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(54) **Disinfectant compositions having residual biocidal activity, and wipes and sprays containing them**

(57) Disinfectant compositions having residual biocidal activity comprise an aqueous solution of from 40 to 95% v/v of a C_1 to C_4 alkanol and at least two antimicrobial agents, the at least two agents having a combined concentration in the solution of up to 2% w/v.

Preferably the alkanol is isopropanol, the first antimicrobial agent is a biguanide compound and the second is a quaternary ammonium compound.

The composition may be impregnated onto a cloth, such as paper or a fabric to form disinfectant wipes or may be used as aerosol sprays.

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SPECIFICATION

Disinfectant compositions having residual biocidal activity

The present invention relates to disinfectant compositions having residual biocidal activity which may be used, for example, in aerosol sprays or impregnated onto cloths to form wipes.

Wipes impregnated with alkanols, such as ethanol or isopropanol, are known. For instance a product sold under the name "Azo-Wipe" comprises a non-woven fabric saturated with isopropyl alcohol. "Azo-Wipe" wipes can be used to wipe hard surfaces but have the disadvantage that their biocidal activity only remains until the alkanol has evaporated. Moreover, the alkanol can cause blood to congeal and thereby make soil removal difficult.

An aerosol spray formulation for feminine hygiene is described in British Patent Specification No. 1,026,831 to Mediline A.G. The formulation contains one or preferably two synthetic bactericides and an emollient in a propellant liquid. The formulation may contain up to 5% of a lower alkanol. The bactericide may be a quaternary ammonium compound, a halogen-phenyl bactericide or a guanide-based bactericide. Preferably a mixture of the first two types are used. The aerosol is not indicated to be of use for disinfecting hard surfaces.

United States Patent Specification No. 4,311,479, assigned to Exterma-Germ Products Ltd., describes a cloth impregnated with an antimicrobial composition. The cloth is activated for use by contact with water. Two compositions described comprise mixture of a quaternary ammonium compound and a polymeric biguanide. These are impregnated onto the cloth as aqueous solutions.

Canadian Patent Specification No. 833,513 granted to Dustlkin Products relates to germicidal paper and describes methods of preparing dry papers having germicidal activity. In use the paper may be used dry as a dust cloth or saturated with water to wipe surfaces. Antibacterial agents used in the dry papers include quaternary ammonium compounds. The Patent does not mention the use of lower alkanols or guanide compounds as antibacterial agents, nor the use of liquid compositions as biocidal agents.

An aerosol spray for disinfecting hard surfaces, containing 0.02% chlorhexidine gluconate in 70% industrial methylated spirit (IMS), is presently on the market. The spray has short-term biocidal activity due to its alcohol content, but the chlorhexidine gluconate has only limited activity against Gram negative organisms, especially Pseudomonas species. It is also inactivated in the presence of organic soil.

According to the present invention, a disinfectant composition comprises an aqueous solution of from 40 to 95% v/v of a C_1 to C_4 alkanol and at least two antimicrobial agents, the at least two agents having a combined concentration in the solution of up to 2% w/v.

The disinfectant composition of the present invention may be used to disinfect and remove soil contaminants from hard surfaces and confer a residual biocidal activity thereon. For example, the compositions in the form of sprays or impregnated wipes may be used for disinfecting or removing soil from hard surfaces, such as operating tables, instruments and machinery in hospitals or surgeries.

The C_1 to C_4 alkanol may be methanol, ethanol, one of the propanols or a mixture of such alkanols, for instance IMS. Preferably the alkanol is isopropanol.

The alkanol preferably comprises 60 to 80% v/v, most preferably about 70% v/v, of the composition. The alkanol is itself a biocidal agent.

The first of the antimicrobial agents is preferably a biguanide compound, for instance 1,1′-hexamethylenebis[5-4-chlorophenyl)biguanide]digluconate, 1,1′-hexamethylene bis [5-(4-chlorophenyl)biguanide]diacetate or 1,1′-hexamethylenebis[5-(4-chlorophenyl)biguanide]dihydrochloride. Most preferably one of the antimicrobial agents is a soluble salt of 1,6-di-(4-chlorophenyl-biguanide)hexane or a polymeric biguanide sold as Vantocil 1B (Registered Trade Mark). Vantocil 1B is manufactured by Imperial Chemical Industries Ltd.

If a biguanide antimicrobial agent is used, it may be possible to reduce the concentration of biguanide antimicrobial agent and other antimicrobial agent(s) in the composition to 1% w/v or less.

Preferably, the second of the antimicrobial agents is a quaternary ammonium compound. Quaternary ammonium compounds which may be used in the composition of the invention include alkyl dimethyl benzyl ammonium halides, dialkyl dimethyl ammonium halides, alkyl trimethyl ammonium halides or mixtures thereof. The alkyl groups conveniently are straight chain and contain from 12 to 18 carbon atoms. The halide is preferably chloride.

Suitable quaternary ammonium compounds include octyl dimethyl benzyl ammonium chloride, octyl decyl dimethyl ammonium chloride, dioctyl dimethyl ammonium chloride, didecyl dimethyl ammonium chloride and dimethyl ethylbenzyl ammonium chloride.

A particularly suitable quaternary ammonium compound is Bardac 205M, manufactured by Lonza of Basle, Switzerland. It is a mixture of alkyl dimethyl benzyl ammonium chlorides and dialkyl dimethyl ammonium chlorides.

Preferably the composition comprises a biguanide agent and a quaternary ammonium compound in an aqueous solution of about 70% isopropanol.

Other antimicrobial agents which may be used in the composition of the present invention include 4-chloro-3,5-xylenol, 2,4,4′-trichloro, 2′-hydroxy-diphenyl ether, 5-brom-5-nitro-1,3-dioxan or

orthophenyl phenol.

The composition may also include a chelating agent, such as ethylenediaminetetra-acetic acid (EDTA), which are known to render some micro-organisms more susceptible to antimicrobial agents.

A surfactant may also be included in the composition to facilitate the cleaning of soiled surfaces. A preferred surfactant is an amphoteric surfactant supplied under the trade name Lexaine C (manufactured by Inoex Chemicals of Philadelphia, U.S.A.). The surfactant should be compatible with all the other components of the mixture.

The compositions of the present invention may also include up to about 0.2% of a fragrance to give the composition a pleasant odour. Suitable fragrances are those supplied by International Flavours and Fragrances Ltd under the designations EAG 5109, EAG 5110, EAG 5198 and EAG 5199.

Preferably the composition is impregnated onto a cloth such as paper or a woven or non-woven fabric to provide a disinfectant wipe. Advantageously the wipe is saturated with the composition.

A particularly suitable cloth for use in providing a wipe is a modified entangled rayon fibre fabric bonded together with a suitable binder. Such fabrics can be obtained from Chicopee Ltd., of New Brunswick, U.S.A.

Alternatively, the composition is mixed with a propellant to provide a formulation suitable for use as an aerosol spray. Conventional propellants and additives, such as mist activators, may be used to provide a sprayable composition. Preferably, the spray can containing the composition is provided with a 360° valve to facilitate cleaning of difficultly-accessible surfaces.

Application of the composition of the present invention to a suitable substrate has an immediate biocidal action on the substrate. The composition has mycobactericidal, fungicidal, virucidal and antibacterial activity. It is effective against both Gram positive and Gram negative bacteria, including Pseudomonas species. Moreover its activity is retained for a considerable time after evaporation of the alkanol. This residual activity is not exhibited by other commercially available compositions.

It is envisaged that the compositions of the present invention, particularly in the form of disinfectant wipes or sprays, will be of use in hospitals and surgeries to clean hard surfaces, such as operating tables and instrument trays, surgical instruments and machinery. The effectiveness of the compositions of the present invention is through to be due to the use of three types of biocidal agent contained therein which provide a broad spectrum of immediate and residual biocidal activity.

Some preferred embodiments in accordance with the present invention will now be described by way of Example.

EXAMPLE 1

The following ingredients were mixed together:

Isopropyl alcohol	700 ml.
Bardac 205M	0.4 g.
Vantocil 1B	25 ml.

The mixture was made up to a volume of 1 l with water.

Vantocil 1B is an aqueous, slightly opalescent, pale yellow liquid containing 20% of a polymeric biguanide hydrochloride. It has a viscosity of 3—5 cp (25°C) and a specific gravity of 1.035 (25°C).

Bardac 205M has the following composition:

Alkyl (C_{14}, 50% C_{12}, 40; C_{16}, 10%) dimethyl benzyl ammonium chloride	20%
Octyl decyl dimethyl ammonium chloride	15%
Dioctyl dimethyl ammonium chloride	7.5%
Didecyl dimethyl ammonium chloride	7.5%
Inerts	50%

The final composition therefore contained 70% v/v isopropyl alcohol, 0.5% w/v active biguanide compound and 0.02% w/v active quaternary ammonium compounds. If desired, up to 0.2% w/v of a fragrance may be added to the composition.

EXAMPLE 2

Disinfectant wipes were prepared by dipping a roll of a non-woven fabric into the composition. The fabric was a modified entangled rayon fibre fabric bonded with 5% of Primal HA8 binder supplied by Chicopee Ltd. of New Brunswick, U.S.A. The impregnated roll was placed in a hermetically-sealed evaporation-resistant container prior to use.

EXAMPLE 3

The composition was also mixed with Arcton 12, a fluorocarbon propellant, in a weight ratio of 70:30, and placed under pressure in an aerosol spray can arranged to produce a fine mist. The aerosol mixture was prepared and placed in a pressurised container using conventional techniques and additives. The container was provided with a 360° valve.

A hard surface was simulated by use of a 6″ × 6″ white ceramic tile. The surface was divided into two equal portions by a line drawn thereon, and both portions were contaminated with bacteria by spraying, using a hand atomiser. The spray contained a test organism at a concentration of between 10^7 and 10^8 organisms per ml. Tests were carried out using *Pseudomonas aeruginosa*, *Staph. aureus*, *E. coli* and *Salmonella choleraesuis.*

The tile was allowed to dry in air for about 10 minutes. It was shown that the dried tiles had approximately 8×10^5 organisms per tile (3.5×10^3 organisms per cm^2).

One portion of the tile was treated by either wiping or spraying with a disinfectant composition. In the case of spraying, care was taken to ensure that the untreated portion of the tile was fully covered. The tile was again allowed to dry in air for up to 10 minutes. Samples were taken from the treated and untreated portions of the tile by taking RODAC plate impressions. The RODAC plates contained 0.75% TWEEN 80 (Registered Trade Mark) and 0.075% lecithin. The TWEEN 80 and lecithin act to neutralise the activity of any biocidal compounds in the sample and are used following the procedure of Babb et al. (J. of Hosp. Inf., *2*, 267—272).

The tile was then recontaminated over the whole area by respraying from the hand atomiser. The tile was allowed to dry in air for approximately 10 minutes. Samples were again taken from the treated and untreated portions and plated using RODAC plates. All the plates were incubated at 32°C for 48 hours.

The plates covered with samples from the untreated portions are called Control 1 and Control 2 and the plates covered with samples from the treated portions are called Treatment and Residual in the following Table 1.

The results given in Table 1 are for use of *Pseudomonas aeruginosa*, but similar results have been obtained using other organisms.

In Table 1, + indicates that confluent growth of the organism was observed, — indicates no growth or a few isolated colonies of growth was observed, test 1 refers to wiping with an Azo-Wipe wipe (a wipe saturated in 70% isopropyl alcohol), test 2 to spraying with DISPRAY 2 (a commercially-available spray containing 0.02% chlorhexidine gluconate in 70% IMS), test 3 to wiping with a wipe including a composition according to the present invention and test 4 to spraying with a composition according to the invention.

TABLE 1

Test	Control 1	Control 2	Treatment	Residual
1	+	+	—	+
2	+	+	—	+
3	+	+	—	—
4	+	+	—	—

It can be seen from the Table that presently-available wipes or sprays are able to confer immediate protection on a hard surface, but this protection is short-lived, whereas wipes or sprays including compositions according to the present invention confer on the surface a residual biocidal activity. This residual activity can last for up to 24 hours.

It is possible that, in the above test procedure, the inactivation effect of the TWEEN 80 and lecithin may not be immediate due to the time needed to complete inactivation. Therefore, to confirm the residual activity of the compositions of the present invention the following test was employed. It is derived from Lowbury and Lilly's technique for determining the number of viable bacteria removed from hands when washing (B.M.J., May 14, 1960, 1448—1450).

A ceramic white tile (6″ × 6″) was treated with a biocide formulation, either by wiping or spraying, and allowed to dry and stand for a certain time. Thereafter a carefully controlled number of organisms was sprayed onto the tile. The tile was placed in a sterile polyethylene bag containing 100 ml of a neutraliser solution (1% TWEEN 80, 1% lecithin). After 1 minute of uniform gentle agitation, 1 ml aliquots were removed, diluted in phosphate buffer and plated out with molten tryptone soya agar. The viable number of surviving organisms can be calculated after incubation at 32°C for 48 hours.

The number of viable organisms recovered from the tile treated with a wipe composition according to the present invention can be calculated as % survivors against those found with the

commercially available Azowipe or Dispray 2.

$$\text{i.e.} \quad \frac{\text{number viable using a composition according to the present invention}}{\text{number viable using either Azowipe or Dispray 2}} \times 100$$

Table 2 shows the results obtained using a wipe of the present invention against commercially available products, with various reinfecting organisms.

TABLE 2
Number (orgs/ml) and % survivors

Organism	Azowipe	v	Wipe*	Dispray 2	v	Wipe*
Staph. aureus	3.5×10^5	v	2.9×10^4	2.1×10^6	v	6.6×10^3
	100%	v	8.2%	100%	v	0.3%
Salm. cholera	2.1×10^5	v	2.3×10^3	1.1×10^5	v	8.8×10^1
	100%	v	1%	100%	v	0.1%
Ps. aeruginosa	4.5×10^5	v	9.2×10^3	6.9×10^5	v	2.2×10^3
	100%	v	6.1%	100%	v	0.4%

* = An impregnated wipe according to the present invention.

This confirms the previous results, and shows that the composition according to the present invention confers a residual biocidal activity relative to the commercially available products.

If a surfactant, such as Lexaine C, is included in the composition, cleaning of soiled surfaces is facilitated.

It was shown that the composition of the present invention is active against a wide range of bacteria, including Pseudomonas, by standard tests.

The active ingredients in the composition according to the invention have proved histories of low toxicity. Therefore its use should present no problems from this point of view. Moreover, the composition may be used, without adverse effects, on a wide variety of substrates, such as most metals, adequately-compounded rubbers and plastics. If a biguanide compound is used, the composition may tarnish copper. Thus the present invention provides a composition which can be used to confer residual biocidal activity on a disinfected surface.

CLAIMS

1. A disinfectant composition having residual biocidal activity comprising an aqueous solution of from 40 to 95% v/v of a C_1 to C_4 alkanol and at least two antimicrobial agents, the at least two antimicrobial agents having a combined concentration in the solution of up to 2% w/v.

2. A composition according to claim 1, wherein the alkanol is isopropanol.

3. A composition according to claim 1 or 2, comprising from 60 to 80% v/v of the alkanol.

4. A composition according to claim 3, comprising about 70% v/v of the alkanol.

5. A composition according to any one of claims 1 to 4, wherein a first of the antimicrobial agents in a biguanide compound.

6. A composition according to claim 5, wherein the biguanide compound is polymeric.

7. A composition according to claim 5 or 6, wherein the combined concentration of the antimicrobial agents is 1% w/v or less.

8. A composition according to any one of the preceding claims, wherein a second of the antimicrobial agents is a quaternary ammonium compound.

9. A composition according to claim 8, wherein the quaternary ammonium compound is an alkyl dimethyl benzyl-, an alkyl trimethyl- or a dialkyl dimethyl-ammonium halide or a mixture thereof.

10. A composition according to claim 9, wherein the alkyl groups are straight chain and have from 12 to 18 carbon atoms.

11. A composition according to claim 9 or 10, wherein the halide is chloride.

12. A composition according to any one of the preceding claims, and including, as an antimicrobial agent, 4-chloro-3,5-xylenol, 2,4,4′-trichloro, 2′-hydroxy diphenyl ether, 5-brom-5-nitro-1,2-dioxan or orthophenyl phenol.

13. A composition according to any one of the preceding claims and including a chelating agent.

14. A composition according to claim 13, wherein the chelating agent is ethylenediaminetetra-acetic acid or a salt thereof.

15. A composition according to any one of the preceding claims, and including a surfactant compatible with the other components of the composition.

16. A composition according to any one of the preceding claims, and including up to 0.2% w/v of a fragrance.

17. A disinfectant composition having residual biocidal activity, substantially as hereinbefore described with reference to the Examples.

18. A disinfectant wipe comprising a cloth, such as a paper or woven or non-woven fabric impregnated with a composition according to any one of claims 1 to 17.

19. A disinfectant wipe according to claim 18, wherein the cloth is saturated with the composition.

20. A disinfectant formulation for use in an aerosol spray comprising a composition according to any one of claims 1 to 17 mixed with a propellant.

21. A disinfectant aerosol spray comprising a formulation according to claim 20 contained under pressure in an aerosol can.

22. A method of disinfecting a substrate comprising wiping it with a composition according to any one of claims 1 to 17.

23. A method according to claim 22, wherein the composition is applied in the form of an aerosol spray.

24. A method according to claim 22, wherein the composition is applied by use of a disinfectant wipe according to either one of claims 18 and 19.

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