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(54) Title: ECO-FRIENDLY NON-AQUEOUS ANTIMICROBIAL COMPOSITION COMPRISING HINOKITOL WITH 1,3-PROPANEDIOL AND/OR SORBITAN CAPRYLATE

(57) Abstract: Disclosed herein is an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising (a) about 0.1 to 20.0 wt% of a Hinokitol; and (b) about 80.0 to 99.9 wt% of bio-derived 1,3-propanediol and/or bio-derived sorbitan caprylate. Also disclosed is a process for preparing and method of using the composition. In accordance with another aspect of the present application, the eco-friendly, nonaqueous antimicrobial composition is capable of inhibiting or killing gram (+) bacteria, gram (-) bacteria, yeasts and/or fungi.



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**ECO-FRIENDLY NON-AQUEOUS ANTIMICROBIAL COMPOSITION
COMPRISING HINOKITOL WITH 1,3-PROPANEDIOL AND/OR SORBITAN
CAPRYLATE**

FIELD OF THE INVENTION

[0001] The present application relates to an antimicrobial composition, and more particularly, to an eco-friendly antimicrobial composition comprising hinokitol and a solvent selected from 1,3-propanediol and/or sorbitan caprylate.

BACKGROUND OF THE INVENTION

[0002] Preservatives are employed in various non-limiting industrial applications including personal care, household, coatings, metalworking fluids, paper, wood, plastics, disinfection, cosmetics, toiletry, pharmaceuticals, food, beverages, oral care, paints, and water treatment to prevent microbial contamination, of which, the personal care products engage significant amount of preservatives. It is mandatory on the part of formulators to give due consideration for product safety and environmental impact of the ingredients of the composition that they develop.

[0003] The prior art discloses use of a variety of glycols for preparing preservative or antimicrobial compositions. Sometimes glycols *per se* are used as a preservative component. In many laboratories ethylene glycol has replaced formaldehyde to preserve organisms. However, the use of ethylene glycol is limited in food and personal care industries due its toxicity. So, there is a necessity to replace ethylene glycol with a solvent which is non toxic. The limitation of ethyleneglycol is partly addressed by chemically synthesized propylene glycol which has been widely used in many applications such as food, cosmetics, personal care, bakery, etc. Such compositions comprising chemically synthesized propylene diols were found to have an irritation potential, and harmful and toxic impurities produced from the chemical processes used to synthesize it.

[0004] Further, the use of diols, glycols and alcohols for preserving cosmetic, dermatological or pharmaceutical, personal care, household, disinfection, toiletry, food, beverages, oral care is limited by statutory regulatory instruments. Countries often have maximum concentration ranges to be employed in their respective approved regulated products. Additionally, the lowering of viscosity is observed with usage of higher percentage

of solvents like alcohols in the end-user applications, thus, there is a limitation to employ higher concentration levels of alcohols.

[0005] To protect end-users against the microbial attack and from the side effects of excessive use levels of antimicrobial active ingredients, it is beneficial to have reduced concentration levels of hinokitiol, an antimicrobial active of the present application. In this regard, mild and harmless efficacy enhancers of hinokitiol could render the opportunity of decreasing the use concentration levels of hinokitiol, an antimicrobial agent.

[0006] US Patent Publication No. 20110086918 discloses a composition having effective broad spectrum preservation activity comprising benzyl alcohol, salicylic acid, sorbic acid, and a compound selected from the group consisting of 1,3-propanediol, glycerin and combinations thereof.

[0007] US Patent Publication No. 20080176957 discloses a preservative compositions comprising 1,3-propanediol, wherein the 1,3-propanediol in said composition has a bio-based carbon content of about 1% to 100%. In addition, it is preferred that the 1,3-propanediol be biologically-derived, and wherein upon biodegradation, the biologically-derived 1,3-propanediol contributes no anthropogenic CO₂ emissions to the atmosphere.

[0008] US Patent Publication No. 20120100085 discloses liquid compositions which contain (a) from 5 to 95% by wt of sorbitan monocaprylate and (b) from 5 to 95% by weight of one or more alcohols of formula (1) R--OH, and wherein the liquid compositions are suitable for the production of cosmetic, dermatological or pharmaceutical products.

[0009] WO2010127227 discloses cleanser compositions suitable for application to the skin and ocular surface comprising linalool, hinokitiol and an alcohol. The alcohol can be a diol, such as a glycol. Exemplary glycols include propylene glycol, and ethylene glycol and dipropylene glycol. The cleanser compositions of the invention may further comprise decylglucoside, sodium trideceth sulfate, cocamidopropyl betaine, dipropylene glycol or mixtures thereof.

[0010] US Patent Publication No. 20120101135 discloses liquid compositions which contain (a) from 40 to 99.9% by wt of sorbitan monocaprylate and (b) from 0.1 to 60% by wt of one or more antimicrobial substances selected from the group consisting of the components (b1) to (b5): (b1) specific organic acids and the salts thereof, (b2) specific

formaldehyde donors, (b3) specific isothiazolinones, (b4) specific paraben esters and the salts thereof, and (b5) specific pyridones and the salts thereof. The liquid compositions are suitable for the production of cosmetic, dermatological or pharmaceutical products.

[0011] In view of foregoing, there remains a need for an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising a solvent which is free from toxins, non-irritant for the skin, and preferably acceptable by various regulatory authorities around the globe.

[0012] Accordingly, it is a primary objective of the present application to provide an antimicrobial composition which is capable of providing effective antimicrobial activity at lower use levels of antimicrobial agent in the presence of said solvent or solvent system, *i.e.*, 1,3- propanediol and/or sorbitan caprylate.

[0013] Another objective of the present application is to provide an antimicrobial composition comprising lower concentration levels of solvents such as alcohols in order to limit the impact on the viscosity of the end user products.

[0014] It is a further objective of the present application to provide an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising (i) hinokitiol; (ii) 1,3-propanediol, a bio-derived solvent; and/or (iii) sorbitan caprylate, a bio-derived solvent.

SUMMARY OF THE INVENTION

[0015] The present application relates to an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising (i) about 0.1 wt% to about 20.0 wt% of a Hinokitiol; and (ii) about 80.0 wt% to about 99.9 wt% of 1,3-propanediol, a bio-derived solvent and/or sorbitan caprylate, a bio-derived solvent.

[0016] In accordance with certain aspects, an eco-friendly non-aqueous antimicrobial composition is provided that is capable of withstanding heat and cold exposure, wherein the composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

[0017] In accordance with another aspect of the present application, the eco-friendly, non-aqueous antimicrobial composition is capable of inhibiting or killing gram (+) bacteria, gram

(-) bacteria, yeasts and/or fungi. The microorganisms of the present application are selected from the group including but are not limited to *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, *Staphylococcus aureus*, *Burkholderia cepacia*, *Aspergillus brasiliensis*, *Penicillium expansum*, *Trichoderma viride* and/or *Candida albicans*.

[0018] In yet another aspect, the eco-friendly, non-aqueous antimicrobial composition of the present application is capable of demonstrating effective synergistic antimicrobial activity against bacteria, fungi and yeast in the presence of 1,3-propanediol, sorbitan caprylate alone or in combination.

[0019] In yet another aspect, the eco-friendly, non-aqueous antimicrobial composition of the present application is employed in the field of cosmetic, toiletry, personal care, household, cleaning, disinfecting, food, beverages, enzyme formulations, feminine care products, foot care products, pet care products, food ingredients, paints, coatings, metal working fluids, nutrients for plants and/or laundry products.

[0020] In accordance with another aspect of the present application, a process for preparing an eco-friendly, non-aqueous and stable antimicrobial solution composition comprises the steps of: (i) preparing a mixture of (a) about 0.1 wt% to about 20.0 wt% of hinokitiol; and (b) about 80.0 wt% to about 99.9 wt% of 1,3-propanediol and/or sorbitan caprylate, a bio-derived solvent; and (ii) heating the mixture of step (i) at about 40°C to yield a homogenous non-aqueous antimicrobial solution.

DETAILED DESCRIPTION OF THE INVENTION

[0021] While this specification concludes with claims particularly pointing out and distinctly claiming that which is regarded as the invention, it is anticipated that the invention can be more readily understood through reading the following detailed description of the invention and study of the included examples.

[0022] The singular forms "a," "an," and "the" include plural forms unless the context clearly dictates otherwise specified or clearly implied to the contrary by the context in which the reference is made. By the term "comprising" herein is meant that various optional, compatible components can be used in the compositions herein, provided that the important ingredients are present in the suitable form and concentrations. The term "comprising" thus encompasses and includes the more restrictive terms "consisting of" and "consisting

essentially of" which can be used to characterize the essential ingredients such as hinokitiol, 1,3-propanediol and/or sorbitan caprylate of the composition.

[0023] All percentages, parts, proportions and ratios as used herein, are by weight of the total composition, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the raw material level.

[0024] All references to singular characteristics or limitations of the present invention shall include the corresponding plural characteristic or limitation, and *vice-versa*, unless otherwise specified or clearly implied to the contrary by the context in which the reference is made.

[0025] The term "about" can indicate a difference of 10 percent of the value specified. Numerical ranges as used herein are meant to include every number and subset of numbers enclosed within that range, whether particularly disclosed or not. Further, these numerical ranges should be construed as providing support for a claim directed to any number or subset of numbers in that range.

[0026] As used herein, the words "preferred," "preferably" and variants refer to embodiments of the invention that afford certain benefits, under certain circumstances. However, other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the invention.

[0027] References herein to "one embodiment", "one aspect" or "one version" or "one objective" of the invention include one or more such embodiment, aspect, version or objective, unless the context clearly dictates otherwise.

[0028] All publications, articles, papers, patents, patent publications, and other references cited herein are hereby incorporated herein in their entireties for all purposes to the extent consistent with the disclosure herein.

[0029] As used, herein, "stable" and "stability" mean a composition which is significantly unaffected in chemical nature, physical homogeneity and/or color upon exposure to conditions reasonably expected to be incurred in transport, storage and use. Stability may be

determined either by empirical observation or by suitable methods of chemical and/or physical examination that would be known to one skilled in the art.

[0030] The term “eco-friendly” as used herein refers to antimicrobial composition comprising naturally-derived or nature-identical non toxic biodegradable ingredients. Further, the term "environmentally friendly" also means, without limitation, no adverse affect on the environment. More particularly, environmentally friendly, (also known as eco-friendly, nature friendly, and green) used to refer to goods and services, laws, guidelines and policies considered to inflict minimal or no harm on the environment or may rebuild or renew resources through their use.

[0031] The term “bio-derived” means produced or generated from a living organism such as one or more strains of bacteria, fungi, yeast and other microbial strains or from a plant or part of a plant through enzymatic reactions and/or simple chemical processes as they occur in nature.

[0032] The term "nature-identical compound" means a compound which has a chemical structure identical to that found in nature. The “nature-identical compound” includes synthetic compounds having the same chemical structure, regioisomeric form and stereo isomeric form as compounds produced by either a plant or animal origin.

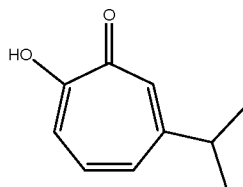
[0033] As used herein, in reference to the compositions of the present application, the term "non-aqueous" means significantly free of water. Water is not purposely added to the compositions of the present application, and no effort has been made to exclude or remove small amount of water from the ingredients used in the compositions.

[0034] The term “sorbitan caprylate” and “sorbitan monocaprylate” is synonymously used in this specification and both the terms would refer to the same compound.

[0035] What is described herein is an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising (i) about 0.1 wt% to about 20.0 wt% of Hinokitiol; and (ii) about 80.0 wt% to about 99.9 wt% of (a) 1,3-propanediol, a bio-derived solvent and/or (b) sorbitan caprylate, a bio-derived solvent.

[0036] The antimicrobial agent hinokitiol (2-Hydroxy-6-propan-2-ylcyclohepta-2,4,6-trien-1-one) of the present application may be obtained from extractions of essential oils derived

from plants, preferably plants of the family *Cupressaceae* such as Hinoki cypress or pine or cedar. The extraction, isolation and purification of hinokitiol from the appropriate plant raw materials can be carried out by the methods that are known for a person skilled in art. However, the hinokitiol for the present application is preferably derived from a synthetic route employing a synthetic route that is known in the prior art. Such laboratory synthesized nature identical compound can be purchased from commercial sources as well.



(a) Hinokitiol

[0037] Further, the term "hinokitiol" is a generic name for β -thujaplicin, one isomer of thujaplicin. The present application may also contain other isomers of hinokitiol such as α -thujaplicin, and γ -thujaplicin.

[0038] Hinokitiol is employed in the range of from about 0.1 wt% to 20.0 wt%. Other preferred ranges of hinokitiol would include, but are not limited to, 0.1 wt% to 0.5 wt%, 0.5 wt% to 1.0 wt%, 1.5 wt% to 2.0 wt%, 2.0 wt% to 2.5 wt%, 2.5 wt% to 3.0 wt%, 3.0 wt% to 3.5 wt%, 3.5 wt% to 4.0 wt%, 4.0 wt% to 4.5 wt% or 4.5 wt% to 5.0 wt%, 5.0 wt% to 5.5 wt%, 5.5 wt% to 6.0 wt%, 6.0 wt% to 6.5 wt%, 6.5 wt% to 7.0 wt%, 7.0 wt% to 7.5 wt%, 7.5 wt% to 8.0 wt%, 8.0 wt% to 8.5 wt%, 8.5 wt% to 9.0 wt%, 9.0 wt% to 9.5 wt%, 9.5 wt% to 10.0 wt%, 10 wt% to 11 wt%, 11 wt% to 12 wt%, 12 wt% to 13 wt%, 13 wt% to 14 wt%, 14 wt% to 15 wt%, 15 wt% to 16 wt%, 16 wt% to 17 wt%, 17 wt% to 18 wt%, 18 wt% to 19 wt%, 19 wt% to 20 wt%.

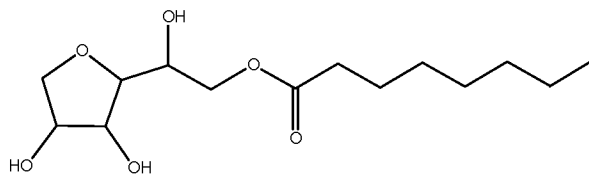
[0039] The 1,3-propane-diol (b) (i), an eco-friendly, naturally occurring bio-derived solvent for dissolving the hinokitiol of the present application is in the range of from about 80 wt% to 99.9 wt%. Other suitable or preferred ranges of 1,3-propane-diol would include but are not limited to 99 wt% to 98 wt%, 98 wt% to 97 wt%, 97 wt% to 96 wt%, 96 wt% to 95 wt%, 95 wt% to 94 wt%, 94 wt% to 93 wt%, 93 wt% to 92 wt%, 92 wt% to 91 wt%, 91 wt% to 90 wt%, 90 wt% to 89 wt%, 89 wt% to 88 wt%, 88 wt% to 87 wt%, 87 wt% to 86 wt%, 86 wt% to 85 wt%, 85 wt%, to 84 wt%, 84 wt% to 83 wt%, 83 wt% to 82 wt%, 82 wt% to 81 wt%, 81 wt% to 80 wt%. The said 1,3-propane-diol is prepared or manufactured according to the

procedures known in the prior art. For example, the 1,3-propane-diol can be prepared in accordance procedures and methods of US20070275139 assigned to Mellissa Joerger. For the purposes of the present invention the commercially available bio-derived 1,3-propanediol, for example Zemea[®], can be employed.



(b) (i) **1,3-Propanediol**

[0040] The sorbitan caprylate **(b) (ii)** is derived from renewable resources. It is eco-friendly, Ecocert-approved, non-listed preservative and can be used globally without regulatory limitations. Further, it has demonstrated literature on its boosting efficacy of classical preservatives such as organic acids, and aromatic alcohols. It is low odor, non-volatile liquid and does not add odor even at high concentration of use levels.



(b) (ii) **Sorbitan caprylate**

[0041] The sorbitan caprylate for dissolving the hinokitiol of the present application is in the range of from about 80 wt% to 99.9 wt%. Other suitable or preferred ranges of sorbitan caprylate would include but not limited to 99 wt% to 98 wt%, 98 wt% to 97 wt%, 97 wt% to 96 wt%, 96 wt% to 95 wt%, 95 wt% to 94 wt%, 94 wt% to 93 wt%, 93 wt% to 92 wt%, 92 wt% to 91 wt%, 91 wt% to 90 wt%, 90 wt% to 89 wt%, 89 wt% to 88 wt%, 88 wt% to 87 wt%, 87 wt% to 86 wt%, 86 wt% to 85 wt%, 85 wt%, to 84 wt%, 84 wt% to 83 wt%, 83 wt% to 82 wt%, 82 wt% to 81 wt%, 81 wt% to 80 wt%. The sorbitan caprylate is derived or manufactured according to the procedures known in the prior art for a person skilled in the art. For the purposes of the present invention the commercially available bio-derived sorbitan caprylate, for example Velsan[®] SC, can be employed.

[0042] According to one important embodiment of the invention, the eco-friendly, non-aqueous and stable antimicrobial solution composition comprising (i) about 0.1 wt% to about 20.0 wt% of a Hinokitiol; and (ii) about 80.0 wt% to about 99.9 wt% of 1,3-propanediol and

sorbitan caprylate, a bio-derived solvent, wherein said 1,3-propanediol and sorbitan caprylate is in the ratio of 1:10 to 10:1. However the preferred ratio of the present application would include but are not limited to 1:1, 1:2, 2:1, 1:3, 3:1, 1:4, 4:1, 1:5, 5:1, 1:6, 6:1, 1:7, 7:1, 1:8, 8:1, 1:9 or 9:1. Most preferred ratio is 1:1, 1:3 or 3:1.

[0043] According to one alternative embodiment of the present application, it is contemplated to employ other biodegradable and eco-friendly glycol based compounds as a suitable solvent for the present application comprising propylene glycol, 1,3-butylene glycol, and 2-methyl-1,3-propanediol.

[0044] As per an optional embodiment of the present application, it is contemplated to employ other sorbitan ester derivatives, such as sorbitan cocoate, diisostearate, dioleate, distearate, isostearate, laurate, oleate, olivate, palmitate, sesquiisostearate, sesquioleate, sesquisteate, stearate, triisostearate, trioleate and the like.

[0045] According to one optional embodiment of the present application, one or more antimicrobial agents is additionally employed in the said antimicrobial preservative composition, preferably in the concentration of 1% to 10% of the total composition. The preferred antimicrobial agents of the present application are selected from the group including, but not limited to, benzoic acid and sodium salt, propionic acid and its salts, salicylic acid and its salts, sorbic acid and its salts, formaldehyde, paraformaldehyde, biphenyl-2-ol (*o*-phenylphenol) and its salts, zinc pyrithione, chlorobutanol, 4-hydroxybenzoic acid its salts and esters, dehydroacetic acid and its salts, formic acid and its sodium salt, 3,3'-dibromo-4,4'-hexamethylene-dioxydibenzamidine, 3,3'-dibromo-4,4'-hexamethylenedioxydibenzamidine isethionate salt, thiomersal, phenylmercuric salts, undec-10-enoic acid and salts, hexetidine, 5-bromo-5-nitro-1,3 dioxane, bronopol, 2,4-dichlorobenzyl alcohol, triclocarban, 4-chloro-*m*-cresol, triclosan, 4-chloro-3,5-xyleneol, 3,3'-bis-(1-hydroxymethyl-2,5-dioximidazolidin-4-yl)-1,1'-methylenediurea, poly(1-hexamethylenebiguanide hydrochloride), 2-phenoxyethanol, hexamethylenetetramine, methenamine-3-chloroallylochloride, 1-(4-Chlorophenoxy)-1-(imidazol-1-yl)-3,3-dimethylbutan-2-one, 1,3-bis(hydroxymethyl)-5,5-dimethylimidazolidine-2,4-dione, benzyl alcohol, 1-hydroxy-4-methyl-6(2,4,4-trimethylpentyl)-2-pyridon and monoethanolamine salt, 6,6-dibromo-4,4-dichloro-2,2'-methylenediphenol, 4-isopropyl-*m*-cresol, mixture of 5-chloro-2-methyl-isothiazol-3(2H)-one (CMIT) and 2-methylisothiazol-3(2H)-one (MIT) with magnesium chloride and magnesium nitrate, 2-benzyl-4-chlorophenol (chlorophene), 2-

chloroacetamide, chlorhexidine digluconate, chlorhexidine diacetate, chlorhexidine dihydrochloride, 1-phenoxypropan-2-ol, alkyl (C₁₂-C₂₂) trimethyl ammonium, bromide and chloride, 4,4-dimethyl-1,3-oxazolidine, N-(hydroxymethyl)-N-(dihydroxymethyl-1,3-dioxo-2,5-imidazolinidyl-4)-N'-(hydroxymethyl) urea, hexamidine isethionate, hexamidine *p*-hydroxy-benzoate, glutaraldehyde (Pentane-1,5-dial), 5-ethyl-3,7-dioxa-1-azabicyclo [3.3.0] octane, 3-(*p*-chlorophenoxy)-propane-1,2-diol (chlorphenesin), sodium hydroxymethylamino acetate (sodium hydroxymethylglycinate), silver chloride deposited on titanium dioxide, benzethonium chloride, benzalkonium chloride, bromide and saccharinate, iodopropynyl butyl-carbamate (IPBC), diazolidinyl urea, imidazolidinyl urea, bromonitropropanediol and combinations thereof.

[0046] According to important embodiment of the invention, at least one UV-filter compound can be added to the eco-friendly, non-aqueous and stable antimicrobial solution composition of the present application. Such UV filter compounds can be selected from organic or inorganic compounds. The non-limiting organic UV filter compounds are selected from the group consisting of 2-ethylhexyl 2-cyano-3,3-diphenylacrylate (octocrylene), ethyl 2-cyano-3,3-diphenylacrylate; 4-methyl benzylidene camphor, 3-benzylidene camphor, camphor benzalkonium methosulfate, polyacrylamidomethyl benzylidene camphor, sulfo benzylidene camphor, sulphomethyl benzylidene camphor, terephthalylidene dicamphor sulfonic acid; ethylhexyl methoxycinnamate, ethoxyethyl methoxycinnamate, isoarnyl methoxycinnamate, cinnamic acid derivatives bond to siloxanes; *p*-aminobenzoic acid derivatives including *p*-aminobenzoic acid, 2-ethylhexyl *p*-dimethylarninobenzoate, N-oxypropylenated ethyl *p*-aminobenzoate, glyceryl *p*-aminobenzoate; benzophenones *e.g.* benzophenone-3, benzophenone-4,2,2',4,4'-tetrahydroxy-benzophenone, 2,2'-dihydroxy-4,4'-dimethoxybenzophenone; di-(2ethylhexyl)-4-methoxybenzalmalonate; organosiloxane compounds with chromophore groups like polysilicones-15, drometrizole trisiloxane; isopropylbenzyl salicylate, benzyl salicylate, butyl salicylate, ethylhexyl salicylate, isooctyl salicylate or homomethyl salicylate; ethylhexyl triazone, diethylhexyl butamido triazone, *bis*-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb® 5); 2,2'-methylene-bis-(6(2H-benzotriazole-2-yl)-4-(1,1,3,3,-tetramethylbutyl)-phenol (Tinosorb® M); encapsulated ethylhexyl methoxycinnamate or microcapsules loaded with UV-filters as revealed in EP1471995; 4-*tert*-butyl-4'-methoxydibenzoyl-methane, dimethoxydibenzoylmethane, isopropylidibenzoylmethane; 2,2-(1,4-phenylene)bis-(1H-benzimidazol4,6-disulfonic acid)

(Neoheliopan AP); 2-(4-diethylamino-2-hydroxybenzoyl)-benzoic acid hexylester; 2,4-bis-[5-1(dimethylpropyl)benzoxazol-2-yl-(4-phenyl)imino] -6-(2 -ethylhexyl)-imino-1,3,5-triazine.

[0047] The preferred list of UV filters for the present application is selected from the group including but not limited to 1-(4-Tert-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione; α -(2-oxoborn-3-ylidene) toluene-4-sulphonic acid and its salts; 2-cyano-3,3-diphenylacrylic acid, octocrylene; polymer of N-[(2 and 4)-[(2-oxoborn-3-ylidene) methyl] benzyl] acrylamide; octyl methoxycinnamate; ethoxylated-ethyl-1-aminobenzoate; isoamyl-*p*-methoxycinnamate; 2,4,6-Trianilino-(*p*-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine (Octyl triazone); phenol-2-2(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-1-(trimethylsilyl)oxy)-disiloxanyl)-propyl (Drometiazole Trisiloxane); benzoic acid, 4,4-((6-(((1,1-dimethylethyl)amino)carbonyl)phenyl)amino)-1,3,5-triazine-2,4-diyl)diimino)*bis*-, *bis*(2-ethylhexyl)ester); 4-methylbenzylidene camphor; 3-Benzylidene camphor; octyl salicylate; 4-dimethyl-aminobenzoate of ethyl-2-hexyl (octyl dimethyl PABA); 2-hydroxy-4-methoxybenzo-phenone-5-sulfonic acid and its sodium salt; 2,2'-Methylene-*bis*-6-(2H-benzotriazol-2-yl)-4-(tetramethyl-butyl)-1,1,3,3-phenol; Monosodium of 2-2'-*bis*-(1,4-phenylene)1Hbenzimidazole-4,6-disulphonic acid; (1,3,5)-Triazine-2,4-bis((4-(2-ethylhexyloxy)-2-hydroxy)-phenyl)-6-(4-methoxyphenyl).

[0048] Accordingly, the preferred inorganic UV filter compounds would include microparticulated Zinc oxide or Titanium dioxide and other known inorganic compounds that are readily available for a person skilled in the art.

[0049] In a preferred embodiment of this application, the eco-friendly, non-aqueous and stable antimicrobial solution composition further comprises sequestering or chelating agent in order to stabilize hinokitiol, an antimicrobial agent and wherein said sequestering or chelating is selected from the group comprising polyols, gluconates, sorbitals, mannitols, carbonates, hydroxamates, catechols, α -amino carboxylates, alkanolamines, metal-ion sequestrants, hydroxy-carboxylic acids, aminocarboxylic acids, amino polycarboxylic acids, polyamines, polyphosphates, phosphonic acids, crown ethers, amino acids, polycarboxylic acids, cyclodextrin, phosphonates, polyacrylates or polymeric polycarboxylates, condensed phosphates, However, the particular sequestering or chelating agents of the present invention would include but are not limited to acetic acid, adenine, adipic acid, ADP, alanine, alanine, albumin, arginine, ascorbic acid, asparagine, aspartic acid, ATP, benzoic acid, n-butyric acid, casein, citraconic acid, citric acid, cysteine, dehydracetic acid, desferri-ferrichrysin, desferri-

ferrichrome, desferri-ferrioxamin E, 3,4-dihydroxybenzoic acid, diethylenetriaminepentaacetic acid (DTPA), hydroxylpropylenediaminetetraacetic acid (DPTA), dimethylglyoxime, dimethylpurpurogallin, EDTA, formic acid, fumaric acid, globulin, gluconic acid and its alkali metal salts, glutamic acid, Tetra sodium glutamate diacetate, Tetrasodium Iminodisuccinate, glutaric acid, glycine, glycolic acid, glycylglycine, glycylsarcosine, guanosine, histamine, salicylic, pimalic and sulfamic acid, salicylic, glutaric, malonic acid, 1,10-phenanthroline, 2-pyridylacetic acid, 5-formylfuran sulfonic acid, N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid, itaconic acid, chelidonic acid, 3-methyl-1,2-cyclopentanedione, glycolamide, histidine, 3-hydroxyflavone, inosine, iron-free ferrichrome, isovaleric acid, itaconic acid, kojic acid, lactic acid, leucine, lysine, maleic acid, malic acid, methionine, methylsalicylate, nitrilotriacetic acid (NTA), nitrilotriacetic acid sodium salts (NTA salts), ornithine, orthophosphate, oxalic acid, oxystearin, phenylalanine, phosphoric acid, phytate, pimelic acid, pivalic acid, polyphosphate, proline, propionic acid, purine, pyrophosphate, pyruvic acid, riboflavin, salicylaldehyde, salicylic acid, sarcosine, serine, sorbitol, succinic acid, tartaric acid, tetrametaphosphate, thiosulfate, threonine, trimetaphosphate, triphosphate, tryptophan, uridine diphosphate, uridine triphosphate, n-valeric acid, valine, xanthosine, triethylenetetraaminehexaacetic acid, N,N'-bis(o-hydroxybenzyl) ethylenediamine-N,N' diacetic acid, ethylenebis-N,N'-(2-o-hydroxyphenyl)glycine, acetohydroxamic acid, desferroamine-B, disulfocatechol, dimethyl-2,3-dihydroxybenzamide, mesitylene catecholamide (MECAM), 1,8-dihydroxynaphthalene-3,6-sulfonic acid, and 2,3-dihydroxynaphthalene-6-sulfonic acid, siderophores molecules, N,N-dicarboxymethyl-2-aminopentanedioic-acid, diethylenetriaminepentaacetic-acid, ethylene-diaminetetraacetates e.g. Tetrasodium EDTA, nitriloacetates or N-(2-hydroxyethyl)nitrilodiacetates), Trisodium Ethylenediamine Disuccinate, 2,2-dichloropropionic acid, 2,2-dibromobutyric acid, trifluoroacetic acid, tribromoacetic acid, trichloroacetic acid, 2,3-dibromopropionic acid, 2,2-dichlorovaleric acid, 3-nitropropionic acid, triiodoacetic acid, 3(2,2,2-trichloroethoxy)propionic acid, 4-nitro-2-chlorobutyric acid, 2-bromo-2-nitropropionic acid, 2-nitroacetic acid, 2,4-dihydroxyphenyl acetic acid, 2,4-dichlorophenyl acetic acid, 3(2',4'-dibromophenoxy)propionic acid, 3(3',5'-dinitrophenoxy)propionic acid, 3-phenyl-2,3-dibromopropionic acid, 3,5-dinitrosalicylic acid, 3(3'-bromo-4'-nitrophenyl)propionic acid, 3(3',4'-dihydroxyphenyl)propionic acid alone or in combination. Further information on sequestering and chelating agents is disclosed in T. E. Furia, CRC Handbook of Food Additives, 2nd Edition, pp. 271-294 (1972), and M. S. Peterson and A. M. Johnson (Eds.), Encyclopedia of Food Science, pp. 694-699 (1978) are

incorporated herein by reference in its entirety. The most preferred metal-ions used to chelate with hinokitiol compound are selected from the group consisting of copper, ferrous, ferric, zinc, magnesium, calcium and manganese.

[0050] Apart from chelation, hinokitiol compound can be complexed with preferred metal ions and used for the purposes of the present application as disclosed in US Patent No. 7427316 assigned to DuPont the disclosure of which is hereby incorporated herein in its entirety.

[0051] One important embodiment of the present application is to provide an antimicrobial solution composition with eco-friendly nature. The composition of the present application provides enhanced compatibility with all cosmetic, toiletry, personal care, household, cleaning, disinfecting, food, beverages, enzyme formulations, feminine care products, foot care products, pet care products, food ingredients, paints, coatings, metal working fluids, nutrients for plants and/or laundry products.

[0052] In accordance with another embodiment of the present application, the antimicrobial composition is capable of inhibiting or killing microorganisms, bacteria, yeasts and fungi, molds or spores that are selected from a group including, but are not limited to, *Candida tropicalis*, *Candida albicans*, *Hansenula anomala*, *Saccharomyces cerevisiae*, *Torulaspora delbreuckii*, *Zygosaccharomyces bailii*, *Zygosaccharomyces rouxii*, *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Salmonella typhimurium*, *Salmonella enteritidis*, *Vibrio parahaemolyticus*, *Pseudomonas aeruginosa*, *Aspergillus niger*, *Aspergillus flavus*, *Penicillium islandicum*, *Penicillium citrinum*, *Penicillium chrysogenum*, *Fusarium oxysporum*, *Fusarium graminearum*, *Fusarium solani*, *Alternaria alternata*, and/or *Mucor racemosus*, *Penicillium funiculosum*, *Aureobasidium pullulans*, *Gliocladium riruns*, *Rhizopus javanicus*, *Penicillium notatum*, *Leuconostoc citreum*, and/or *Leuconostoc gelidium*. The preferred microorganisms of the present application is *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, *Staphylococcus aureus*, *Burkholderia cepacia*, *Aspergillus brasiliensis*, *Penicillium expansum*, *Trichoderma viride* and/or *Candida albicans*.

[0053] Further, the use levels of hinokitiol required for an adequate preservation of the desired products can be significantly decreased in combination with 1,3-propanediol and/or

sorbitan caprylate by their unexpected synergism. In so doing, the use of hinokitiol is often sufficient enough for the preservation of desired products.

[0054] The minimum inhibitory concentration (MIC) level of hinokitiol is reduced by 50% in presence of 1,3-propanediol (Zemea) against *Escherichia coli* and *Staphylococcus aureus*. Similarly, the sorbitan caprylate (Velsan SC) is able to reduce the MIC level of hinokitiol by 50% against *Escherichia coli*.

[0055] The following is a representative list of some of the numerous possible applications of the preservative antimicrobial composition. It should be understood that this list is presented for illustrative purposes only and does not represent any limitation as to possible applications.

[0056] (i) Cosmetic products: sunscreens; suntan lotions; after-sun gels, lotions and creams; antiperspirants; deodorants (solutions, powders, gels, roll-ons, sticks, sprays, pastes, creams, lotions); cleansing creams; skin conditioners; skin moisturizers; protectants; skin aging products; skin wrinkle reduction products; products for treatment of acne; products for treatment of rosacea; age-spot reduction products; stretch-mark reduction products; pimple treatment products, skin soothing products; skin infection and lesion treatment products; skin-redness reduction products; stretch-mark reduction products; varicose and spider-vein reduction products; lotions; oils; hand/body creams; shaving gels/creams; body washes; liquid and solid soaps; blood microcirculation improvement products, cellulite reduction products, body toning products, skin penetration enhancers; skin whitening products; cosmetics; shampoos; shower gels; bubble baths; hair treatment products, e.g., conditioning shampoos, medicated shampoos, mousses, waxes, conditioners, styling agents, lotions, pomades, spray gels, hair dyes and tints, colorant and non-colorant rinses, detangling lotions, hair curling and hair straightening products, hair wave products, hair styling gels, hair reparatives, hair tonics, hair fixatives, hair mousses, etc. hand (or mechanical) dishwashing compositions, hand sanitizers, disinfectants, lipsticks and lip balms, salves, collodion, impregnated patches and strips for skin treatment, skin surface implants, impregnated or coated diapers, moisturizing compositions, skin toners, skin cleansers, night creams, skin creams, shaving creams, skin care lotions, make-up, foundation, liquid, powder-based make-up, mascara, lipstick, blush, gloss, eye-liner, sunscreens, fragrances, massage oil, bath and shower gels, liquid soaps, moisturizing pressed powder formulations, bath additives, foaming soaps and body washes, sanitizing wipes, hand sanitizers, towelettes and wipes and the like. It

should be understood, based on this brief disclosure that a wide range of cosmetic and toiletry formulations can be benefitted from the compositions of the present application.

[0057] (ii) Dental care: mouthwash; dentifrice; dental floss coated and/or impregnated with the composition; protective coating for teeth; toothbrush bristles coated and/or impregnated with the composition; orthodontic appliance coated and/or impregnated with the composition; orthodontic appliance adhesive; denture appliance coated and/or impregnated with the composition; denture appliance adhesive; endodontic composition coated and/or impregnated with the composition; composite-type dental restorative materials; dental cement; dental liner; dental bonding agent; and the like.

[0058] (iii) Foods and food products: food-stuffs; animal feed-stuffs; grains; breads; bakery products; confectionary; potato products; pasta products; salads; soups; seasonings; condiments; syrups; jams, jellies and marmalades; dairy products; egg-based products; meats and meat-based products; poultry and poultry-based products; fish and fish-based products; crustaceans and crustacean-based products; fresh and dried fruit products; vegetables and vegetable products; greens; salads; sauces; beverages, e.g., wines, tea extracts, beers, juices; and the like.

[0059] (iv) Plastics and miscellaneous products, coated and/or impregnated with the composition, including: medical items, e.g., thermometers, catheters, surgical sutures, blood lines, implants, bandages, surgical dressings, surgical apparel, respirators, etc.; food packaging; drug and cosmetic packaging; eating utensils; shower curtains; bath mats; sponges; mops; toilet seats, rubber gloves; contact lenses; hearing aids; shelving paper; carpet pads; pool covers; animal bedding and cat litter; computer covers and computer keys; doorknobs; tampons and sanitary napkins; dental chairs; dryer sheets; dishcloths; paints and coatings; powdered, liquid, gel and spray cleaners for floors sinks, counter-tops, walls, tiles, floors, carpets; deodorizing liquids, solids, sprays, gels and powders; filters; foams; hair brushes; combs; diaper rash preventer; plasma bag treatment; disposable glove treatment; additive to pasteurized cow milk; additive to blood sample tubes to inactivate HIV, HCMV, and other viruses (safety measure for lab technicians and healthcare providers); additives for condoms, band-aids, or bandages; additive for paint; or animal or plant treatment for microbial infections; and the like.

[0060] (v) Fibers and fabrics coated and/or impregnated with the composition, including natural and synthetic fibers and fabrics manufactured from such fibers; wipes, cloths; surgical gauze; crib covers; bassinet covers; bed linens; towels and wash cloths; tents; draw sheets; cubicle curtains; shower curtains; wall coverings; wood and wood products; hospital clothing such as examination robes, physicians' coats, nurses uniforms, etc.; apparel; paper, non-woven fabric, knitted fabric, woven fabric, brick, stone, plastic, polymer, latex, metal, tile, walls, floors, gurneys, tables, or trays; shoes and the like.

[0061] (vi) Industrial products: Agricultural sector, pesticide preparations, polymer dispersions, adhesives, thickeners, paints, coatings, metal working, pigment dispersions, photographic materials.

[0062] (vii) Cleaning and disinfecting: It is contemplated that the preservative composition of the present application is useful for cleaning, disinfecting or inhibiting microbial growth on any hard surface. Examples of surfaces, which may be contacted with the composition of the invention are surfaces of process equipment used e.g. dairies, chemical or pharmaceutical process plants, water sanitation systems, oil processing plants, paper pulp processing plants, water treatment plants, and cooling towers. Additionally, the preservative composition be used for cleaning surfaces and cooking utensils in food processing plants and in any area in which food is prepared or served such as hospitals, nursing homes, restaurants, especially fast food restaurants, delicatessens and the like. It may also be used as a preservation agent or a disinfection agent in water based paints, microbial control of water lines, and for disinfection of water, in particular for disinfection of industrial water.

[0063] Suitable application forms for delivering the present antimicrobial preservative composition include, but are not limited to, emulsion, lotion, milk, fluid, cream, alcoholic or aqueous/alcoholic solution, liquid soap, shampoo, stick or makeup, stick, roll-ons, spray, pump-spray, aerosol, soap bar, powder, solution, gel, cream, balm, towelettes and wipes and lotion. However the preferred form for delivering the present composition is a solution.

[0064] One important embodiment discloses a process for preparing an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising the steps of: (i) preparing a mixture of (a) about 0.1 to 20.0 wt% of a hinokitiol; and (b) about 80.0 to 99.9 wt% of 1,3-propanediol and/or sorbitan caprylate, a bio-derived solvent; and (ii) heating the mixture of step (i) at about 40°C to yield a homogenous non-aqueous antimicrobial solution.

[0065] In yet another embodiment, the present application provides an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising: about 0.1 to 20.0 wt% of a Hinokitiol; and about 49.95 to 40.0 wt% of (i) 1,3-propanediol, a bio-derived solvent; and about 49.95 to 40.0 of (ii) sorbitan caprylate, a bio-derived solvent.

[0066] Another embodiment of the present application provides a method for inhibiting or killing microbial growth comprising mixing a effective amount of antimicrobial composition of the present invention with an appropriate product selected from the group consisting of cosmetic, toiletry, personal care, household, cleaning, disinfecting, food, beverages, enzyme formulations, feminine care products, foot care products, pet care products, food ingredients, paints, coatings, metal working fluids, nutrients for plants and/or laundry products, wherein, the effective amount of preservative composition is in the range of from about 0.01 wt% to about 25 wt% of the total composition. The other preferred effective amount of preservative composition ranges includes but not limited to 0.01 wt% to 5 wt%, 5 wt% to 10 wt%, 10 wt% to 15 wt%, 15 wt% to 20 wt% or 20 wt% to 25 wt%. The most preferred effective amount of preservative composition range is 0.01 wt% to 5 wt%.

[0067] Further, certain aspects of the present invention are illustrated in detail by way of the following examples. The examples are given herein for illustration of the invention and are not intended to be limiting thereof.

[0068] EXAMPLE 1: 1% Hinokitiol and 99% 1,3-propanediol or sorbitan caprylate

[0069] The antimicrobial solution composition is prepared by mixing (a) about 1.0 wt% of a hinokitiol; (b) about 99 wt% of a 1,3-propanediol or sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	1
1,3-Propane-diol or Sorbitan caprylate	99

[0070] EXAMPLE 2: 1% Hinokitiol and 99% 1,3-propanediol and sorbitan caprylate

[0071] The antimicrobial solution composition is prepared by mixing (a) about 1.0 wt% of a hinokitiol; (b) about 99 wt% of a 1,3-propanediol and sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	1
1,3-Propane-diol and Sorbitan caprylate (1:1 ratio)	99

[0072] EXAMPLE 3: 2% Hinokitiol and 98% 1,3-propanediol and sorbitan caprylate

[0073] The antimicrobial solution composition is prepared by mixing (a) about 2.0 wt% of a hinokitiol; (b) about 98 wt% of a 1,3-propanediol and sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	2
1,3-Propane-diol and Sorbitan caprylate (1:1 ratio)	98

[0074] EXAMPLE 4: 2% Hinokitiol and 98% 1,3-propanediol and sorbitan caprylate

[0075] The antimicrobial solution composition is prepared by mixing (a) about 2.0 wt% of a hinokitiol; (b) about 98 wt% of a 1,3-propanediol and sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution.

The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	2
1,3-Propane-diol and Sorbitan caprylate (3:1 ratio)	98

EXAMPLE 5: 2% Hinokitiol and 98% 1,3-propanediol and sorbitan caprylate

[0076] The antimicrobial solution composition is prepared by mixing (a) about 2.0 wt% of a hinokitiol; (b) about 98 wt% of a 1,3-propanediol and sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	2
1,3-Propane-diol and Sorbitan caprylate (1:3 ratio)	98

[0077] EXAMPLE 6: 2% Hinokitiol and 98% 1,3-propanediol or sorbitan caprylate

[0078] The antimicrobial solution composition is prepared by mixing (a) about 2.0 wt% of a hinokitiol; (b) about 98 wt% of 1,3-propanediol or sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	2
1,3-Propane-diol or Sorbitan caprylate	98

[0079] EXAMPLE 7: 3% Hinokitiol and 97% 1,3-propanediol and sorbitan caprylate

[0080] The antimicrobial solution composition is prepared by mixing (a) about 3.0 wt% of a hinokitiol; (b) about 97 wt% of a 1,3-propanediol and sorbitan caprylate and heating the resultant mixture at about 40°C to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	3
1,3-Propane-diol and Sorbitan caprylate (1:1 ratio)	97

[0081] EXAMPLE 8: 3% Hinokitiol and 97% 1,3-propanediol or sorbitan caprylate

[0082] The antimicrobial solution composition is prepared by mixing (a) about 2.0 wt% of a Hinokitiol; and (b) about 98 wt% of a 1,3-propanediol or sorbitan caprylate to yield a homogenous non-aqueous antimicrobial solution. The composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.

Antimicrobial Composition	wt %
Hinokitiol	3
1,3-Propane-diol or Sorbitan caprylate	97

[0083] EXAMPLE 9: Antimicrobial Activity (MIC study) for (1) Hinokitiol and 1,3-Propanediol, (2) Hinokitiol and sorbitan caprylate:

[0084] The antibacterial and antifungal studies were conducted for compositions of example 6 at concentrations ranging from 20ppm to 500ppm of the antimicrobial active (Hinokitiol) to obtain the Minimum Inhibitory Concentration (MIC) of the above said compositions, for the selected bacterial and fungal strains.

[0085] The individual concentrations of the test-product were weighed into sterile Erlenmeyer flasks and mixed with 100ml of an appropriate growth media at a maximum temperature of about 40 to 50°C. Equal amounts of mixtures were poured into four Petri dishes. After cooling, the Petri dishes were inoculated with the respective standard strains. During the experiment, the Petri dishes were kept for 2 to 3 weeks at room temperature of about 20 to 25°C in the dark. The following two different types of culture media were employed for the present studies:

- i. Bacteria-Agar: merchantable Caso - Agar
pH-Value: 7.3 ± 0.2
- ii. Fungi/Yeast-Agar: merchantable Malt extract - Agar (3%)
pH-Value: 5.6 ± 0.2

[0086] The preferred bacterial strains for the present application are *Pseudomonas aeruginosa* (DSM 1128), *Staphylococcus aureus* (DSM 799), *E. Coli* (DSM 1576), *Proteus mirabilis* (DSM 788) and *Burkholderia cepacia* (DSM 7288), and the preferred fungal strains are *Aspergillus brasiliensis* (DSM 1988), *Penicillium expansum* (DSM 1282), *Trichoderma viride* (DSM 63064), and the yeast is *Candida albicans*, (DSM 1386). After 2nd and 3rd weeks macroscopic evaluations were performed, the ratings are as follows:

Evaluation criteria for Bacteria and Yeast:

- +++ Strong growth
- ++ Growth
- + Slight growth
- No growth

Evaluation criteria for Fungi:

- +++ Petri dish completely overgrown
- ++ Petri dish 50% overgrown
- + Growth only at inoculation points
- No growth

[0087] The *formulation* under examination is considered to be efficient if the following conditions are duly fulfilled *i.e.* (i) after 2 - 3 weeks no growth of the tested culture is visible; (ii) with rising concentration of the tested formulation, the germ growth should

macroscopically be reduced until it is not visible any more. The obtained MIC levels are disclosed in Table 1 and 2.

[0088] Table 1: MIC levels for bacterial strains of Example 6:

Antimicrobial strain	MIC (ppm)		
	Hinokitiol	Hinokitiol + 1,3-Propandiol	Hinokitiol + Sorbitan caprylate
<i>Pseudomonas aeruginosa</i>	500	500	>500
<i>Escherichia coli</i>	100	50	50
<i>Staphylococcus aureus</i>	100	50	100
<i>Burkholderia cepacia</i>	500	500	>500

[0089] Table 2: MIC levels for fungal strains of Example 6:

Antifungal strain	MIC (ppm)		
	Hinokitiol	Hinokitiol + 1,3-Propandiol	Hinokitiol + Sorbitan caprylate
<i>Aspergillus brasiliensis</i>	100	100	100
<i>Trichoderma viride</i>	100	100	250

[0090] EXAMPLE 10: Antimicrobial study of Example 6 in hair gel product:

[0091] The preserved and non-preserved (control) hair gel products were weakly inoculated 4 times with 10^5 cfu/g and strongly inoculated once with 10^7 - 10^8 cfu/g of a bacterial and a fungal composite. The microbes inoculated products were preserved with 0.8%, 1.3%, 2.0% and 3.0% of the total composition of example 6. The hair gel products were evaluated several times for microbial counts at various days intervals after the first, the third and the fifth inoculation. The hair gel products were free of microbes 5 days after the first (weak) inoculation and 2 days after the fifth inoculation (strong). The unpreserved hair gel product was still heavily contaminated at the end of the 10 weeks of observation.

[0092] EXAMPLE 11: Antimicrobial study of Example 6 in cream product:

[0093] The preserved and non-preserved (control) hair gel products were weakly inoculated 4 times with 10^5 cfu/g and strongly inoculated once with 10^7 - 10^8 cfu/g of a bacterial and fungal strain. The microbes inoculated products were preserved at 0.8%, 1.3%, 2.0% and

3.0% of the total composition of example 6. The cream products were evaluated several times for microbial counts at different days intervals after the first, the third and the fifth inoculation. The cream products were free of microbes 5 days after the first (weak) inoculation and 5 days after the fifth inoculation (strong). The unpreserved (control) cream product was still heavily contaminated at the end of the 10 weeks of observation.

[0094] While this invention has been described in detail with reference to certain preferred embodiments, examples and explanations set forth herein are provided for illustrative purposes only, it should be appreciated that the present invention is not limited to those precise embodiments, examples and explanations. Rather, in view of the present disclosure, various modifications and variations would present themselves to those skilled in the art without departing from the scope and spirit of this application and scope of the appended claims.

We Claim:

1. An eco-friendly, non-aqueous and stable antimicrobial solution composition comprising:
 - a. about 0.1 to 20.0 wt% of a Hinokitiol; and
 - b. about 80.0 to 99.9 wt% of (i) 1,3-propanediol, a bio-derived solvent and/or (ii) sorbitan caprylate, a bio-derived solvent.
2. The antimicrobial composition according to claim 1, wherein said (i) 1,3-propanediol and (ii) sorbitan caprylate are present in the ratio of 1:10 to 10:1.
3. The antimicrobial composition according to claim 1, wherein said (i) 1,3-propanediol and (ii) sorbitan caprylate are present in the ratio of 1:1, 1:3 or 3:1.
4. The antimicrobial composition according to claim 1, wherein the composition is stable for at least two years at room temperature or stable for at least 5 freeze/thaw cycles when the temperature is cycled from 50°C to -24°C in every 24 hours or stable for at least 4 weeks at about 50°C.
5. The antimicrobial composition according to claim 1, wherein the composition is capable of inhibiting or killing *gram* (+) bacteria, *gram* (-) bacteria, yeasts and/or fungus.
6. The antimicrobial composition according to claim 1 capable of inhibiting or killing *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, *Staphylococcus aureus*, *Burkholderia cepacia*, *Aspergillus brasiliensis*, *Penicillium expansum*, *Trichoderma viride* and/or *Candida albicans*.
7. The antimicrobial composition according to claim 1, wherein said 1,3-propanediol demonstrated synergistic antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus*.
8. The antimicrobial composition according to claim 1, wherein said sorbitan caprylate demonstrated synergistic antimicrobial activity against *Escherichia coli*.
9. The antimicrobial composition according to claim 1 employed in the field of cosmetic, toiletry, personal care, household, cleaning, disinfecting, food, beverages, enzyme formulations, feminine care products, foot care products, pet care products, food ingredients,

paints, coatings, metal working fluids, nutrients for plants, construction and/or laundry products.

10. The antimicrobial composition according to claim 1 employed in the field of personal care compositions.

11. The antimicrobial composition according to claim 1 employed in the field of shampoo, hair conditioners, skin care lotions, bar soaps, baby bath washes, moisturizers, conditioners, in-shower body moisturizers, body washes, shower gels, hand soaps, wet wipes, hand sanitizers, medicinal creams, cosmetic products, laundry formulations and/or oral care products.

12. The antimicrobial composition according to claim 10 wherein the personal care composition is produced in a form selected from stick, roll-on, spray, pump-spray, aerosol, soap bar, powder, solution, gel, cream, wet wipes, balm and lotion.

13. A process for preparing an eco-friendly, non-aqueous and stable antimicrobial solution composition comprising the steps of:

- i. preparing a mixture of (a) about 0.1 to 20.0 wt% of a hinokitiol; and (b) about 80.0 to 99.9 wt% of 1,3-propanediol, a bio-derived solvent and/or sorbitan caprylate, a bio-derived solvent; and
- ii. heating the mixture of step (i) at about 40°C to yield a homogenous non-aqueous antimicrobial solution.

14. A method for inhibiting or killing microbial growth comprising mixing an effective amount of antimicrobial composition of claim 1 with an appropriate product selected from the group consisting of cosmetic, toiletry, personal care, household, cleaning, disinfecting, food, beverages, enzyme formulations, feminine care products, foot care products, pet care products, food ingredients, paints, coatings, metal working fluids, construction, nutrients for plants and/or laundry products.

15. The method of claim 14 wherein the effective amount of preservative composition is in the range of from about 0.001 wt% to about 25 wt% of the total composition.

16. The method of claim 14 wherein the effective amount of preservative composition is in the range of from about 0.001 wt% to about 5 wt% of the total composition.

17. An eco-friendly, non-aqueous and stable antimicrobial solution composition comprising:

- a. about 0.1 to 20.0 wt% of a Hinokitiol; and
- b. about 49.95 to 40.0 wt% of (i) 1,3-propanediol, a bio-derived solvent; and about 49.95 to 40.0 wt% of (ii) sorbitan caprylate, a bio-derived solvent.

18. An eco-friendly, non-aqueous and stable antimicrobial solution composition comprising:

- a. about 2.0 wt% of a Hinokitiol; and
- b. about 49.0 wt% of (i) 1,3-propanediol, a bio-derived solvent; and about 49.0 wt% of (ii) sorbitan caprylate, a bio-derived solvent.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 13/33284

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A01N 25/34 (2013.01)

USPC - 424/405

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

USPC: 424/405

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC: 424/404 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PUBWEST; Google Scholar

search terms: Hinokitiol, antimicrobial, 1,3-propanediol, sorbitan caprylate, Escherichia coli

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011/0177146 A1 (Cahill et al.) 21 July 2011 (21.07.2011) abstract; para [0014], [0100], [0102]	1-18
Y	US 2012/0101135 A1 (Klug et al.) 26 April 2012 (26.04.2012) abstract; [0009], [0065]-[0066], [0107]-[0108], [0110], [0112], [0206]	1-18
Y	US 2011/0086918 A1 (Ciccognani et al.) 14 April 2011 (14.04.2011) abstract; para [0017], [0021]	1-18
A	US 2008/0176957 A1 (Joerger et al.) 24 July 2008 (24.07.2008) entire document	1-18
A	US 2012/0100085 A1 (Klug et al.) 26 April 2012 (26.04.2012) entire document	1-18
A	US 2008/0253976 A1 (Scott et al.) 16 October 2008 (16.10.2008) entire document	1-18
A	US 2011/0182959 A1 (Cahill et al.) 28 July 2011 (28.07.2011) entire document	1-18
A	US 2010/0266510 A1 (Tamarkin et al.) 21 October 2010 (21.10.2010) entire document	1-18
A	US 2008/0299220 A1 (Tamarkin et al.) 04 December 2008 (04.12.2008) entire document	1-18
A	WO 2010/127227 A1 (Gilbard et al.) 04 November 2010 (04.11.2010) entire document	1-18

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

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03 May 2013 (03.05.2013)

Date of mailing of the international search report

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