



167167

12 JAN 2005

- 1 -

**TITLE: ALKYL POLYGLUCOSIDES CONTAINING DISINFECTANT
COMPOSITIONS ACTIVE AGAINST PSEUDOMONAS MICROORGANISM**

TECHNICAL FIELD

5 This invention relates to a disinfectant cleansing composition.

BACKGROUND ART

 It is known that infection is spread via skin contact through the transmission of pathogenic microorganisms. Hitherto, in order to reduce the presence of such organisms it has been known to scrub the skin with a solution containing a surfactant
10 followed by application of an antiseptic.

 In recent years it has been suggested that it would be desirable to combine the washing and disinfectant actions in a single operation by providing a composition comprising both an antimicrobial agent and a surfactant. It has been found however that many antimicrobial agents such as chlorhexidine [N,N'-bis(4-chlorophenyl)- 3,12-
15 diimino 2,4,11,13-tetraazatetradecanediimidamide] digluconate and other chlorhexidine salts are incompatible with anionic surfactants, and are reduced in their antimicrobial activity by nonionic surfactants, thus requiring addition of more antimicrobial agent in order to retain sufficient biocidal activity at the amount of surfactant required for satisfactory foam formation.

20 In particular, US 3,855,140 assigned to Imperial Chemical Industries describes a skin cleansing composition comprising a soluble salt of chlorhexidine in combination with a polyoxyethylenepolyoxypropylene block copolymer. In order to obtain sufficient sudsing of the polymer it is necessary to use high proportions of the surfactant in amounts of the order of 20-25%. High amounts of chlorhexidine are
25 consequently required to maintain the desired antimicrobial activity. Such high amounts are undesirable as it is known that surfactants may affect the skin adversely by defatting, and causing in combination with biocides such as chlorhexidine, irritation to the skin. Further the ingredients of the composition can be costly.



000001

It would be desirable therefore to provide a composition in which the amount of antimicrobial agent and surfactant is reduced whilst maintaining sufficient antimicrobial activity and sudsing ability.

In this regard, in order to provide such a composition, WO 95/09605 teaches one to combine a phenolic disinfectant with an alkylpolyglucoside surfactant. As indicated in that patent however, such compositions although showing good biocidal activity against most microorganisms, are incapable of disinfecting surfaces contaminated by the microorganism *Pseudomonas aeruginosa* to which the compositions are inactive.

It is an object of the invention to substantially ameliorate the disadvantages of the prior art.

DESCRIPTION OF THE INVENTION

According to a first aspect of the invention, there is provided an antiseptic cleansing composition comprising an antimicrobial agent, an effective amount of an alkylpolysaccharide surfactant, at least one alkyl alcohol and at least one aryl alcohol.

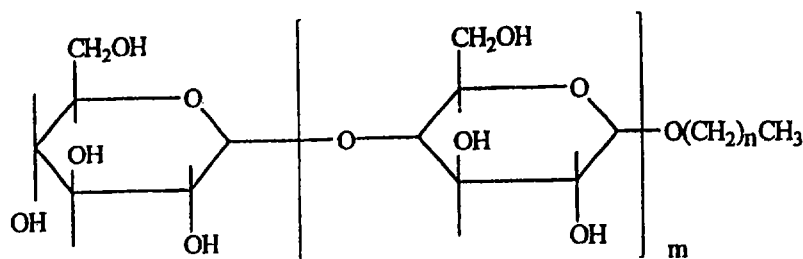
According to a second aspect of the invention there is provided a method of decontaminating surfaces contaminated with bacteria including the *Pseudomonas* microorganism, which method comprises contacting the surface with the disinfectant cleansing composition of the first aspect.

Typically the cleansing composition comprises an inert carrier, and optionally other additives.

The alkylpolysaccharide surfactants are also known in the art as alkylpolyglucosides, however, for the purposes of the following discussion, the surfactant will be termed an alkylpolysaccharide.

Preferably, the content of the surfactant present in the composition does not exceed 6% w/v.

Preferably the alkylpolysaccharide is an alkylpolysaccharide of the formula:



wherein n is an integer between 5 and 19, and

m is an integer between 1 and 3.

In the above formula the surfactant alkyl polysaccharide shown contains
 5 glucose units, however the invention is not limited thereto and other sugar units can be substituted for one or more of the glucose units. Other sugar units which might be included in the alkylpolysaccharide include maltose, arabinose, xylose, mannose, galactose, gulose, idose, talose, allose, altrose, sucrose, fructose, sorbose, levulose, lactose, allulose, tagatose, alloheptulose, sedoheptulose, glucoheptulose,
 10 mannoheptulose, guloheptulose, idoheptulose, galactoheptulose, taloheptulose and derivatives thereof.

Suitable antimicrobial agents include chlorhexidine and its salts; dichlorophene, other chlorophenol derivatives such as p-chloro-m-xyleneol, chlorophene and o-phenylphenol, 2,4,4-trichloro-2-hydroxy-diphenylether (triclosan);
 15 octenidindihydrochloride ($\text{CH}_3 - (\text{CH}_2)_7 - \text{NHON} - (\text{CH}_2)_{10} - \text{NO} - \text{NH}(\text{CH}_2)_7 - \text{CH}_2$) or any other salt thereof and quaternary ammonium compounds.

Suitable salts of chlorhexidine include the gluconate, isethionate, formate, acetate, glutamate, succinamate, monodiglycolate, dimethanesulfonate, lactate, diisobutyrate or the glucoheptonate salts.

20 Preferably the antimicrobial agent has a water solubility of at least 0.001% w/v at ambient temperature.

When the antimicrobial agent is chlorhexidine digluconate it is used in an amount preferably not exceeding 4.5% w/v. When the antimicrobial agent is 2,4,4-trichloro-2-hydroxydiphenylether (triclosan) it is used in an amount preferably not
 25 exceeding 3% w/v.

The alkyl alcohol is preferably a lower alkyl alcohol (herein defined as an alcohol having less than 6 carbon atoms) such as ethanol, iso or n-propanol, most preferably the alkyl alcohol is isopropanol or n-propanol. The alcohol content preferably does not exceed 70% w/v. When the composition is in an aqueous carrier (for example for use in hand washing) the alcohol is desirably iso or n-propanol or a combination thereof and is preferably present in an amount of from 3 to 10% w/v, most preferably 4 to 8% w/v. When the composition is an alcoholic solution (for example for a rapid cleaning self-drying solution) the alkyl alcohol will be preferably be 55-75% w/v.

10 The aryl alcohol is preferably a benzylalcohol, phenylethylalcohol, phenoxyethanol, phenoxypropanol or a chlorinated derivative thereof. For application to skin, phenoxyethanol and phenoxypropanol are preferred. Preferably the aryl alcohol is present in an amount not exceeding 3% w/v.

An inert carrier can be used - for example water or a lower alcohol such as
15 ethanol.

The composition may further comprise one or more of the following integers:

- (a) a solubilising agent for example propylene glycol, a hydrotrope or mixtures thereof. Suitable hydrotropes include urea, cumene sulphonate, toluene sulfonate, xylenesulphonate and the ethanolamine salts of citric and other
20 hydroxycarboxylic acids.
- (b) a foaming agent such as an alkylaminooxide, alkylmono or diethanolamides. Examples of foaming agents are lauryl or cocodiethanolamide or monoethanolamide condensates or the lauryl or cetyl dimethylamineoxides.
- (c) viscosity modifiers such as cellulose derivatives, guar resins and
25 carbopol resins.
- (d) preservatives such as imidazolidinyl, urea derivatives (Germabenes), methyl or propyl parabens (p-hydroxy benzoic esters).
- (e) other conventional additives such as colouring agents, fragrances, antioxidants, emollients, moisturisers, stabilising agents and thickeners such as
30 carboxymethylcellulose.

(f) optionally, additional surfactants including amphoteric surfactants, anionic surfactants and nonionic surfactants. Suitable additional surfactants include quaternary ammonium compounds or a small amount of a high foaming anionic surfactant such as laurylethoxysulfonate, sarcosinates, sodium laurylethersulphate.

- 5 The additional ingredients are selected to avoid possible incompatibility with any of the other ingredients of the composition and especially with regard to the antimicrobial agents.

The pH of the composition is typically adjusted to pH 5 to 7, most preferably 5.5 but is not limited to this pH. When chlorhexidine is used as the antimicrobial
10 agent, a pH greater than 8 should be avoided to prevent precipitation of the chlorhexidine free base. Most organic acids compatible with the composition, such as lactic, acetic, citric and gluconic acids, preferably gluconic acid, can be used to adjust the pH.

The term "comprising" as herein used is used in an inclusive sense, that is to say in the sense of "including" or "containing". The term is not intended in an
15 exclusive sense ("consisting of" or "composed of").

BEST MODES FOR CARRYING OUT THE INVENTION

The following examples illustrate preferred embodiments of the present invention. They should not be construed as limiting.

- 20 It will also be understood by those skilled in the art that while the present invention is described herein with reference to a concentrate, such a concentrate could be diluted prior to sale (for example to 55%) or use.

EXAMPLES

25 Example I - Comparative composition in accordance with WO 95/09605

	Sodium laurylsulfate (100%)	4.67% w/v
	Alkylpolysaccharide (100%)	3.92% w/v
	Coconut Betaine (100%)	0.90% w/v
	Triclosan	0.49% w/v
30	Propylene glycol	0.254% w/v
	Glycerine	0.254% w/v

12 JAN 2005

- 6 -

Sodium chloride	0.49% w/v
Citric acid	up to 10% w/v
Water	to 100% by volume

5

**Example II - Comparative Commercial Antibacterial Skin Cleanser
Containing 2.0% (Triclosan) Full Composition Unknown**

**Example III - Comparative Composition of Commercial Antiseptic Surgical
Scrub**

10

Chlorhexidine Gluconate (CHG)	4.0% w/v
Nonionic Surfactant* (100%)	25.00% w/v
Lauryl Dimethylamineoxide (100%)	2.60% w/v
Water	to 100.0% by volume

15

(formula as per published data (Manuf. Chemist, October 1973, p. 25-27 and disclosed in US Patent 3 855 140)

*polyoxyethylene/polyoxypropylene block copolymer PLURONIC F87
(BASF, Germany).

20

Example IV - Inventive Composition containing Triclosan

Same composition as Example 1 to which n-propanol 5.0% w/v and phenoxyethanol 1% w/v have been added.

25

Example V - Inventive Composition containing Triclosan

Same composition as Example 1 to which 5.0% w/v n-propanol and 1% w/v phenoxyethanol have been added and the triclosan increased to 1% w/v.

Example VI - Inventive Composition Containing Chlorhexidine**Gluconate**

5	Chlorhexidine Gluconate (CHG)	2.0% w/v
	Alkylpolysaccharide* (100%)	4.00% w/v
	Cocodiethanolamide (100%)	2.00% w/v
	Propylene Glycol	2.0% w/v
	Isopropanol	8.0% w/v
10	Phenoxyethanol	2.0% w/v
	Water	to 100% by volume
	*Oramix TM NS10 55% w/v (Sepic SA, France).	

Example VII - Inventive Compositions Containing Chlorhexidine**Gluconate**

	Chlorhexidine gluconate (CHG)	1.0% w/v
	Alkylpolysaccharide* (100%)	4.00% w/v
	Cocodiethanolamide (100%)	0.80% w/v
20	Propylene glycol	2.0% w/v
	n-propanol	6.0% w/v
	Phenoxypropanol	1.0% w/v
	Water	to 100.0% by volume

* Any commercial alkylpolysaccharide can be used such as PlantarenTM 2000
 25 (Henkel) or AtlasTM G73500 (ICI).

12 JAN 2005

- 8 -

Example VIII - Inventive Composition Containing Triclosan

	Triclosan	1.0% w/v
5	Alkylpolysaccharide* (100%)	4.00% w/v
	Sodium 2 laurylethersulfate (100%)	0.20% w/v
	Cocodiethanolamide (100%)	2.00% w/v
	Isopropanol	8.0% w/v
	Propylene Glycol	10.0% w/v
10	Preservative**	1.0% w/v
	Phenoxyethanol	2.0% w/v
	Water	to 100.0% by volume
	*Oramix TM NS12 (Sepic SA, France)	
	**Germabene TM II 0.2% w/v	

15

Example IX - Inventive Composition Containing Triclosan

	Triclosan	1.0% w/v
	Alkyl polysaccharide* (100%)	4.00% w/v
20	Sodium 2 laurylethersulphate (100%)	0.25% w/v
	Sodium cumene sulfate (100%)	4.00% w/v
	Ethyl alcohol	4.0% w/v
	n-propanol	4.0% w/v
	Phenoxyethanol	1.5% w/v
25	Water	to 100% by volume

*Any commercial alkylpolysaccharide can be used such as PlantarenTM 2000 (Henkel) or AtlasTM G73500 (ICI).

12 JAN 2005

Example X - Inventive Composition Containing Triclosan

	Triclosan	1.00% w/v
5	Alkylpolysaccharide (100%)	2.75% w/v
	Cocodiethanolamide (100%)	0.80% w/v
	Sodium xylene sulphonate (100%)	4.00% w/v
	Isopropanol	8.0% w/v
	Propylene glycol	2.0% w/v
10	Phenoxyethanol	1.0% w/v
	Carboxymethyl cellulose	0.6% w/v
	Phenoxypropanol	1.0% w/v
	Water	to 100.0 by volume %

15 **Example XI - Inventive Composition Containing Dichlorophene**

	Dichlorophene	1.5% w/v
	Alkylpolysaccharide (100%)	4.00% w/v
	Sodium 2 laurylethersulfate (100%)	0.20% w/v
20	Cocodiethanolamide (100%)	2.00% w/v
	Isopropanol	5.0% w/v
	Phenoxyethanol	1.0% w/v
	Water	to make 100.0% by volume

Example XII - Inventive Composition Containing Dichlorophene

Dichlorophene	1.5% w/v
Alkylpolysaccharide (100%)	4.00% w/v
Sodium 2 laurylethersulphate (100%)	0.50% w/v
Cocodiethanolamide (100%)	1.00% w/v
Ethanol	5.0% w/v
Phenoxyethanol	1.0% w/v
Water	to make 100.0% by volume

adjust pH to 7.0 - 7.2 with triethanolamine.

Suspension tests were performed (in accordance with European Standard CEN/TC216/WG IN) in the presence of a number of organisms. The results are shown in the following table:

TABLE I - SUSPENSION TESTS

RESULTS EXPRESSED AS: log reduction

Test temperature: 23°C; Contact time: 60 seconds

Neutralising Medium: Tween80 100 g/L, Lecithin 50 g/L, Histidine 1 g/L

TEST ORGANISM	E. coli NCTC 8196	S. aureus NCTC 4163	P. aeruginosa NCTC 6749	S. faecalis NCTC 775
Concentration	Neat	Neat	Neat	Neat
Contact Time (secs)	60	60	60	60
Formulations:				
Comparative Example I 0.49% w/v Triclosan	NG	NG	>2	>2
Inventive Example IV 0.49% w/v Triclosan	NG	NG	NG	NG
Comparative Example II 2% w/v Triclosan	>2	>2	>2	>2
Inventive Example V 1.0% w/v Triclosan	NG	NG	NG	NG
Comparative Example III 2% w/v CHG	NG	3.8	NG	3.9
Inventive Example VI 2.0% w/v CHG	NG	NG	NG	NG
Inoculum Level	2.5×10^8	2.8×10^8	1.3×10^8	1.8×10^8

NG: Means NO GROWTH

Suspension tests were also conducted for the composition of Example X (1.0% w/v Triclosan). The results were as follows:

Microbicidal Results

5 Suspension test - 30 sec contact/con. 75%
Expressed as a Log reduction of microorganisms.

	<u>Microorganism</u>	<u>Inoculum level</u>	<u>Reduction</u>
	S. aureus ATTC 6538	Log 6.8	> 5.8
10	E. coli ATTC 11229	Log 6.9	> 5.9
	PS aeruginosa ATTC 15442	Log 7.0	> 6.0
	P. mirabilia ATTC 14153	Log 6.8	> 6.0

Compositions according to the invention have the same or greater
15 effectiveness with respect to biocidal activity and are less toxic, at much lower concentrations of the antimicrobial agent in comparison with conventional prior art compositions.

In preferred embodiments, the use of an alkylpolysaccharide surfactant in amounts below 6% (w/v), the amount of triclosan can be successfully reduced from
20 1.0% to 0.5% (w/v) with substantially no loss in biocidal activity. Surprisingly the amount of chlorhexidine can be reduced 4% to 2% (w/v) whilst maintaining good biocidal activity and foaming properties.

Further, by use of alkylpolysaccharides in amounts as low as 2% it is possible to obtain sufficient foaming skin cleansing properties not obtainable with other
25 conventional surfactants. Further, the known interference with the antimicrobial properties of biocides with surfactants is considerably reduced.

Further, by the inclusion of an alkyl and aryl alcohol combination, the compositions of the invention are effective against the pseudomonas microorganism.

The invention is a significant and important improvement on the art as taught
30 in US 3,855,140 as illustrated by the fact that, while the composition of US Patent 3,855,140 showed no activity against Pseudomonas, the compositions of the present

12 JAN 2005

- 12 -

invention are effective against *Pseudomonas* at concentrations containing as low as 0.49% triclosan.

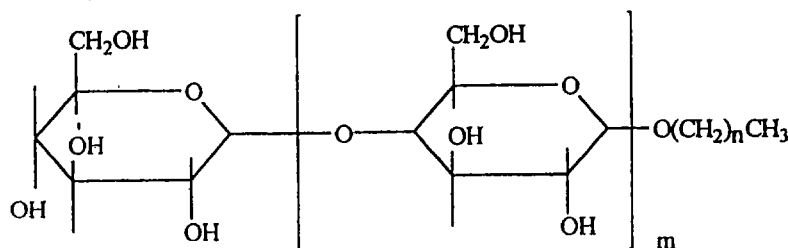
Compositions according to the invention are especially suitable for skin and hand disinfection, surface disinfection, impregnation of sponges, woven and non-
5 woven textiles and the like.

The composition of the invention is suitable for cleansing any object. The composition of the invention is particularly suitable for cleansing hands in clinical situations and before surgery but can also be used for cleansing inanimate objects such as surgical instruments.

12 JAN 2005

THE CLAIMS OF THE INVENTION ARE AS FOLLOWS

1. An antiseptic cleansing composition effective against *Pseudomonas* comprising an antimicrobial agent, an effective amount of an alkylpolysaccharide surfactant, at least one alkyl alcohol and at least one aryl alcohol.
- 5 2. A cleansing composition according to claim 1 further comprising an inert carrier.
3. A composition according to claim 1 or claim 2 wherein the content of the surfactant present in the composition does not exceed 6%.
4. A composition according to any one of the preceding claims wherein the
- 10 alkylpolysaccharide is an alkylpolysaccharide of the formula:



wherein n is an integer between 5 and 19, and

m is an integer between 1 and 3.

5. A composition according to any one of claims 1 to 3 wherein the surfactant
- 15 alkyl polysaccharide contains one or more sugar units selected from the group consisting of maltose, arabinose, xylose, mannose, galactose, gulose, idose, talose, allose, altrose, sucrose, fructose, sorbose, levulose, lactose, allulose, tagatose, alloheptulose, sedoheptulose, glucoheptulose, mannoheptulose, guloheptulose, idoheptulose, galactoheptulose, taloheptulose and derivatives thereof.
- 20 6. A composition according to any one of the preceding claims wherein the antimicrobial agent is selected from the group consisting of chlorhexidine, chlorhexidine salt, chlorophenol derivative, octenidindihydrochloride $(\text{CH}_3 - (\text{CH}_2)_7 - \text{NHON} - (\text{CH}_2)_{10} - \text{NO} - \text{NH}(\text{CH}_2)_7 - \text{CH}_2)$ or any other salt thereof, and quaternary ammonium compounds.
- 25 7. A composition according to claim 6 wherein the salt of chlorhexidine is selected from the group consisting of gluconate, isethionate, formate, acetate,

glutamate, succinamate, monodiglycolate, dimethanesulfonate, lactate, diisobutyrate or the glucoheptonate salts.

8. A composition according to any one of claims 1 to 7 wherein the antimicrobial agent is chlorhexidine digluconate.
- 5 9. A composition according to claim 8 wherein the chlorhexidine does not exceed 4.5% w/v.
10. A composition according to claim 6 wherein the chlorophenol derivative is selected from the group consisting of dichlorophene, p-chloro-m-xyleneol, chlorophene, o-phenylphenol, and 2,4,4-trichloro-2-hydroxy-diphenylether.
- 10 11. A composition according to claim 10 wherein the antimicrobial agent is 2,4,4-trichloro-2-hydroxydiphenylether.
12. A composition according to claim 11 wherein the 2,4,4-trichloro-2-hydroxydiphenylether does not exceed 3% w/v.
13. A composition according to any one of the preceding claims wherein the
15 antimicrobial agent has a water solubility of at least 0.001% w/v at ambient temperature.
14. A composition according to any one of the preceding claims wherein the alkyl alcohol is a lower alkyl alcohol.
15. A composition according to claim 14 wherein the lower alkyl alcohol is
20 ethanol, isopropanol or n-propanol.
16. A composition according to claim 15 wherein the lower alkyl alcohol is isopropanol or n-propanol or a combination thereof.
17. A composition according to any one of the preceding claims wherein the alcohol content does not exceed 70% w/v.
- 25 18. A composition according to any one of the preceding claims wherein the alcohol content is between 55-70% w/v.
19. A composition according to claim 17 wherein the alcohol is present in an amount of from 3 to 10% w/v.
20. A composition according to claim 19 wherein the alcohol is present in an
30 amount of from 4 to 8% w/v.

21. A composition according to any one of the preceding claims wherein the aryl alcohol is selected from the group consisting of a benzylalcohol, a phenylethylalcohol, a phenoxyethanol, a phenoxypropanol or a chlorinated derivative thereof.
22. A composition according to claim 21 wherein the aryl alcohol is selected
5 from the group consisting of phenoxyethanol and phenoxypropanol.
23. A composition according to any one of the preceding claims wherein the aryl alcohol does not exceed 3% w/v.
24. A composition according to any one of the preceding claims further including an inert carrier.
- 10 25. A composition according to claim 24 wherein the inert carrier is water
26. A composition according to claim 24 wherein the inert carrier is a lower alcohol.
27. A composition according to claim 26 wherein the inert carrier is a ethanol.
28. A composition according to any one of the preceding claims further including
15 one or more of the integers selected from the group consisting of
- (a) a solubilising agent
 - (b) a foaming agent
 - (c) one or more viscosity modifiers
 - (d) preservatives
 - 20 (e) other conventional additives
 - (f) additional surfactants
29. A composition according to claim 28 wherein the solubilising agent is propylene glycol, a hydrotrope or mixtures thereof.
30. A composition according to claim 29 wherein the hydrotrope is selected from
25 the group consisting of urea, cumenesulfonate, toluenesulfonate, xylenesulphonate and the ethanolamine salts of citric and other hydroxycarboxylic acids.
31. A composition according to any one of claims 28 to 30 wherein the foaming agent is an alkylaminooxide, alkylmono or diethanolamide.
32. A composition according to claim 31 wherein the foaming agent is selected
30 from the group consisting of lauryl condensates, cocodiethanolamide condensates,

12 JAN 2005

monoethanolamide condensates, lauryl dimethylamine oxides and cetyl dimethylamine oxides.

33. A composition according to any one of claims 28 to 32 wherein the viscosity modifier is selected from the group consisting of cellulose derivatives, guar resins and carbopol resins.
34. A composition according to any one of claims 28 to 33 wherein the preservative is selected from the group consisting of imidazolidinyl derivatives, urea derivatives (Germabenes), methyl parabens (p-hydroxy benzoic esters) or propyl parabens (p-hydroxy benzoic esters).
35. A composition according to any one of claims 28 to 34 wherein the conventional additives are selected from the group consisting of colouring agents, fragrances, antioxidants, emollients, stabilising agents and thickeners
36. A composition according to claim 35 wherein the thickener is carboxymethylcellulose.
37. A composition according to any one of claims 28 to 36 wherein the additional surfactant is selected from the group consisting of amphoteric surfactants, anionic surfactants and ionic surfactants.
38. A composition according to claim 37 wherein the additional surfactants include a quaternary ammonium compound or a high foaming anionic surfactant.
39. A composition according to claim 38 wherein high foaming anionic surfactant is selected from the group consisting of laurylethoxysulfonate, a sarcosinate and sodium 2 laurylethersulphate.
40. A composition according to any one of claims 28 to 39 wherein additional ingredients are selected to avoid possible incompatibility with any of the other ingredients of the composition and especially with regard to the antimicrobial agent.
41. A composition according to any one of the preceding claims wherein the pH is 8 or less.
42. A composition according to any one of the preceding claims wherein the pH is in the range 5 to 7.
43. A composition according to claim 40 wherein the pH is 5.5

44. A composition according to any one of claims 1 to 40 wherein the pH is controlled to avoid precipitation of ingredients.
45. A composition according to any one of the preceding claims wherein the pH is adjusted by an organic acid.
- 5 46. A composition according to claim 45 wherein organic acid is selected from the group consisting of lactic acid, acetic acid, citric acid and gluconic acid.
47. A composition according to claim 46 wherein the organic acid is gluconic acid.
48. A method of decontaminating surfaces contaminated with bacteria including the pseudomonas microorganism, which method comprises contacting the surface with a disinfectant
10 cleansing composition according to any one of the preceding claims.
49. A disinfectant cleansing composition substantially as herein described with reference to any one of the examples.
50. A method of decontaminating surfaces substantially as herein described with reference to any one of the examples.
- 15 51. An antiseptic composition effective for cleansing and disinfecting a surface and effective against pseudomonas comprising an antimicrobial agent, at least 2% w/v of an alkyl polysaccharide surfactant, at least one alkyl alcohol, at least one aryl alcohol and wherein the total weight of said alkyl and aryl alcohols exceeds 55% w/v of the composition.