

ANTI-MICROBIAL COMPOSITION

This invention relates to anti-microbial compositions and to formulations including the anti-microbial compositions. In particular, the invention relates to anti-microbial compositions
5 that can be used on skin.

Micro-organisms such as bacteria and viruses, for example norovirus, polio virus and adenovirus, are well known to present health hazards due to infection or contamination. Along with fungi, yeasts and other micro-organisms they can also cause spoilage of items
10 such as food, clothing and produce unpleasant odours. When micro-organisms are present on the surface of a substrate, such as skin, they can replicate rapidly to form colonies.

Many anti-microbial agents can destroy micro-organisms that are present in a wide range
15 of environments. For example, anti-microbial agents that may be used in medical, industrial, commercial, domestic and marine environments are known. Many of the known anti-microbial agents have previously been included in compositions for use in these environments for various applications.

20 Known anti-microbial agents and the compositions that contain these anti-microbial agents act via a number of different mechanisms.

For example, many anti-microbial agents are poisonous to microorganisms and, therefore, destroy microorganisms with which they are contacted. Examples of this type of anti-
25 microbial agent include hypochlorites (bleaches), phenol and compounds thereof, and salts of copper, tin and arsenic.

However, whilst many of these anti-microbial agents are effective against micro-organisms and appropriate for certain environments, their mechanisms can make them unsuitable or
30 disadvantageous for topical application to human skin due to their detrimental effects to human health or on skin condition. For example, hypochlorite bleach is very effective at killing micro-organisms on solid surfaces, but inappropriate for application to skin due to its corrosive properties. Also, these materials tend to be effective in a wet environment for sterilization and cleansing but stop working shortly after drying.

35 Many skin sanitizers are alcohol-based. These are typically an alcohol-containing preparation designed for application to the hands for reducing the number of viable

microorganisms on the hands. Such preparations typically contain 60%-95% ethanol or isopropanol. However, while isopropyl alcohol has established antibacterial properties, it has the disadvantage that, when used regularly, it can cause dryness and skin irritation. As a result some people may be reluctant to use such creams, soaps and other compositions comprising significant levels of isopropanol.

Some anti-microbial agents are highly toxic to humans and animals and are dangerous to handle. Specialist handling, treatment and equipment are therefore required in order to handle them safely. The manufacture and disposal of compositions comprising this type of anti-microbial agent can, therefore, be problematic. There can also be problems associated with the use of compositions containing this type of anti-microbial agent, particularly in consumer materials where it is difficult to ensure that they are used for designated purposes.

Herein, unless the context indicates otherwise, "toxicity" is intended to refer to toxicity to complex organisms such as mammals. References to "toxic" are to be construed accordingly.

Increasing scrutiny of the environmental credentials of chemicals is further restricting the usage of anti-microbial agents not just for topical application on skin but for general use. For example, some anti-microbial agents once they enter the environment can harm other organisms. They can also be very stable and persist in the environment for long periods causing concerns around build-up and residual levels.

Because of these factors the list of effective and available anti-microbial agents, particularly for use on skin, is becoming more restricted and the burden of registering new anti-microbials more prohibitive. At the same time the public are becoming increasingly concerned with sanitization, both of person and property following outbreaks such as MRSA in hospitals.

There is a need to provide compositions for a variety of applications and uses, such as compositions for use on skin, for example hand sanitising agents, that have anti-microbial properties and that address one or more of the problems set out above. However, it is not a straight forward matter to do this. There are regulations such as the Biocidal Products Regulations (Directive 98/8/EC) which regulates the use of anti-microbial agents both in terms of the nature and the amount of a given anti-microbial agent that may be used. Additionally, the potential reactivity of an anti-microbial agent once in a composition is

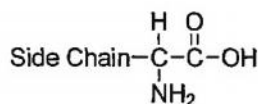
important as some anti-microbial agents are rendered inactive by chemical reaction. Even where an anti-microbial agent is not deactivated by chemical reaction it may have its activity suppressed by other components of the composition.

- 5 The present inventors have surprisingly found that the foregoing deficiencies can be overcome by certain combinations of components. It has also been found that compositions containing these combinations of components can have some surprising and unexpected properties.
- 10 The listing or discussion of an apparently prior-published document in this specification should not necessarily be taken as an acknowledgment that the document is part of the state of the art or is common general knowledge.

The present invention provides an antimicrobial composition comprising:

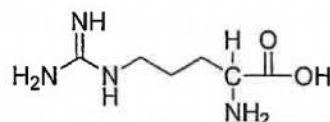
- 15 (i) an amino acid, a derivative of an amino acid, a salt of an amino acid, or a salt of a derivative of an amino acid or a mixture thereof;
- (ii) an anti-microbial component comprising two or more anti-microbial quaternary ammonium compounds or at least one anti-microbial quaternary ammonium compound and chlorhexidine, or a chlorhexidine salt; and
- 20 (iii) a polar solvent.

- Amino acids are well known organic compounds that are essential for life. They are characterised by having an amine (NH₂) functional group attached to the carbon adjacent to a carboxylic acid (CO₂H) functional group, along with a side-chain that is specific to the
- 25 amino acid. An amino acid has the general formula shown below.



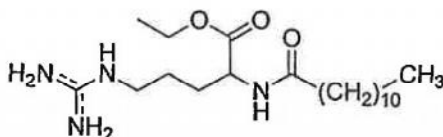
- Because amino acids have both an amine and carboxylic acid group they can act as both
- 30 a base and an acid. At low pH the predominant form will have a neutral carboxylic acid group and a positive Ammonium ion (net charge +1). At high pH it will have a negative carboxylate and neutral amino group (net charge -1). At an intermediate pH, the amino acid will usually contain both a negative carboxylate and a positive ammonium group, so has net zero charge.

Arginine is one of the most common amino acids and is shown below.



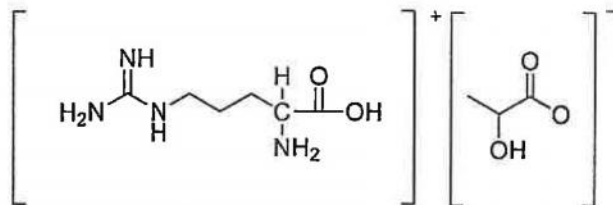
- 5 Some further examples of common amino acids are glycine, lysine, glutamate, glutamine, aspartate, asparagine, histidine, proline, methionine, cysteine, serine, threonine, isoleucine, phenylalanine, tyrosine, tryptophan, valine and leucine. The structures of these amino acids are well documented.
- 10 By the term "amino acid" we also include chains of amino acids such as peptides and polypeptides. Peptides are formed when individual amino acids are linked together via peptide (amide) bonds formed by the reaction of the amine group of one amino acid with the carboxyl group of another. The shortest peptides are dipeptides consisting of two amino acids joined by a single peptide bond, followed by tripeptides, tetrapeptides and so
- 15 on. A polypeptide is a long, continuous, and unbranched peptide chain.

- By the term "derivative of an amino acid" we mean an amino acid in which the alpha-amino and/or carboxyl functional groups are substituted by an alternative organic group, or an amino acid in which the functional groups in the side chain of an amino acid are substituted
- 20 by an alternative organic group, or an amino acid in which the alpha-amino and/or carboxyl functional groups are substituted by an alternative organic group and/or the functional groups in its side chain are also substituted by an alternative organic group. Alternative organic groups include, but are not limited to, alkenyl, phenyl, amide, ester, alcohol, and ether groups or combinations thereof. An example of a derivative of an amino acid is N-
- 25 lauroyl-L-arginine ethyl ester whose structure is shown below.

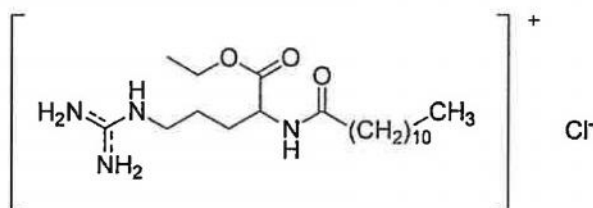


- By the term "salt of an amino acid" we mean the cationic or anionic form of the amino acid combined with a counter-ion, which is an ion of opposite charge. The cationic form of the amino acid is formed by the transfer of a positively charged hydrogen ion from an acid to an amino group in the amino acid. The counter-ion is derived from the acid from which the
- 30

- hydrogen ion is transferred from. The anionic form of the amino acid is formed by the loss of a positively charged hydrogen ion from the carboxylic acid group in the amino acid. In this case the counter-ion is derived from the base to which the hydrogen ion is transferred to. An example of an amino acid salt is arginine lactate which is commercially available in
- 5 *AH Care L65*. *AH Care L65* is composed of a lactic acid; arginine mixture. The structure of arginine lactate is shown below.



- 10 By the term "salt of the derivative of an amino acid" we mean the cationic or anionic form of the amino acid derivative, as defined above, combined with a counter-ion, which is an ion of opposite charge. The cationic form of the amino acid is formed by the transfer of a positively charged hydrogen ion from an acid to an amino group in the amino acid derivative. The counter-ion is derived from the acid from which the hydrogen ion is
- 15 transferred from. The anionic form of the amino acid derivative is formed by the loss of a positively charged hydrogen ion from the carboxylic acid group in the amino acid derivative. In this case the counter-ion is derived from the base to which the hydrogen ion is transferred to. An example of a salt of a derivative of an amino acid is N-lauroyl-L-arginine ethyl ester mono-hydrochloride which is commercially available as *Aminat G*
- 20 whose structure is shown below.



- Salts of amino acids or amino acid derivatives used in the present invention include, but
- 25 are not limited to, hydrochloride, tartrate, malonate, succinate, succinamate, malate, glutamate, pyroglutamate and aspartate. In one aspect, the salt of the amino acid or amino acid derivative is not a phosphonate salt or a phosphorus containing salt, such as a monoalkyl phosphate ion, a monoalkenyl phosphate ion, a monoalkyl phosphonate ion, or

a monoalkenyl phosphonate ion, such as those having a linear or branched alkyl or alkenyl group with 8 to 20 carbon atoms.

Component (i) may comprise a hydrophilic amino acid or a salt or a derivative of such an amino acid or a salt of such a derivative. Hydrophilic amino acids may have a hydrophilic side chain or may be positively or negatively charged having a hydrophilic side chain.

Component (i) may, for example, comprise a positively charged amino acid or a salt or a derivative of such an amino acid or a salt of such a derivative.

A derivative of an amino acid may be hydrophilic as a result of the modification made to the amino acid. For example, an amino acid may be modified so that it is positively or negatively charged.

Hydrophilic amino acids as defined above are typically water soluble.

By water soluble we mean that the amino acid or a salt or a derivative of such an amino acid or a salt of such a derivative typically have a solubility in water at 25°C of at least about 0.5 g per kg of water. For example, at least about 1 g per kg of water, such as at least about 10 g per kg of water, or at least about 50 g per kg of water.

The salts and derivatives of amino acids and salts of such a derivative suitable for use in the present invention are typically water soluble.

Amino acids that are suitable for use in the present invention can also be classified by their hydropathy Index. This index is described in, for example, Kyte, J. and Doolittle, R., 1982, "A simple method for displaying the hydropathic character of a protein", J mol. Biol. 157: 105-132. As the skilled reader will appreciate, the more positive the value on the Hydropathy Index, the more hydrophobic an amino acid is. Suitable amino acids for use in the present invention include amino acids having a Hydropathy Index value of 0 (zero) or less, such as -2 or less. Salts and derivatives of such amino acids and salts of such a derivative are suitable for use in the present invention. Arginine and its salts and derivatives and salts of such a derivative are suitable for use in the present invention. Arginine has a Hydropathy Index value of -4.5.

Alternatively or additionally, amino acids suitable for use in the present invention can be classified by their isoelectric point (pI); that is the pH at which the net charge on the amino

acid is zero. At a pH below its isoelectric point an amino acid will be positively charged. In certain compositions of the invention, it is preferred that the amino acid is positively charged. In this aspect, an amino acid that has a pI that is greater than the pH of the composition is used.

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Amino acids that are suitable for use in the present invention include those with a pI 5 or greater, such as 6 or 6.25 or greater; or 8 or 10 or greater. Salts and derivatives of such amino acids and salts of such a derivative are suitable for use in the present invention. Arginine and its salts and derivatives and salts of such a derivative are suitable for use in the present invention. Arginine has a pI of 10.76.

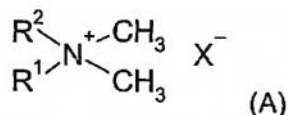
Amino acids that are particularly suitable for use in the present invention include those having a hydrophathy index of value of 0 (zero) or less, such as -2 or less and a pI of 6 or greater, 6.25 or greater or 8 or greater or 10 or greater. Salts and derivatives of these amino acids and salts of such a derivative are also particularly suitable for use in the present invention.

The compositions of the invention comprise chlorhexidine or a chlorhexidine salt. Examples of suitable chlorhexidine salts include the acetates, formates, gluconates, hydrochlorides, isoethionates, lactates, and succinamates of chlorhexidine. For example, suitable salts include, but are not limited to chlorhexidine diphosphanilate, chlorhexidine digluconate, chlorhexidine diacetate, chlorhexidine dihydrochloride, chlorhexidine dichloride, chlorhexidine dihydroiodide, chlorhexidine diperchlorate, chlorhexidine dinitrate, chlorhexidine sulfate, chlorhexidine sulfite, chlorhexidine thiosulfate, chlorhexidine di-acid phosphate, chlorhexidine difluorophosphate, chlorhexidine diformate, chlorhexidine dipropionate, chlorhexidine di-iodobutyrate, chlorhexidine di-n-valerate, chlorhexidine dicaproate, chlorhexidine malonate, chlorhexidine succinate, chlorhexidine succinamate, chlorhexidine malate, chlorhexidine tartrate, chlorhexidine dimonoglycolate, chlorhexidine mono-diglycolate, chlorhexidine dilactate, chlorhexidine di- α -hydroxyisobutyrate, chlorhexidine diglucoheptonate, chlorhexidine di-isothionate, chlorhexidine dibenzoate, chlorhexidine dicinnamate, chlorhexidine dimandelate, chlorhexidine di-isophthalate, chlorhexidine isoethionate chlorhexidine di-2-hydroxy-napthoate, and chlorhexidine embonate.

A specific example of a chlorhexidine salt that may be used in the compositions of the invention is chlorhexidine di-gluconate.

The quaternary ammonium anti-microbial agent(s) used in the present invention are typically water soluble at room temperature and pressure.

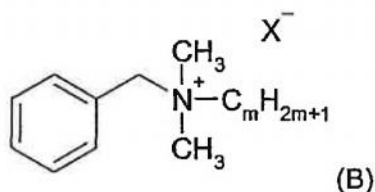
Suitable anti-microbial quaternary ammonium compounds include compounds of formula (A) shown below.



wherein R^1 and R^2 are each independently a straight chain, unsubstituted and uninterrupted C_{8-12} alkyl group. In one aspect, the groups R^1 and R^2 contain the same number of carbon atoms but this is not essential and compounds in which R^1 and R^2 contain different number of carbon atoms can be used. X^- is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, carbonate or bicarbonate.

In one aspect, X^- is not a phosphonate salt or a phosphorus containing salt, such as a monoalkyl phosphate ion, a monoalkenyl phosphate ion, a monoalkyl phosphonate ion, or a monoalkenyl phosphonate ion, such as those having a linear or branched alkyl or alkenyl group with 8 to 20 carbon atoms.

Suitable anti-microbial quaternary ammonium compounds also include benzalkonium compounds having the formula (B) shown below.



wherein m is from 8 to 18, and X^- is a halide anion such as chloride, bromide, fluoride, iodide, sulphonate, saccharinate, carbonate or bicarbonate. The compounds of formula (B) are generally called benzalkonium compounds. The benzalkonium chloride is provided and/or used as a mixture of C_{8-18} alkyl groups, particularly a mixture of straight chain, unsubstituted and uninterrupted alkyl groups $n\text{-C}_8\text{H}_{17}$ to $n\text{-C}_{18}\text{H}_{37}$, mainly $n\text{-C}_{12}\text{H}_{25}$ (dodecyl), $n\text{-C}_{14}\text{H}_{29}$ (tetradecyl), and $n\text{-C}_{16}\text{H}_{33}$ (hexadecyl). Preferably m is 8, 10, 12, 14 and/or 16. Most preferably m is from 8 to 12 for example 8, 10 and/or 12 or from 12 to 16, for example 12, 14 and/or 16.

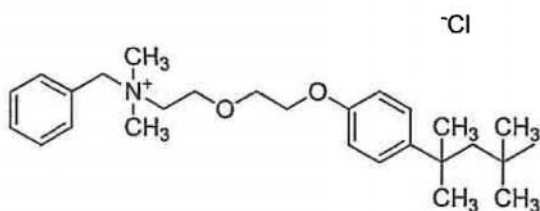
In the compounds of formula (A) each group R^1 and R^2 is independently a straight chain, unsubstituted, uninterrupted C_{8-12} alkyl group, for example an alkyl group containing 8, 9, 10, 11 or 12 carbon atoms. R^1 and R^2 may be the same, for example R^1 and R^2 may both be alkyl groups containing 8, 9, 10, 11 or 12 carbon atoms.

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By benzalkonium compounds we also include derivatives of benzalkonium compounds whereby the alkyl group C_mH_{2m+1} shown below can be substituted by another organic group. Such organic groups include but are not limited to alkenyl, phenyl, amide, ester, alcohol, and ether groups or combinations thereof.

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An example of such a derivative of a benzalkonium compound is diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride, whose INCI name is benzethonium chloride (typically abbreviated to BENZ). The structure of benzethonium chloride is shown below.



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The anion of each quaternary ammonium compound in the compositions of the invention may be the same or different. For example, the anion of a compound of formula (A) may be the same or different to the anion of a compound of formula (B). In one aspect, the anion for each compound is chloride.

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In an aspect of the invention, where the composition comprises two or more anti-microbial quaternary ammonium compounds, a compound of formula (A) and a compound of formula (B) may be present, or the composition may comprise more than one compound of formula (A) or more than one compound of formula (B).

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Examples of quaternary ammonium compounds of formula (A) include di-n-decyldimethyl ammonium chloride, octyl decyl dimethyl ammonium chloride and dioctyl dimethyl ammonium chloride.

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Examples of commercially available compounds of formula (A) include Acticide DDQ 40 from Thor, Bardac 2240 from Lonza, Bardac 2280 from Lonza and Maquat 4480E, from Mason Chemical Company, USA.

Examples of quaternary ammonium compounds of formula (B) include N,N-benzyl dimethyloctylammonium chloride, N,N-benzyl dimethyldecylammonium chloride, N-dodecyl-N-benzyl-N,N-dimethylammonium chloride, N-tetradecyl-N-benzyl-N,N-dimethylammonium chloride, N-hexadecyl-N,N-dimethyl-N-benzylammonium chloride, N,N-dimethyl N-benzyl N-octadecyl ammonium chloride and mixtures thereof.

It will be appreciated that a single CAS number often refers to more than one blend or mixture. A CAS classification for a commercial preparation typically covers blends comprising specified compounds in amounts within defined ranges. The compositions having the CAS numbers quoted above are only examples of compositions having a given CAS number that may be used in the present invention.

In the compositions of the present invention the anti-microbial quaternary ammonium compound is typically not polymerised.

Examples of commercially available compounds of formula (B) include Acticide BAC 50M from Thor, Barquat MB50/80 from Lonza, Lonzagard Benzethonium Chloride USP from Lonza.

Typically, the anti-microbial quaternary ammonium compound or compounds used in the composition of the invention is selected from the group consisting of di-n-decyl dimethyl ammonium chloride (DDAC (CAS number 7173-51-5)), benzalkonium chloride (BAC) such as benzalkonium chloride of formula (B) above wherein m is 8. This benzalkonium chloride has CAS number 68424-85-1, and benzethonium chloride (BENZ).

The amount of component (i) and anti-microbial component (ii) present in the compositions of the present invention will vary depending on a number of factors, such as the intended use of composition and the particular compound(s) used.

For example, as will be appreciated by the person skilled in the art, higher concentrations of (i) and/or (ii) may be required in order to provide sterilisation compared to providing sanitisation or disinfection.

Anti-microbial component (ii) may consist essentially of at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt.

Anti-microbial component (ii) may consist of at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt.

Alternatively anti-microbial component (ii) may consist essentially of two or more anti-microbial quaternary ammonium compounds without chlorhexidine.

The compositions of the invention may contain two or more anti-microbial quaternary ammonium compounds or at least one anti-microbial quaternary ammonium compound and chlorhexidine, or a chlorhexidine salt as the only anti-microbial compounds in the composition. Alternatively, the compositions of the invention may comprise other suitable anti-microbial agent(s) (b), such as those described in the EPA (United States Environmental Protection Agency) Listing and Annex I and Annex 3 of the EC Biocides Directive.

Typically, the compounds included in the anti-microbial component (ii) are those that are suitable for application to the skin. For example, compounds that meet the required regulatory approval for human hygiene, such as those compounds approved by the European Commission, when used in products of Product-type 1 as listed in Annex II of the European Commission's delegated regulation (EU) No. 1062/2014 of 4 August 2014 and/or those approved by the FDA (Food and Drugs Administration).

Suitable anti-microbial agents (b) that may be included in the anti-microbial component (ii) include anti-microbial agents that are not quaternary ammonium compounds. Preferably, these additional antimicrobial agent(s) are water soluble at room temperature and pressure.

Examples of suitable additional antimicrobial agents include but are not limited to polymeric biguanidines (e.g. polyhexamethylene biguanidine (PHMB)), lactic acid, silver, salts of silver for example silver chloride, silver carbonate, silver citrate, silver dihydrogen citrate, octenidine HCl, amphoteric compounds, iodophores, phenolic compounds, amine anti-microbial agents and nitrogen based heterocyclic compounds, ortho phenyl phenol (OPP), and nitro bromopropanes (e.g. bronopol (INN), 2-bromo-2-nitropropane-1,3-diol), naturally derived biocidal compounds (e.g. honey and extracts of honey such as those comprising methyl glyoxal), flavenoid based antimicrobials, and essential oils.

In one aspect, the compositions of the invention are free of inorganic antimicrobial agents such as those comprising silver. In this aspect, any additional antimicrobial agent is an organic antimicrobial agent.

- 5 In one aspect, the compositions of the invention do not comprise PHMB or they may be free of polymeric biguanides. For example, they do not contain a biguanide in addition to chlorhexidine.

- 10 In one aspect of the invention the anti-microbial composition does not comprise any isothiazalones and/or any nitrobropropenes such as bronopol and/or any hypochlorites.

In one aspect of the invention the anti-microbial composition does not contain antimicrobial compounds that are poorly soluble in water such as phenolic compounds.

- 15 Typically, when formulated as a ready to use composition, the amount of component (i) may be from about 0.0005 to 10% by weight of the composition, for example from about 0.005 to about 5% by weight of the composition, such as from about 0.01 to about 1% by weight of the composition. These compositions may contain about 0.5% by weight of the composition or less of component (i), such as from 0.02 to 0.3% by weight of the composition, such as about 0.2% by weight or 0.1% by weight.

- 25 Typically, when formulated as a ready to use composition, the total amount of antimicrobial component (ii) and component (b) if present (ie the combined amount of antimicrobial quaternary ammonium compound and chlorhexidine or a salt thereof and any additional antimicrobial component (b)), may be from about 0.001 to about 10% by weight of the composition, for example from about 0.005 to about 5% by weight of the composition, such as from about 0.01 to about 1% by weight of the composition.

- 30 When the composition of the invention formulated for use as a hand sanitizer, the amount of antimicrobial component (ii) may be from about 0.05 to about 0.5% by weight.

- 35 The antimicrobial component (ii) may comprise equal amounts of quaternary ammonium compound and chlorhexidine, or salt thereof. For example, if the total amount of antimicrobial component is about 0.2% by weight of the composition, the amount of quaternary ammonium compound would be about 0.1% and the amount of chlorhexidine, or salt thereof, would be about 0.1%.

Alternatively, the anti-microbial component may comprise different amounts of quaternary ammonium compound and chlorhexidine.

Typically, in the compositions of the invention, the ratio of component (i) to anti-microbial
5 component (ii) ranges from 10:1 to 1:10.

The compositions of the invention comprise a polar solvent (iii). Suitable polar solvents include, but are not limited to, water, alcohols, glycol ethers and mixtures thereof.

10 Suitable alcohols include, but are not limited to, straight or branched chain C_1 to C_5 alcohols, such as methanol, ethanol, n-propanol, iso-propanol, mixtures of propanol isomers, n-butanol, sec-butanol, tert-butanol, iso-butanol, mixtures of butanol isomers, 2-methyl-1-butanol, n-pentanol, mixtures of pentanol isomers and amyl alcohol (mixture of isomers), and mixtures thereof.

15 Preferred polar solvents for use in the compositions of the invention include, but are not limited to, water, ethanol, isopentylol, mono propylene glycol, hexylene glycol, 3-Methoxy-3-methyl-1-butanol (MMB), n-propanol, isopropanol, ethylene glycol ethers, propylene glycol ethers, butyl diglycol (BDG) and mixtures thereof. In one aspect, the composition
20 comprises water or a mixture of water and one or more alcohols selected from the alcohols described above. In such mixtures, water is preferably the major component. The polar solvent may consist essentially of water or consist of water.

If the compositions of the invention comprise an alcohol, the alcohol is typically present in
25 an amount lower than the amount necessary for the alcohol to provide an antimicrobial effect, but at a level that it is believed improves drying of the composition on skin. For example, the compositions of the invention may comprise up to about 30% by weight alcohol, such as between 20 and 30% by weight alcohol or less than about 20% by weight alcohol, such as from about 15 to about 20% by weight alcohol.

30 It will be appreciated that the percentage of alcohol may depend on the use of the composition. For example, when used on a wipe, the composition of the invention may comprise up to 20% alcohol.

35 In one aspect, the compositions of the invention are substantially free of alcohol. For example, the compositions may contain 1% or less by weight alcohol. For example, the compositions may contain less than 1% or less than 0.5% by weight or 0.1% by weight or

less of an alcohol such as isopropanol. As an example, compositions of the invention may comprise no isopropanol or may comprise no alcohol.

5 In another aspect, the compositions of the invention may comprise an alcohol up to a level of 70% by weight, e.g. up to about 50% by weight.

The composition may comprise water or a mixture of water and one or more alcohols selected from the alcohols described above. In such mixtures, water is preferably the major component.

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For example, the polar solvent may consist of or consist essentially of water. As another example, the polar solvent may be water and from about 0 to about 20% by weight, such as from about 15 to about 20% by weight of an alcohol, for example ethanol or isopropanol.

15 The compositions of the invention can be provided in concentrated form for dilution before use or in ready to use form. It is preferred that the compositions of the invention are provided in ready to use form and, unless otherwise stated, information about amounts (such as weight% or ppm) provided in this document relate to ready to use compositions.

A concentrate is typically provided such that when diluted the concentrate is 5 to 30% by weight, e.g. 10 or 20% by weight of resulting diluted product.

20 Typically, but not essentially, the compositions of the invention have a concentration of amino acid component (i) of from about 0.0005 weight% to about 10 weight%, such as from about 0.005 weight% to about 5 weight%, or 0.01 weight% to 1.0 weight% and a concentration of anti-microbial component (ii) of from about 0.001 weight% to about 10 weight%, such as from about 0.005 weight% to about 5.0 weight%, or 0.01 weight% to 1 weight%. These compositions may contain about 0.5% by weight of the composition or
25 less of component (i), such as from 0.02 to 0.3% by weight of the composition, such as about 0.2% by weight or 0.1% by weight.

30 The pH of the compositions and formulations used can vary within wide limits, for example from about pH 2 to about pH 12, more preferably from about pH 3 to about pH 10 or about pH 4.5 to 8. The pH of a formulation used in the invention may be similar to that of known formulations which are intended to be used for the same purpose or a similar purpose. For example, a formulation that is intended to come into contact with the skin such as a personal care or first aid formulations will typically have a pH which will not irritate the skin,

for example from about pH 3 to about pH 8, such as from about pH 4.5 to about pH 7.5 or from about pH 5 to about pH 6.

When used as a hand sanitizer, the pH of the compositions of the invention is typically
5 from about 5 to about 6.

It will be appreciated that the compositions of the invention can comprise other ingredients commonly used in the art. The nature of any other ingredients used will depend on the nature and intended purpose of the composition. The person of ordinary skill in the art will
10 know which additional ingredients are suitable for use in compositions for different applications.

The compositions of the present invention may comprise additional materials such as surfactants, complexing agents, buffering agents, thickening agents, skin conditioning
15 compounds, polar solvents and fragrances.

The selection of surfactants will depend on the nature of and the intended purpose of the composition. Suitable surfactants for use in formulations intended for different purposes will be within the knowledge of the person of ordinary skill in the art. Likewise, the selection
20 of suitable amounts of surfactant will be within the knowledge of the person of ordinary skill in the art. Suitable surfactants may be selected from non-ionic, cationic or amphoteric and mixtures thereof.

Some compositions of the invention may comprise a non-ionic surfactant. Suitable non-
25 ionic surfactants include, but are not limited to, amine oxides, alkyl polyglucosides, linear and branched 1° and 2° alcohol ethoxylates, and ethoxylated/propoxylated (EOPO) block polymers.

In one aspect, the composition is substantially free of or free of anionic surfactant. In
30 another aspect, the compositions of the invention do not comprise an amphoteric surfactant.

Some compositions of the invention may comprise an amphoteric surfactant. Suitable amphoteric surfactants include but are not limited to C₆-C₂₀ alkylamphoacetates or
35 amphodiacetates (such as cocoamphoacetates), C₁₀-C₁₈ alkyldimethyl betaines, C₁₀-C₁₈ alkyl amidopropyldimethyl betaines. Examples include but are not limited to coconut

amphoteric surfactant cocoamidopropyl betaine (CAPB) (Surfac B4, CAS 61789-40-9), coco imidazoline betaine, oleo amido propyl betaine, and tall oil imidazoline.

Some compositions of the invention may comprise a cationic surfactant. Suitable cationic
5 surfactants include but are not limited to undecylenamidopropyltrimonium methosulphate and cetrimonium chloride

Typically, the amount of surfactant present in the compositions of the invention is in an amount of from about 0.01 to 20% by weight. The amount of surfactant depends on a
10 number of factors such as the pH of the composition and the intended use of the composition.

The compositions of the invention may comprise complexing agents. The terms sequestering agents or chelates are sometimes used interchangeably with the term
15 complexing agents. For the purpose of describing this invention, the term complexing agents include both sequestering agents and chelates. Complexing agents can be used to help provide a clear composition even when the compositions of the invention are used with hard water. Examples of suitable complexing agents include but are not limited to EDTA (Ethylenediaminetetraacetic acid), Gluconate, GLDA (Glutamic acid diacetic acid) -
20 Trade name Dissolvine GL, EDDS (Ethylenediamine-N,N'-disuccinic acid), citrates and gluconates or salts of glutaric, adipic and succinic acids and mixtures thereof. If the complexing agent contains a counter ion that counter ion is preferably metallic. Suitable metallic counter ions include but are not limited to Na, Ca, Fe, K, Zn, Mg and Mn.

25 Preferred complexing agents are GLDA (Dissolvine) and EDTA.

The complexing agents are typically present in an amount of from about 100 to 10,000 ppm, preferably from about 400 to 3,000 ppm, for example from about 500 to 2000ppm.

30 Buffering agents may be included to adjust the pH of the composition to the required value and maintain it at or close to that pH value during storage and use.

Suitable pH modifiers include but are not limited to acids such as citric, sulfamic, hydrochloric, phosphoric, nitric, lactic, formic, acetic glycolic or gluconic acids or other
35 mineral or organic acids or bases such as sodium or potassium hydroxide, triethanolamines and carbonates and mixtures thereof.

Thickening agents can be included to adjust the viscosity of the composition to the required value for such purposes as to make the composition more stable; facilitate application of the composition; or for aesthetic benefits. Examples of thickening agents include but are not limited to hydroxypropylmethylcellulose stearoxy ether supplied commercially by Daido chemical corporation under the tradename Sangelose 90, and a polyquaternium 37
5 supplied by Rheo Lab under the tradename Kleasol 200ST.

The compositions of the invention may contain skin conditioning compounds. Suitable skin conditioning compounds include, but are not limited to, panthenol, tocopheryl acetate, glycerine, polyquaternium compounds, PEG-7-glyceryl cocoate, and silicones and mixtures thereof. Typically, the compositions of the invention do not comprise mucopolysaccharides.
10

The compositions of the invention may alternatively or additionally contain salts such as the halides of alkali metals or alkaline earth metals such NaCl or KCl. In some situations, the use of salts can facilitate the formation of a stable composition.
15

The compositions of the invention may also contain other ingredients that are standard in the art such as colorants, fragrances, emollients, antioxidants and mixtures thereof.
20

The compositions of the invention may be free of anionic materials. Within the meaning of anionic materials, we do not include counterions that may for present in any of the ingredients used in the invention, such as counterions associated with a quaternary ammonium compound. The compositions of the invention may, for example, be free of anionic polyelectrolytes, such as high molecular weight, anionic mucomimetic polymers, polystyrene sulfonic acid polymers and cationic exchange resins.
25

It has been found that in use compositions of the invention have advantageous anti-microbial effects, and particularly when applied to the surface of skin. For example, such compositions have an anti-microbial effect when initially applied to a surface (so called "wet kill") and they can also have a residual anti-microbial effect in that they control, reduce or prevent the formation of new microbial colonies at the surface (so called "dry kill") that may otherwise result in the formation of more persistent biofilms.
30

The compositions of the invention are also resistant to washing with water and to wiping. This means that the compositions of the invention provide a residual anti-microbial effect
35

even when the surface which has been treated is subsequently wiped and/or washed or rinsed with water.

The compositions of the invention are particularly suitable for use as skin or hand sanitizers
5 or on other surfaces. Some compositions are suitable for use on other surfaces. The compositions of the invention typically provide a residual anti-microbial effect.

Such compositions may be used in a wide variety of formats and applications for the purpose of skin sanitization. For example, the compositions of the invention are particularly
10 suitable for formulation into mousses, gels, creams, lotions, liquids, sprays and wipes to be used in body or skin sanitisation, such as hand sanitizers.

When used in a wipe format, the substrates used to prepare the wipes may be made of any suitable woven or non-woven material. Suitable wipe materials include, but are not
15 limited to, non-woven fibrous sheet materials and those made of fibres from natural sources such as wood pulp, and viscose or other cellulose based materials, silk fibres and keratin fibres. The materials comprise from 1 to 100% by weight of a cellulosic material. For example, 100% cellulosic materials such as viscose or wood pulp may be used. Other preferred materials include blends of cellulosic and non-cellulosic materials, such as blend
20 of viscose with synthetic substrates such as polyester or polypropylene. Blended materials may comprise from 1 to 99.9 % by weight of a cellulosic material such as viscose, for example from 20 to 80% by weight or from 30 to 70 % by weight of a cellulosic material such as viscose.

25 The compositions of the invention can be used on humans and animals for both therapeutic and non-therapeutic purposes. Examples of products for non-therapeutic uses include personal care and personal hygiene products. Examples of products for therapeutic purposes include first aid and skin care products.

30 Compositions of the invention may also be in the form of a liquid and packed into suitable dispensers to provide a foam, mousse or spray in use. Compositions of the invention may be used for foot hygiene products, including those for direct use on the foot and those for the treatment/deodorisation of footwear, particularly sports footwear. Compositions of the invention can also be used in other personal care products which are used for direct
35 application on skin or hair for example soap, bath and shower products, hair care products including shampoo, and anti-dandruff shampoos, hair conditioners hair styling products such as hair mousses, gels and sprays, skincare products such as shaving products,

cosmetics and products for hair removal, deodorant and antiperspirant products, baby products including baby cleaning and cleansing products such as baby bath, soaps, wipes, moisturisers, nappy rash cream, products for cleaning surfaces that have regular and high incidence of infant and baby contact.

5

Compositions of the invention may be used as hygienic cleansers in pet products for direct application to the skin surface of the animal or its coat or fur for the purpose of eradicating or inhibiting micro-organisms which may otherwise have a detrimental effect on the animal's health, well-being or cleanliness. Such compositions can also be applied to
10 materials such as surfaces which come into contact with animals and to which micro-organisms may be transferred from the animal. The benefit of such applications is again to eradicate or inhibit such micro-organisms which otherwise may be transferred to another animal or human and also to control or eliminate the by-products that such organisms may produce such as malodour. Such pet applications may include but not be limited to stain
15 and odour removal sprays, disinfectant sprays and wipes, outdoor hutch cleaners, cage cleaners, antibacterial cat litter tray sprays and wipes, dog shampoos and spritzers and dog ear cleaning wipes.

Compositions of the invention may be used for First Aid topical applications to skin to
20 sanitize abrasions or wounds on the surface of the skin to prevent or deter infection, or to prevent minor infections such as athletes' foot, verruca, warts, spot/acne prevention/treatment products. Thus, the invention provides products for these uses, such as wound care or first aid products that comprise a composition of the invention.

25 Compositions of the invention may also be used for medical applications such as sterilization of catheters, dialysis and other medical equipment; inhibiting or eradicating viruses such norovirus, polio virus or adenovirus; and prevention or eradication of persistent biofilms.

30 Compositions of the invention may also be used on surfaces other than skin. Examples of applications of the invention to surfaces other than skin include but are not limited to: surface cleaners such as those intended for use in bathrooms, kitchens, living areas; hard floor cleaners; carpet cleaners; furniture cleaners; glass/mirror cleaners; toilet care products including solid toilet cleaners such as rim devices and those designed to be
35 placed in the cistern; liquid toilet cleaners excluding those comprising hypochlorite bleaches; dishwashing products such as washing up liquids and preparations from dishwashing machines such as dishwashing solids (in powder or tablet format) & liquids;

Laundry products such as solid detergents (in powder or tablet format); liquid detergents; fabric conditioners and "2 in 1" products comprising detergent and fabric conditioner; cleaning products intended for use outdoors such as those for cleaning for wood, stone, concrete or plastics, for example patio cleaner, garden furniture cleaners/treatments, BBQ
5 cleaners, wall and fence cleaners/treatments; plant sprays such as those intended to remove insects such as aphides from plants; food sprays, such as those suitable for use in food preservation.

For the avoidance of doubt, in this specification when we use the term "comprising" or
10 "comprises" we mean that the composition or formulation or component being described must contain the listed ingredient(s) but may optionally contain additional ingredients. When we use the term "consisting essentially of" or "consists essentially of" we mean that the composition or formulation or component being described must contain the listed ingredient(s) and may also contain small (for example up to 5% by weight, or up to 1% or
15 0.1% by weight) of other ingredients provided that any additional ingredients do not affect the essential properties of the composition, formulation or component. When we use the term "consisting of" we mean that the composition or formulation or component being described must contain the listed ingredient(s) only. These terms can be applied in an analogous manner to processes, methods and uses.

20

By "substantially free" we mean that the composition or formulation or component being described contains less than 3% by weight, preferably less than 1%, more preferably 0.1% or less by weight of the stated ingredient. For example, the compositions of the invention that are substantially free of alcohol contain less than 3% by weight of alcohol, preferably
25 less than 1% by weight of alcohol, more preferably 0.1% or less alcohol.

By the term "anti-microbial" we mean a compound or composition that kills and/or inhibits the growth of microbes (microorganisms). The term "microbiocidal" is used to refer to compounds or compositions that kill microbes. The compositions of the invention are anti-
30 microbial and/or microbiocidal.

By the term "sanitising" or "sanitizer" we mean the reducing in the total number of microbes on a surface.

35 By the term "sterilising" we mean the elimination of microbiological organisms to achieve asepsis (a sterile microbial environment).

A microorganism or microbe is an organism that is microscopic (too small to be seen by the human eye). Examples of microorganisms include bacteria, fungi, yeasts, moulds, mycobacteria, algae spores, archaea and protists. Microorganisms are generally single-celled or unicellular organisms. However, as used herein, the term "microorganisms" also
5 includes viruses.

The compositions of the invention may be anti-bacterial, anti-fungal, anti-algal, anti-sporal, anti-viral, anti-yeast and/or anti-mould.

10 The compositions of the invention are particularly suitable for use against bacteria, such as E.coli.

As used herein, the terms anti-bacterial, anti-fungal, anti-algal, anti-viral, anti-yeast and anti-mould agents are intended to refer to agents that inhibit the growth of the respective
15 microorganisms but do not necessarily kill the microorganisms and agents that kill the respective microorganisms. Thus, for example, within the term anti-bacterial we include agents that inhibit the growth of bacteria but may not necessarily kill bacteria and bactericidal agents that do kill bacteria.

20 Examples of anti-bacterial agents include mycobactericides and tuberculocides. Preferably, the compositions of the invention comprise at least one agent selected from anti-bacterial, anti-fungal, anti-algal, anti-sporal, anti-viral, anti-yeast and anti-mould agents and mixtures thereof. More preferably, the compositions of the invention comprise at least one anti-bacterial, anti-viral, anti-fungal and/or anti-mould agent.

25 The compositions of the invention can be effective against a wide range of organisms, including Gram negative and Gram positive bacteria, fungi, yeasts, viruses and some spore forming bacteria

30 An advantage of the invention is that it is possible to prevent a broad range of microorganisms from adhering and attaching to the surface, and, therefore, from forming a biofilm. Large numerous colonies are also substantially prevented from forming. Thus, the ability of the colony to grow is substantially reduced or even prevented. The invention is therefore general in its control of microorganisms.

35 In an aspect of the invention, the compositions may be used to reduce or control the formation of a biofilm.

As described previously, the compositions of the invention advantageously provide a residual antimicrobial effect whereby the antimicrobial action continues for a significant period after the initial application of the composition.

- 5 Typically, the compositions of the invention do not need to contain materials that are highly toxic to mammals. The anti-microbial agents used in the anti-microbial compositions are typically well known and widely understood and tested anti-microbial agents. The efficacy of the known anti-microbial agents is amplified in the formulations of the invention. Therefore, anti-microbial agents that have a low toxicity can be used in the anti-microbial
10 compositions. In contrast, many "new" anti-microbial agents for known techniques of sanitization use "stronger", more toxic and/or little tested materials.

- The anti-microbial compositions of the invention do not contain materials that produce highly persistent residues or rinsates or products that contain heavy metals and their salts.
15 Thus, there is a greatly reduced risk of long term hazards.

- The anti-microbial compositions of the invention do not interfere with the biochemical reproductive pathways of the micro-organisms they control. The risk of resistance build up and the development of resistant strains is, therefore, low.
20

- The anti-microbial compositions of the invention can have a dual effect in that not only do they provide an anti-microbial effect in use but they can also have a preservative effect on the composition. This means that it is typically not necessary to include additional preservatives in the formulations of the invention.
25

- The compositions of the invention do not typically give surfaces to which they are applied a greasy feel.

- According to a further aspect of the invention, there is provided the use of composition of
30 the invention to control, reduce or prevent the formation of colonies of micro-organisms on a surface at which it is provided.

- The present invention provides a method for providing a residual antimicrobial benefit to a surface such as a hard surface or skin, which method comprises applying a composition
35 as defined herein to that surface or skin. The composition may, for example, be applied to the surface or skin by spraying the composition on the surface or wiping the composition onto the surface or skin. In one method of the invention, it is not necessary for the method

to include any steps in addition to simply applying the composition to the surface. Thus, a method that consists essentially of or consists of applying the composition to the surface or skin is provided.

- 5 In an aspect of the invention, the surface to which the composition of the invention is applied is a surface of the body, such as skin.

The anti-microbial compositions of the invention can typically degrade when submersed in water, to provide a rinsate/leachate of low toxicity and which has a short residence time in
10 the environment.

According to a further aspect of the invention, there is provided the use of an anti-microbial composition of the invention to reduce or prevent the formation of colonies of microorganisms on a surface at which it is provided, such as skin.

15

The anti-microbial compositions of the invention are typically made by a process as described below.

A process for preparing an anti-microbial composition as herein described comprising:

- 20 (i) combining component (iii) and component (ii) with stirring; and
(ii) adding component (i) to components (iii) and (ii).

In some aspects, the pH of the solution obtained after step (ii) may require adjusting. Therefore, the present invention also describes a process in which (iii) the pH of the
25 solution is adjusted after step (ii).

Preferences and options for a given aspect, feature or parameter of the invention should, unless the context indicates otherwise, be regarded as having been disclosed in combination with any and all preferences and options for all other aspects, features and
30 parameters of the invention.

The invention will now be illustrated by the following non-limiting Examples.

35

Example 1 - Preparation of Test Samples and Controls

The compositions as described in Table 1 were prepared using the method of Example

- 5 1. The commercially available compounds used in the compositions are listed below.

Aminat G is a 20% solution of N-lauroyl-L-arginine ethyl ester mono hydrochloride in glycerine, supplied by Seppic. Its principal component is a salt of a derivative of the amino acid L-arginine.

10

AH Care L65 is an amphoteric hydroxy complex, containing an amino acid, arginine and lactic acid. It is supplied by BASF. Both *Aminat G* and *AH Care L65* are commercial examples that contain component (i) of the invention.

- 15 *Acticide DDQ 40* supplied by Thor contains 40% *di-n-decyldimethyl ammonium chloride* (DDAC). This is an example of component (ii) of the invention, being of Formula Type A.

Acticide BAC 50M supplied by Thor contains 50% *Benzalkonium chloride* (BAC) is also an example of component (ii) of the invention, being of Formula Type B.

20

Chlorhexidine di-gluconate (CHDG), supplied by Evonik as a 20% solution is a further example of component (ii) of the invention.

- 25 *Benzethonium Chloride USP* supplied by Lonza is a Benzalkonium derivative and contains 100% Diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride (BENZ) otherwise known as Benzethonium Chloride. It is a further example of component (ii) of the invention.

- 30 The polar solvent (component (iii)) was placed in a suitably sized vessel (typically of 1 litre capacity). A small amount of the polar solvent was retained to allow for final weight adjustment. The required amount of the biocide(s) (component (ii)), was then added to the vessel, with the vessel being stirred for 5 minutes after addition of each biocide before the next biocide is added. The required amount of the amino acid, derivative or salt (component (i)) was then added and the vessel stirred for a further 5 minutes. The
- 35 pH was checked and was adjusted using lactic acid or sodium hydroxide solution if required. The solution was then made up to 100% by weight by adding the retained polar solvent and stirred for a final 10 minutes.

The Control Samples were prepared following the same method but by leaving out one or more of the components (i), (ii) or (iii) of the invention.

In Table 1 the % weights of compositional components (i) of the invention, Aminat G and AH Care L65, refers to the amount of the commercially available material and the % weights of component (ii) of the invention refers to the amount of the active chemical component, namely DDAC-*di-n-decyldimethyl ammonium chloride*; CHDG-*Chlorhexidine digluconate*; BENZ-*Benzethonium Chloride*; or BAC-*Benzalkonium Chloride*.

10

Table 1

Composition	Compositional component (i) of the invention		Compositional component (ii) of the invention		Compositional component (iii) of the invention	
	Components	% by weight	Components	% by weight	Components	% by weight
Formulation 1	Aminat G	0.25	DDAC CHDG	0.10 0.10	Water	99.55
Formulation 2	Aminat G	0.25	DDAC BAC	0.10 0.10	Water	99.55
Formulation 3	AH Care L65	0.50	DDAC CHDG	0.10 0.10	Water	99.30
Control 1	-	-	DDAC	0.20	Water	99.80
Control 2	Aminat G	0.25	-	-	Water	99.75
Control 3	-	-	DDAC CHDG	0.10 0.10	Water	99.80
Control 4	-	-	DDAC BAC	0.10 0.10	Water	99.80
Control 5	AH Care L65	0.5	-	-	Water	99.50
Control 6	Aminat G	0.25	DDAC	0.20	Water	99.55
Control 7	Aminat G	0.25	BAC	0.20	Water	99.55
Control 8	-	-	CHDG	0.20	Water	99.80
Control 9	Aminat G	0.25	CHDG	0.20	Water	99.55
Control 10	AH Care L65	0.5	DDAC	0.20	Water	99.30
Control 11	AH Care L65	0.5	CHDG	0.20	Water	99.30
Control 12	-	-	DDAC CHDG	0.10 0.10	Water	99.80

Example 2 - Evaluation of Residual Anti-microbial Efficacy of Test Samples

25 micro litres (0.025ml) of test sample was applied to a 2cm x 2cm section of Vitro-Skin (as supplied by IMS, Inc.) in duplicate in a Petri dish. The test sample was spread on the vitro-skin® surface with a sterile inoculation loop ensuring that approximately a 0.5 cm perimeter was left untreated to the edge. The test sample was allowed to dry on the vitro-skin®*₂ at 20°C in an oven with the Petri dish lid left off for one hour. The Petri dish was then removed from the oven and a strip of polypropylene wipe saturated with a sterile

tryptone/saline solution placed inside. The lid was closed and then placed back in the oven for 4 hours at 20°C. After this time the Petri dish was removed from the oven and 10ul of a $1-1.5 \times 10^8$ cfu/ml. suspension of *E. coli* K12*, prepared in tryptone/saline solution was added to the surface of the vitro-skin® containing the test sample and spread with a sterile
5 inoculation loop ensuring the suspension stayed within the treated area of the vitroskin. The bacterial suspension was left in contact with the vitroskin for 5 minutes. After this time the vitro-skin® was removed from the petri dish and placed in a test tube containing 10ml of neutralisation solution. It was shaken gently and left for a further 5 minutes after which the tube was vortex mixed for 1 minute to recover the bacteria from the surface of the
10 vitroskin. A 1 ml sample of this suspension was then plated with tryptone soya agar and incubated for 48 hours at 37°C. After this time the log reduction in *E. coli* K12 was calculated by comparison with the water-treated control.

*₁ NB. *E. coli* K12 suspension prepared from a '2a' culture grown on tryptone soya agar
15 for 24 hours at 37 °C, as described in BS EN microbiology standards e.g. EN1276:2009)

*₂ vitro-skin® is a testing substrate that mimics the surface properties of human skin. It is a synthetic non-biological product that has been formulated to have topography, pH, critical surface tension and ionic strength that are similar to human skin. It is a well-known and used substrate for those trained in the art to evaluate the benefits of topological
20 applications of skin-care products to skin, which includes the evaluation of biocidal efficacy of actives applied to skin. Examples of published, peer-reviewed work with vitro-skin include US 20090202463 A1 which describes a method for evaluating antimicrobial compositions that provide enhanced immediate and residual anti-viral and antibacterial efficacy on the surface of skin; evaluation of the efficacy of organic acids in Hand
25 Cleansers for the prevention of rhinovirus infections as described in the Journal of Antimicrobial Agents and Chemotherapy; 48(7); 2004 July; 2595-2598; US 20120141396 A1 describes disinfectant compositions that provide a prolonged antimicrobial property to a variety of surfaces, including skin, evaluated using vitro-skin.

30 Results of Example 2

Formulation 1

Formulation 1 and Control Samples 1, 2, 3 6, 8 & 9 were made to the compositions
35 described in Table 1 following the method described in Example 1. Samples of Formulation 1 and the Control Samples were then tested for anti-microbial efficacy using the method described in Example 2. The results of these tests are shown in Table 2 below.

Table 2

Composition	Log R E.coli K12	Standard error
Formulation 1	4.58	0.26
Control 1	2.98	0.06
Control 2	Tntc*	-
Control 3	2.64	0.04
Control 6	3.54	0.00
Control 8	Tntc*	-
Control 9	Tntc*	

*Tntc=too numerous to count

The results in table 2 show that the composition of the invention, namely DDAC combined with CHDG and Aminat G has superior anti-microbial performance compared to Control 3 that does not have Aminat G (component (i) of the invention).

Formulation 1 also has superior anti-microbial performance compared to Controls 6 and 9 which are DDAC and CHDG used individually with Aminat G respectively, and Controls 1 and 8 which are DDAC and CHDG used individually without Aminat G respectively.

Control 2 shows that Aminat G has no anti-microbial activity.

Formulation 2

Formulation 2 and Control Samples 1, 2, 4, 6 & 7 were made to the compositions described in Table 1 following the method described in Example 1. Samples of Formulation 2 and the Control Samples were then tested for anti-microbial efficacy following the method described in Example 2. The results of these tests are shown in Table 3 below.

Table 3

Composition	Log R E.coli K12	Standard error
Formulation 2	3.88	0.04
Control 1	2.98	0.06
Control 2	Tntc*	-
Control 4	1.88	0.02
Control 6	3.54	0.00
Control 7	2.42	0.12

*Tntc=too numerous to count

The results in table 3 show that the composition of the invention, namely DDAC combined with BAC and Aminat G has superior anti-microbial performance compared to Control 4 that does not have Aminat G (component (i) of the invention).

Formulation 2 also has superior anti-microbial performance compared to Controls 6 and 7 which are DDAC and BAC used individually with Aminat G respectively, and Control 1 which is DDAC used alone without Aminat G.

- 5 Control 2 shows that Aminat G has no anti-microbial activity.

Formulation 3

- 10 Formulation 3 and Control Samples 5, 10, 11 & 12 were made to the compositions described in Table 1 following the method described in Example 1. Samples of Formulation 3 and the Control Samples were then tested for anti-microbial efficacy following the method described in Example 2. The results of these tests are shown in Table 4 below.

Table 4

Composition	Log R E.coli K12	Standard error
Formulation 3	>5.22	0.00
Control 12	2.48	0.03
Control 5	Tntc*	-
Control 10	2.75	0.25
Control 11	Tntc*	-

*Tntc=too numerous to count

- 15 The results in table 4 show that the composition of the invention, namely DDAC combined with CHDG and AH Care L65 has superior anti-microbial performance compared to Control 12 that does not have AH Care L65 (component (i) of the invention).
- 20 Formulation 3 also has superior anti-microbial performance compared to Controls 10 and 11 which are DDAC and CHDG used individually with AH Care L65 respectively.

Control 5 shows that AH Care L65 has no anti-microbial activity.

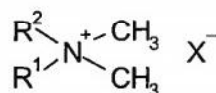
25

Claims

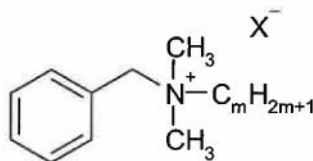
1. An anti-microbial composition comprising:

- (i) an amino acid component which is arginine, N-Lauroyl-L-arginine ethyl ester, arginine lactate or N-Lauroyl-L-arginine ethyl ester monohydrochloride or a mixture thereof;
- (ii) an anti-microbial component consisting of at least one anti-microbial quaternary ammonium compound and chlorhexidine or a chlorhexidine salt and optionally an additional anti-microbial component (b) selected from polymeric biguanidines, silver, octenidine HCl, amphoteric compounds, iodophores, isothiazalones, nitro bromopropanes, nitrogen based heterocyclic compounds, alkyl betaines, alkyl amine oxides, anionic amino acid based surfactants and amine anti-microbial agents and mixtures thereof; and
- (iii) a polar solvent;

wherein the anti-microbial quaternary ammonium compound is at least one compound of formula (A)



wherein R_1 and R_2 are each independently a straight chain, un-substituted and uninterrupted C_{8-12} alkyl group and X^- is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, carbonate or bicarbonate and/or at least one benzalkonium compound of formula (B)



wherein m is from 8 to 18 and X^- is a halide anion such as chloride, bromide, fluoride, iodide or sulphonate, saccharinate, carbonate or bicarbonate; and/or benzethonium chloride.

2. A composition according to any one of the preceding claims, wherein the chlorhexidine is chlorhexidine di-gluconate.

3. A composition according to any one of the preceding claims, wherein the benzalkonium compound of formula (B) is benzyldimethyl-n-tetradecyl-ammonium chloride, benzyldimethyl-n-dodecyl-ammonium chloride, benzyl-C₁₂-C₁₆-alkyl-dimethyl-ammonium chloride, diisobutylphenoxyethoxyethyl-dimethylbenzyl ammonium chloride (otherwise known as Benzethonium Chloride) or benzyl-cocoalkyl-dimethyl-ammonium chloride and/or the compound of formula (A) is di-n-decyldimethyl ammonium chloride, octyl decyl dimethyl ammonium chloride or dioctyl dimethyl ammonium chloride.
4. A composition according to any one of the previous claims, wherein the anti-microbial quaternary ammonium compound is selected from the group consisting of di-n-decyldimethyl ammonium chloride (DDAC), benzalkonium chloride (BAC), and benzethonium chloride (BENZ).
5. A composition according to any one of the preceding claims, wherein the anti-microbial component (ii) comprises (a) chlorhexidine or a chlorhexidine salt and (b) di-n-decyldimethyl ammonium chloride and/or a benzalkonium chloride of formula (B).
6. A composition according to claim 5, comprising benzalkonium chloride of formula (B) wherein m is 8, 10 or 12.
7. A composition according to any one of the preceding claims comprising a quaternary ammonium compound of CAS number 7173-51-5 and/or 68424-85-1.
- 8.. A composition according to any one of the preceding claims, wherein the amount of component (i) is from 0.0005 to 10% by weight of the composition.
9. A composition according to claim 8, wherein the amount of component (i) is from 0.005 to 5% by weight of the composition.
10. A composition according to claim 9, wherein the amount of component (i) is from 0.01 to 1% by weight of the composition.
11. A composition according to any one of the preceding claims, wherein the total amount of component (ii) and component (b) if present is from 0.001 to 10% by weight of the composition.

12. A composition according to claim 11, wherein the total amount of component (ii) and component (b) if present is from 0.005 to 5% by weight of the composition.
- 5 13. A composition according to claim 12, wherein the total amount of component (ii) and component (b) if present is from 0.01 to 1% by weight of the composition.
14. A composition according to any one of the preceding claims, wherein the pH of the composition is from 4.5 to 8.
- 10 15. A composition according to any one of the preceding claims, wherein the composition further comprises a complexing agent.
- 15 16. A composition according to claim 15, wherein the complexing agent is selected from EDTA (Ethylenediaminetetraacetic acid), Gluconate, GLDA (Glutamic acid diacetic acid), EDDS (Ethylenediamine-N,N'-disuccinic acid), DPTA (Diethylene triamine pentaacetic acid), HEDTA (Hydroxyethyl-ethylenediamine triacetic acid), MGDA (Methyl glycine diacetic acid), PDTA (1,3-propylenediaminetetraacetic acid), and EDG (Ethanoldiglycineic acid) and mixtures thereof.
- 20 17. A composition according to any one of the preceding claims, wherein the polar solvent is selected from water, ethanol, n-propanol, isopropanol, ethylene glycol ethers, propylene glycol ethers, butyl diglycol (BDG) and dipropylene glycol methyl ether (Trade name Dowanol DPM) and mixtures thereof.
- 25 18. A composition according to claim 16 or 17, wherein the composition is free of alcohol.
- 30 19. A composition according to any one of the preceding claims, wherein the salt of the amino acid or amino acid derivative is not a phosphate salt or a phosphorus containing salt.
20. A composition according to any one of the preceding claims for use in reducing or controlling the formation of microbial colonies on or at a surface.
- 35 21. A composition according to any one of claims 1 to 20 for use to reduce or control the formation of microbial colonies on the skin or a wound.

22. A composition according to any one of claims 1 to 20 for use to reduce or control the formation of biofilms on the skin or a wound.
- 5 23. A composition according to any one of claims 1 to 20 for use to disrupt, prevent or reduce the adhesion and/or attachment of micro-organisms to the skin or a wound.
- 10 24. A personal care or personal hygiene product comprising an anti-microbial composition as defined in any one of claims 1 to 20 or a composition for use as defined in any one of claims 21 to 23.
- 15 25. A hand sanitizer comprising an anti-microbial composition as defined in any one of claims 1 to 20 or a composition for use as defined in any one of claims 21 to 23.
- 20 26. A wound care product comprising an anti-microbial composition as defined in any one of claims 1 to 20 or a composition for use as defined in any one of claims 21 to 23.
27. An anti-microbial wipe comprising a substrate and an anti-microbial composition as defined in any one of claims 1 to 20 or a composition for use as defined in any one of claims 21 to 23.
- 25 28. A pet product comprising an anti-microbial composition as defined in any one of claims 1 to 20 or a composition for use as defined in any one of claims 21 to 23.
29. The use of a composition according to any one of claims 1 to 20 to reduce or control the formation of microbial colonies on or at a hard surface.
- 30 30. Use of claim 29 to reduce or control the formation of biofilms.
- 35 31. A method of reducing or controlling the formation of microbial colonies on or at a hard surface, which method comprises applying a composition according to any one of claims 1 to 20 to that surface.
32. A method according to claim 31 to reduce or control the formation of biofilms.

33. A method of disrupting, preventing or reducing the adhesion and/or attachment of micro-organisms to a hard surface, which method comprises applying a composition according to any one of claims 1 to 20 to that surface.



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(57) Abstract: This invention relates to anti-microbial compositions comprising: an amino acid, a derivative of an amino acid, a salt of an amino acid, a salt of a derivative of an amino acid or mixtures thereof; an anti-microbial component comprising two or more anti-microbial quaternary ammonium compounds, or at least one anti-microbial quaternary ammonium compound and chlorhexidine or a salt thereof; and a polar solvent, and to formulations including the anti-microbial compositions. In particular, the invention relates to anti-microbial compositions that can be used on skin.