Surf. B** $R^1O(CH_2CH(CH_3)O)_5(CH_2CH_2O)_9H$

where R^1 is 2-ethylhexyl.

Example: Synergistic effect of glutaraldehyde and Surf A and B against anaerobic sulfate-reducing bacteria

20 Inside an anaerobic chamber (Bactron anaerobic chamber), a deoxygenated sterile salt solution (3.1183 g of NaCl, 1.3082 mg of $NaHCO_3$, 47.70 mg of KCl, 72.00 mg of $CaCl_2$, 54.49 mg of $MgSO_4$, 172.28 mg of Na_2SO_4 , 43.92 mg of Na_2CO_3 in 1 L water) was inoculated with *Desulfovibrio longus* ATCC 51456 to a final bacterial concentration of 10^6 to 10^7 CFU/mL. Aliquots of this cell suspension were then treated with glutaraldehyde, and
25 each of Surf A and B at selected active concentrations. After incubation at 35°C for 2 hours, viable bacteria in the aliquots were enumerated using serial dilution method. Synergistic combinations and their biocidal efficacy as well as Synergy Index were summarized in Table 1 and Table 2.

The test results for demonstration of synergy of the combinations are shown in the
30 tables below. Each table shows the results for combinations of two components against the microorganisms tested with incubation times; the end-point activity in ppm measured by the level of kill for compound A alone (CA), for component B alone (CB), and the mixture (Ca) and (Cb); the calculated SI value; and the range of synergistic ratios for each combination tested. SI is calculated as follows:

$$Ca/CA + Cb/CB = \text{Synergy Index ("SI")}$$

Wherein:

Ca = Concentration of biocide A required to achieve a certain level of bacterial kill when used in combination with B

5 CA = Concentration of biocide A required to achieve a certain level of bacterial kill when used alone

Cb = Concentration of biocide B required to achieve a certain level of bacterial kill when used in combination with A

10 CB = Concentration of biocide B required to achieve a certain level of bacterial kill when used alone

When the sum of Ca/CA and Cb/CB is greater than one, antagonism is indicated. When the sum is equal to one, additivity is indicated, and when less than one, synergism is demonstrated.

15

Table 1. Biocidal efficacy of glutaraldehyde (Glut) and Surf. A against anaerobic sulfate-reducing bacteria, and Synergy Index

Active weight ratio of Glut:Surf. A	Concentration (active ppm) for complete bacterial kill in 2 hours		Synergy Index
	Glut	Surf. A	
1:0	13.2	0.0	
8:1	8.8	1.1	0.68
6.7:1	5.9	0.9	0.45
5:1	5.9	1.2	0.46
3:1	3.9	1.3	0.31
1:1	3.9	3.9	0.34
0:1	0.0	>100	

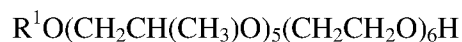
20

Table 2. Biocidal efficacy of glutaraldehyde (Glut) and Surf. B against anaerobic sulfate-reducing bacteria, and Synergy Index

Active weight ratio of Glut:Surf. B	Concentration (active ppm) for 99.99% bacterial kill in 2 hours		Synergy Index
	Glut	Surf B	
1:0	5.9	0.0	
7.6:1	3.9	0.5	0.67
3.4:1	3.9	1.2	0.67
1:1	3.9	3.9	0.70
1:3.4	3.9	13.2	0.79
0:1	0.0	>100	

CLAIMS

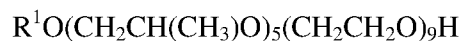
1. A synergistic microbicidal composition comprising: (a) a nonionic surfactant with structure:



where R^1 is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:1.

2. A method for controlling the growth of microorganisms in an aqueous medium; the method comprising adding to the aqueous medium the synergistic microbicidal composition of claim 1.

3. A synergistic microbicidal composition comprising: (a) a nonionic surfactant with structure:



where R^1 is 2-ethylhexyl; and (b) glutaraldehyde; wherein a weight ratio of the glutaraldehyde to nonionic surfactant is from 8:1 to 1:4

4. A method for controlling the growth of microorganisms in an aqueous medium; the method comprising adding to the aqueous medium the synergistic microbicidal composition of claim 3.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/19270

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A01N 25/30, 35/02 (2016.01) CPC - A01N 25/30, 35/02; A61L 2/18 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) IPC(8): A01N 25/30, 35/02; A01P 1/00; A61L 2/18 (2016.01) CPC: A01N 25/30, 35/02; A61L 2/18 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) PatSeer; Google Scholar; Pubmed; EBSCO; Dow Global Technologies, Yin, glutaraldehyde, 2-ethylhexyl, synergistic, microbicial, antimicrobial, disinfectant, pesticide, pentaisopropoxy, hexaethoxy, hexaethyleneglycol, glycol, ethylhexyl, polypropylene glycol, polyethylene glycol, glutaraldehyde, PPG, PEG, Polypropylene oxide, polyethylene oxide, oligomer, copolymer, pentapropylene		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2014/046990 A1 (DOW GLOBAL TECHNOLOGIES LLC) 27 March 2014; abstract; page 2, line 10; page 4, lines 5-20; page 16, lines 30-35; page 17, lines 1-15	1-4
Y	EP 1 138 203 B1 (BODE CHEMIE GMBH AND CO) 28 September 2005; English translation; claims 1, 5	1-4
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> Sec patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 11 April 2016 (11.04.2016)		Date of mailing of the international search report 03 MAY 2016
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300		Authorized officer Shane Thomas PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774