Antimicrobial actives and their compositions thereof

The present invention relates to antimicrobial actives and their compositions. Antimicrobial actives such as compounds of formulae (I) to (XI) individually or in mixtures are found to be active against various microbes such as dandruff-causing and/or malodour-causing and/or pathogenic microorganisms by significantly reducing the population of such microorganisms. It particularly relates to antimicrobial compositions for use in personal care formulations.

Field of the Invention

Antimicrobial actives such as compounds of formulae (I) to (XI) individually or in mixtures are found to be active against dandruff-causing, malodour-causing, and/or pathogenic microorganisms by significantly reducing the population of such microorganisms. The antimicrobial compositions used in personal care products for malodour counteraction, dandruff prevention, and/or personal cleaning.

The present invention relates to compounds of formulae (I) to (XI) individually or in combinations as antimicrobial actives particularly as antibacterial and antidandruff compounds for use in personal care formulations such as but not limited to shampoo, hair conditioner, hair tonic, hair oil, hair serum, hair gel, cream rinse, body wash, bubble bath, bath oil, facial cleanser, cleansing mask, cleansing milk, micellar water, make-up remover, cleansing wipes, perfume, talc, soaps, shaving soaps, shaving foams, cleansing foams, face mask, face cream, hand cream and body lotion, deodorants and roll-on.

The invention provides the use of compounds of formulae (I) to (XI),

Compounds	IUPAC name
Compound of formula (I)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one
Compound of formula (II)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol
Compound of formula (III)	4-(4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (IV)	4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (V)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-one
Compound of formula (VI)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-ol
Compound of formula (VII)	4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (VIII)	Combination of 1. 2',5,5-trimethyl-4,4a,5,6,7,8-hexahydro-3H-spiro[naphthalene-2,5'-[1,3]dioxane], 2. 2',5,5-trimethyl-3,4,4a,5,6,7-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane], and 3. 2',5,5-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (IX)	2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (X)	2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (XI)	8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]

Illustrative embodiments are also the following compositions and mixture

Composition	Mixture of one or more of any of the compound(s) of formula (I) to formula (XI) and Diethyl adipate (for example 1:1 by weight)
Composition	Mixture of Compound of formula (I) and Diethyl adipate (for example 1:1 by weight)
Mixture of compounds	Mixture of Compound of formula (I) and Compound of formula (II) (for example 1:1 by weight)

Background Art

EP1238645A2 discloses synergistic anti-dandruff compositions which contain climbazole, zinc pyrithione, and piroctone olamine as active substances and their use in scaling the hair-covered skin, especially the scalp.

EP2787823B1 discloses an antimicrobial composition and a method for disinfection involving the antimicrobial composition. It particularly relates to an antimicrobial composition for personal cleaning, oral care, or hard surface cleaning applications.

IN3636MU2013 (A) discloses a process for synthesis of alloisolongifolene and/or derivatives and/or isomers. It particularly discloses a process for synthesis of 3-Penten-2-one, 4-(octahydro-l,7a-dimethyl-l,4-methano-4H-inden-4-yl)-,[lS-[1α,3αβ,4β,7αβ]] and its isomers or derivatives. Further, reports the use of these compounds and their mixtures as odorants or fragrances or perfumery compositions or cosmetic ingredients.

US5219835A and GB2018251A have reported spiro tricyclic compounds like hydrospiro[furan-2(3H),2'(1'H)naphthalene] derivatives as perfumery molecules. Similar type of compounds have also reported for ambergris like olfactory properties (Jingxi Yu Zhuanyong Huaxuepin (2006).

US10874599B2 discloses composition comprising at least 30% of compound N-((3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)methyl)-N-methyloctanamide / N-((3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)methyl)-N-methylhexanamide for inhibiting microorganisms, as well as related processes, formulations, concentrates and uses.

The term antimicrobials used in this invention are the substances used to prevent or treat infections caused by bacteria, yeasts, and funguses, commonly termed as antibacterial, and antifungal. They are used as antidandruff compounds and bacteriostatic compounds.

The term "cosmetics formulations" has been used interchangeably with "Personal care compositions". Also, the term "formulations" and "compositions" have been interchangeably used.
The term "mixture(s)" and "combination(s)" used interchangeably when more than one compound is used in the composition(s).

The term "w/w%" is defined here as relative weight %. The term "cfu/ml" is defined here as colony-forming units per millilitre.

Body odour is a common problem caused by the presence of skin bacteria such as *Corynebacterium xerosis* (*C. xerosis*), *Staphylococcus epidermidis* (*S. epidermidis*) and *Staphylococcus aureus* (*S. aureus*). These bacteria on the skin and axilla break down protein and other molecules within sweat and produce malodour. These bacteria are also responsible for various diseases and infections. Anti-bacterial compound Triclosan (5-chloro-2-(2,4-dichlorophenoxy)phenol) is used as an antiseptic, preservative, and disinfectant in cosmetics and household cleaning products.

Dandruff is a major problem, experienced by many people, which causes the flaking of the scalp's skin and also causes inflammation and itchiness of the scalp. Malassezia yeasts are associated with dandruff. Malassezia species, such as *Malassezia furfur* (*M. furfur*) or Malassezia globosa (*M. globosa*), are the main cause of dandruff as they decompose fats into

fatty acids. Antidandruff compounds include the compounds such as Climbazole (1- (4-chlorophenoxy) -1- (1H-imidazolyl) -3,3-dimethyl-2-butanone, Zinc Pyrithione (bis(2-pyridylthio)zinc 1,1'-dioxide) and Piroctone Olamine (2-aminoethanol;1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)pyridin-2-one), Selenium sulphide (hexathiadiselenocane), Ketoconazole (1-[4-[4-[[(2S,4R)-2-(2,4-dichlorophenyl)-2-(imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazin-1-yl]ethanone). These compounds are used commercially in cosmetic compositions to treat dandruff.

Objective of the invention:

The objective of the present invention relates to antimicrobial compounds and their compositions thereof. Thus, it provides a safe and advantageous alternative to commonly used antimicrobial compounds e.g. Triclosan, Zinc pyrithione, Piroctone olamine, Climbazole, Ketoconazole, and Selenium sulphide.

Compounds of formulae (I) to (XI) are effective, nontoxic, liquid and act as anti-microbial compounds. It is particularly suitable for producing of anti-dandruff and antibacterial formulations.

The compounds of formulae (I) to (XI) individually or in mixtures are active against various microbes such as dandruff-causing, malodour-causing and/or pathogenic microbes. They are compatible with most surfactants, additives, and other active ingredients used in personal care formulations.

One of the additional advantages of the compounds of formulae (I) to (XI) consists in their unexpected fragrance activity, i.e. conferring interesting olfactory notes when incorporated in the antimicrobial personal care formulations according to the present invention; e.g. this property allows to reduce or even remove the content of the additional perfumery molecules which are usually introduced as fragrances in corresponding personal care formulations.

Description of the Invention

The present invention is defined by its claims.

The compounds of formulae (I) to (XI), and/or their mixtures and/or compositions comprising said compound(s) or mixture(s) thereof, showed a decrease in the level of microorganisms on a surface when used in an antimicrobial composition.

Said compounds of formula (I) to (XI) have the following IUPAC names

Compounds	IUPAC name
Compound of formula (I)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one
Compound of formula (II)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol
Compound of formula (III)	4-(4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (IV)	4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (V)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-one
Compound of formula (VI)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-ol
Compound of formula (VII)	4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (VIII)	Combination of 1. 2',5,5-trimethyl-4,4a,5,6,7,8-hexahydro-3H-spiro[naphthalene-2,5'-[1,3]dioxane], 2. 2',5,5-trimethyl-3,4,4a,5,6,7-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane], and

	3. 2',5,5-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (IX)	2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (X)	2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (XI)	8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]

Illustrative examples of the synthesis paths for producing the claimed compounds (I) to (XI).

Synthesis

The Compound of formulae (I) to (VII) can be prepared by using the below-mentioned process.

The alloisolongifolene undergoes Kondakov reaction with acyl anhydride such as acetic anhydride, propionic anhydride and like; or acyl chlorides in presence of Lewis acids such as zinc chloride or organic acid such as methane sulphonic acid to yield the corresponding ketone compound of the formula (I)

The ketone compound can be reduced to corresponding alcohol of formula (II) by using sodium borohydride in alcoholic solvents such as methanol, ethanol and like; or lithium aluminium hydride in etheral solvents such as tetrahydrofuran, diethyl ether or mixture thereof.

These alcohols can further be converted to corresponding ethers of formula (III) by means of O-alkylation reaction. This conversion can be performed by using bases such as sodium hydride, sodium or potassium tert-butoxide and like; and alkyl or alkenyl halides in solvent such as DMF, DMA, THF and like.

Using the similar protocols mentioned above one can prepare compounds of formulae (V), (VI) and (VII) by employing corresponding anhydrides and alkyl halides in respective steps.

General Synthetic procedures

Step-1: General Procedure for Kondakov reaction

A mixture of 1,7a-dimethyl-4-(prop-1-en-2-yl)octahydro-1H-1,4-methanoindene (Alloisolongifolene, 1 mol) and acyl anhydride (2.8 mol) was stirred in an oven dried 2L three neck RBF. Zinc (II) chloride (0.5 mol) was added to the reaction and the reaction mixture was heated to 80 °C. The reaction was stirred for 16h at same temperature and the progress of reaction was monitored by GC. The reaction was cooled to room temperature and quenched with water (3 vol) The resulted mixture was extracted thrice with ethyl acetate (2 vol x 3). Combined organic layer was subsequently washed with 10% $NaHCO_3$ (1 vol), brine (1 vol) and dried over anhydrous sodium sulfate. Solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (100-200 mesh) using hexane-ethyl acetate as eluent to afford corresponding compound (I) as oil in 30-60% yields.

Step-2: General procedure for reduction of enone to corresponding α-hydroxy alkenes

Procedure: To a solution of the compound (I) in methanol (10 vol), $NaBH_4$ (1 mol) was added at 0-5 °C in portion wise manner over the period of 20 -30 min. The reaction was allowed to stir at room temperature for 1 hr and the progress of reaction was monitored by TLC. The reaction was quenched with water (4 vol) and extracted with ethyl acetate (2 x 5 vol). Combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure. The crude product was purified by column chromatography over silica gel using hexane-ethyl acetate as an eluent to give corresponding alcohol of formula (II) in 60-70 % yield

Step-3: General procedure for O-alkylation

Procedure: To a mixture of Compound of formula (II, 1 mol) and DMF (10 vol) or THF (10 vol), sodium hydride (1.5 mol) or potassium tert-butoxide (1.5 mol) was added at 0-5 °C in portion wise manner. The reaction was stirred for 10 min and an alkyl halide (3 mol) was

added in drop wise manner. The reaction was stirred for 16 h at 25- 60 °C and the reaction was monitored by TLC. The reaction was quenched with aqueous ammonium chloride solution (5 vol) and extracted with ethyl acetate (2 x 5 vol). The combined organic layer was washed with brine (3 vol), dried on anhydrous sodium sulphate and concentrated under reduced pressure. The crude mass was purified by column chromatography over silica gel using hexane-ethyl acetate as an eluent to get compound of formula (III) in 40-50 % yield.

Examples (compounds)

Compound formula (I): 4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one was synthesized following method described in IN3636MU2013 (A) .

Compound formula (II): (E)-4-((1S,3aS,4R,7aS)-1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol (II)

Commercially available (E)-4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one (**compound formula I**) was subjected to reduction with sodium borohydride in methanol using the protocol mentioned in **step-2** gave the titled compound in 69% yield.

IR (cm^{-1}): 3388.3 (Broad), 1655

^1H NMR (400 MHz, $CDCl_3$) δ ppm: 5.24 – 5.09 (m, 1H), 4.65 – 4.49 (m, 1H), 1.63 – 1.60 (m, 3H), 1.58 – 1.40 (m, 9H), 1.35 (d, J = 12.6 Hz, 2H), 1.21 (t, J = 6.3 Hz, 4H), 1.01 (ddd, J = 10.6, 7.9, 5.4 Hz, 1H), 0.86 (s, 3H), 0.75 (s, 3H) (-OH is not observed in NMR)

Compound formula (III): (1S,3aS,4R,7aS)-4-((E)-4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene

(E)-4-((1S,3aS,4R,7aS)-1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol (**Compound formula II**) was subjected to O-alkylation using the protocol mentioned in **step-3** provided the titled compound in 50% yield

IR (cm^{-1}): 1655.7

^1H NMR (400 MHz, $CDCl_3$) δ ppm : 5.01 (t, J = 8.4 Hz, 1H), 4.08 (dq, J = 8.8, 6.3 Hz, 1H), 3.23 (d, J = 1.4 Hz, 3H), 1.61 (dd, J = 2.6, 1.3 Hz, 3H), 1.60 – 1.51 (m, 5H), 1.51 – 1.35 (m, 5H), 1.33 – 1.24 (m, 2H), 1.18 (dd, J = 6.3, 3.8 Hz, 3H), 1.06 – 0.99 (m, 1H), 0.88 (s, 3H), 0.77 (d, J = 2.0 Hz, 3H).

Compound formula (IV): E)-4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene

(E)-4-((1S,3aS,4R,7aS)-1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol (**Compound formula II**) was subjected to O-alkylation reaction with potassium tert-butoxide and n-butyl bromide along with catalytic potassium iodide using the protocol mentioned in **step-3** gave the titled compound in 46 % yield

IR (cm^{-1}): 1655.7

^1H NMR (400 MHz, $CDCl_3$) δ ppm: 5.11 – 4.96 (m, 1H), 4.15 (dq, J = 8.6, 6.3 Hz, 1H), 3.40 (dt, J = 9.3, 6.8 Hz, 1H), 3.34 – 3.18 (m, 1H), 1.63 – 1.58 (m, 4H), 1.58 – 1.53 (m, 4H), 1.53 – 1.43 (m, 6H), 1.41 – 1.30 (m, 4H), 1.27 – 1.20 (m, 1H), 1.17 (dd, J = 6.3, 3.7 Hz, 3H), 1.05 – 0.97 (m, 1H), 0.93 – 0.85 (m, 6H), 0.77 (d, J = 2.2 Hz, 3H).

Compound formula (V): (E)-5-(1,7a-dimethyloctahydro-1,3a-methanoinden-5-yl)hex-4-en-3-one

Alloisolongifolene on reaction with propionic anhydride and zinc chloride using the protocol mentioned in **step-1** provided the titled compound in 36% yield.

IR (cm^{-1}): 1685, 1606

^1H NMR (400 MHz, $CDCl_3$) δ 6.01 (s, 1H), 2.44 (q, *J* = 7.3 Hz, 2H), 2.10 (s, 3H), 1.74 – 1.70 (m, 1H), 1.69 – 1.65 (m, 1H), 1.63 – 1.43 (m, 7H), 1.41 – 1.35 (m, 1H), 1.32 – 1.23 (m, 2H), 1.08 – 0.98 (m, 4H), 0.89 (s, 3H), 0.78 (s, 3H).

Compound formula (VI): ((E)-5-(1,7a-dimethyloctahydro-1H-1,4-methanoinden-5-yl)hex-4-en-3-ol

(E)-5-(1,7a-dimethyloctahydro-1,3a-methanoinden-5-yl)hex-4-en-3-one **(compound formula V)** was subjected to sodium borohydride reduction using the protocol mentioned in **step-2** gave the titled compound in 64% yield

IR (cm^{-1}): 3345.2 (Broad), 1655.4

^1H NMR (400 MHz, $CDCl_3$) δ 5.15 – 5.05 (m, 1H), 4.35 – 4.25 (m, 1H), 1.64 – 1.61 (m, 4H), 1.60 – 1.51 (m, 5H), 1.51 – 1.42 (m, 6H), 1.24 – 1.17 (m, 1H), 1.05 – 0.97 (m, 1H), 0.90 – 0.83 (m, 6H), 0.76 (s, 3H). (-OH is not observed in ^1H NMR)

Compound formula (VII): ((E)-4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene

(E)-4-(1,7a-dimethyloctahydro-1H-1,4-methanoinden-5-yl)hex-4-en-3-ol (14 g, 53.3 mmol) (Compound **VI**) was subjected to O-alkylation reaction with methyl iodide and sodium hydride using the protocol mentioned in **step-3** gave the titled compound in 38% yield

IR (cm^{-1}): 1655.2

^1H NMR (400 MHz, $CDCl_3$) δ 5.02 – 4.90 (m, 1H), 3.89 – 3.77 (m, 1H), 3.21 (s, 3H), 1.68 – 1.60 (m, 5H), 1.59 – 1.50 (m, 5H), 1.49 – 1.29 (m, 6H), 1.28 – 1.18 (m, 1H), 1.06 – 0.98 (m, 1H), 0.87 (s, 3H), 0.83 (t, J = 7.5 Hz, 3H), 0.77 (s, 3H).

Compound formula (VIII): was synthesized following method described in US5219835A and GB2018251A.

Compounds of formulae (IX) to (XI) can be prepared by using the below-mentioned process.

General procedure for synthesis of Cyclic ketals

To a solution of (8,8-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalene-2,2-diyl)dimethanol (CAS: 940006-76-8, 1 mmol), corresponding ketone (10 mmol) and pTSA (1mol% to 5mol%) were added at room temperature and the reaction was stirred overnight for 16 to 20h at same temperature. The progress of reaction was monitored by GC and TLC. Upon completion of the reaction, the reaction mixture was quenched with water (5 vol) and extracted with ethyl acetate (2 x 5 vol). Combined organic layer was washed with brine (5 vol) and dried over anhydrous sodium sulphate. Solvent was removed under reduced pressure and the crude product was purified by column chromatography using hexane-ethyl acetate as eluent to give the corresponding cyclic ethers in 30-35% yields.

Using this synthetic protocol, the following compounds were synthesized-

Compound formula (IX): 2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]: This was synthesized in 30% yield from (8,8-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalene-2,2-diyl)dimethanol and butan-2-one by using the above synthetic protocol.

IR (cm^{-1}): 1453,1179, 1078

GCMS m/z: 278.1 [M+]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.62 – 3.48 (m, 4H), 2.01 – 1.77 (m, 6H), 1.77 – 1.68 (m, 2H), 1.62 – 1.50 (m, 3H), 1.49 – 1.38 (m, 3H), 1.38 – 1.29 (m, 3H), 1.02 – 0.83 (m, 9H).

Compound formula (X): 2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]: This was synthesized in 33% yield from (8,8-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalene-2,2-diyl)dimethanol and pentan-3-one by using the above synthetic protocol.

IR (cm^{-1}): 1461, 1157, 1083

GCMS m/z: 292.2 [M+]

^{1}H NMR (400 MHz, CDCl3) δ 3.65 – 3.45 (m, 4H), 1.93 – 1.77 (m, 6H), 1.76 – 1.68 (m, 4H), 1.60 – 1.53 (m, 2H), 1.52 – 1.36 (m, 4H), 1.00 – 0.92 (m, 6H), 0.92 – 0.81 (m, 6H).

Compound formula (XI): 8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]: This was synthesized in 30% yield from (8,8-dimethyl-1,2,3,4,5,6,7,8-octahydronaphthalene-2,2-diyl)dimethanol and cyclohexanone by using the above synthetic protocol.

IR (cm^{-1}): 1445, 1156, 1096

GCMS m/z: 304.2 [M+]

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (d, J = 3.5 Hz, 4H), 1.93 – 1.79 (m, 6H), 1.79 – 1.71 (m, 4H), 1.60 – 1.55 (m, 2H), 1.55 – 1.47 (m, 6H), 1.45 – 1.36 (m, 4H), 1.02 – 0.85 (m, 6H).

In one embodiment, the present invention relates to an antimicrobial compound of formula (I), (II), (III), (IV), (V), (VI), (VII), (VIII), (IX), (X) or (XI), and/or a mixture of two or more compounds thereof, for use as a medicament,

wherein the compounds of formula (I) to (XI) have the following IUPAC names

Compounds	IUPAC name
Compound of formula (I)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one

Compound of formula (II)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol
Compound of formula (III)	4-(4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (IV)	4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (V)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-one
Compound of formula (VI)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-ol
Compound of formula (VII)	4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (VIII)	Combination of 1. 2',5,5-trimethyl-4,4a,5,6,7,8-hexahydro-3H-spiro[naphthalene-2,5'-[1,3]dioxane], 2. 2',5,5-trimethyl-3,4,4a,5,6,7-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane], and 3. 2',5,5-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (IX)	2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (X)	2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (XI)	8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]

In an embodiment of the present invention, an antimicrobial composition for use as a medicament is provided, said composition comprising

i. one or more of compounds of formulae (I) to (XI) at 0.01 to 90 % by weight,

ii. cosmetically acceptable ingredient(s) at 10 to 99.99 % by weight,

where the combined weight of i and ii is at least 90 weight percent of the composition, preferably 100%.

In an embodiment, the antimicrobial composition comprises one or more of compounds of formulae (I) to (XI) in a content comprised between 0.01 % and 40 % by weight, for example between 0.01 % and 20 % by weight.

Preferably, the cosmetically acceptable ingredient(s) is selected amongst anionic surfactants, nonionic surfactants, amphoteric/zwitterionic surfactants, cationic surfactants, cationic polymers, conditioning agents, suspending agents, silicone polymers, humectants, preservatives, high melting point fatty compounds, pH adjusting agents, emulsifiers, additives, skin and hair benefiting ingredients solvents and/or a mixture of two or more carriers thereof.

Preferably, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition for use as antibacterial or antifungal medicament.

In an embodiment, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition for use as a medicament in a method for the treatment of malodour, dandruff and/or pathogenic microorganisms.

In an embodiment, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition for use as a medicament in a method for the treatment of dandruff due to the presence of *Malassezia furfur*, or for the treatment of malodour caused by the presence of *Corynebacterium xerosis*, *Staphylococcus epidermidis* and/or *Staphylococcus aureus*.

In an embodiment, the antimicrobial compound antimicrobial composition is an antimicrobial compound or antimicrobial composition wherein the compounds are selected from antimicrobial compounds of formula (I), (II), (III), (VI), (VIII), or a mixture of compounds of formula (I) and formula (II), for use as a medicament in a method for the treatment of dandruff due to the presence of *Malassezia furfur*.

In an embodiment, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition wherein the compounds are selected from antimicrobial compounds of formula (I), (II), (VI), (VIII), (X), or (XI), or wherein the compound of the composition is the compound formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Corynebacterium xerosis*.

In an embodiment, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition wherein the compounds are selected from antimicrobial compounds of formula (I) or (VIII), or wherein the compound of the composition is the compound formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Staphylococcus epidermidis*.

In an embodiment, the antimicrobial compound or antimicrobial composition is an antimicrobial compound or antimicrobial composition wherein the compounds are selected from antimicrobial compound of formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Staphylococcus aureus*.

In an embodiment, the antimicrobial compound or antimicrobial composition is formulated as a rinse-off and/or wash-off personal care formulation for the treatment of human scalp or human skin or underarms for use as a medicament in a method for the treatment of malodour, dandruff and/or pathogenic microorganisms.

In an aspect, the present invention provides a process for decreasing the level of microorganisms like *Malassezia furfur*, *Corynebacterium xerosis*, *Staphylococcus epidermidis*, and/or *Staphylococcus aureus* on a surface by treating said surface with a personal care composition as defined hereinabove.

A corresponding antimicrobial composition for use as a medicament is advantageously used in personal care compositions such as rinse-off and wash-off skin or hair care compositions such as but not limited to shampoo, hair conditioner, hair tonic, hair oil, hair serum, hair gel, cream rinse, body wash, hand wash, bubble bath, bath oil, facial cleanser, cleansing mask, cleansing milk, micellar water, make-up remover, cleansing wipes, perfume, talc, soaps, shaving soaps, shaving foams, cleansing foams, face mask, face cream, hand cream and body lotion, deodorants and roll-on.

The surface on which the above-mentioned cosmetic compositions are applied is skin more specifically human skin or underarms and on hairs more specifically on the human scalp.

Formulations and Ingredients

According to the present invention, the compounds of formulae (I) to (XI) can be suitably formulated into a personal care composition. The personal care compositions described herein can be used on skin or hair for malodour masking or cleaning and conditioning purpose. The personal care composition specifically for skin and hair including rinse-off or leave-on formulations such as but not limited to shampoos, hair conditioner, hair tonic, hair oil, hair serum, hair gel, cream rinse, body wash, hand wash, bubble bath, bath oil, facial cleanser, cleansing mask, cleansing milk, micellar water, make-up remover, cleansing wipes, perfume, talc, soaps, shaving soaps, shaving foams, cleansing foams, face mask, face cream, hand cream and body lotion, deodorants and roll-on.

Personal care compositions for use in the invention include one or more cosmetically accepted ingredients such as anionic surfactants, nonionic surfactants, amphoteric/zwitterionic surfactants, cationic surfactants, cationic polymers or conditioning agents, suspending agents, silicone polymers, humectants, preservatives, high melting point fatty compounds, pH adjusting agents, emulsifiers, skin and hair benefiting ingredients, additives and solvents.

The examples of cosmetically accepted ingredients are as follows:

Anionic surfactants are negatively charged surfactant ions which are used as a primary ingredient in all cleansing products. Personal care compositions typically comprise one or more anionic surfactants such as but not limited to alkyl ether, alkyl ether phosphates, alkyl ether carboxylic acids, alkyl ether sulfates, sodium lauryl sulfate, sodium lauryl isethionate, sodium oleyl succinate, ammonium lauryl sulfosuccinate, disodium lauryl Sulfosuccinate, sodium lauryl ether sulphate, ammonium lauryl sulphate, ammonium lauryl ether sulphate, alkyl glycinates, acyl glutamates, acyl taurates and salts thereof, such as sodium, ammonium, magnesium, and mono-, di- and triethanolamine salts, sodium dodecylbenzene sulfonate,

triethanolamine dodecylbenzene sulfonate, alkaryl sulphonates, N-alkyl sarcosinates, alkyl phosphates, alkyl glycinates and salts thereof, sodium cocoyl isethionate, sodium N-lauryl sarcosinate or mixtures thereof.

Nonionic surfactants are combination of uncharged hydrophilic and hydrophobic group used as an emulsifiers and foaming agents, it also reduces irritation and provide conditioning effect. Personal care compositions typically comprise one or more non-ionic surfactants include but not limited to alkanolamides such as cocamide monoethanolamide and cocamide monoisopropanolamide; alkyl polyglucosides such as cocoglucoside and lauryl glucoside; and acyl glucamides such as cocoyl methyl glucamide, polysorbate-20, polysorbate-21, polysorbate-40, polysorbate-60, or mixtures thereof.

Amphoteric or Zwitterionic surfactants carry both a positive and a negative charge, used as a cleansing agent as well as to increase the foam and viscosity of the product. Personal care compositions typically comprise one or more amphoteric or zwitterionic surfactants include but not limited to cocamidopropyl betaine, alkyl amidopropyl betaines, alkyl betaines, alkyl amine oxides, alkyl sulphobetaines, alkyl carboxyglycinates, alkyl glycinates, alkyl amphopropionates, alkylamphoglycinates, alkyl amphoacetates, alkyl amidopropyl hydroxysultaines, alkylamphoglycinates, acyl taurates and acyl glutamates or mixtures thereof.

Cationic surfactants are positively charged surfactant ions which are used as conditioning agents specifically for hair care products. Personal care compositions typically comprise one or more cationic surfactants include but not limited to di-long alkyl quaternized ammonium salt, mono-long alkyl amine; a mono-long alkyl cationic neutralized amino acid esters; cetrimonium chloride, brassicamidopropyl dimethylamine, behenamidopropyl dimethylamine, behentrimonium methosulfate, stearamidopropyl dimethylamine and behentrimonium chloride or mixtures thereof.

Personal care compositions can include one or more cationic polymers and conditioning agents include but not limited to cationic polysaccharide polymers such as cationic cellulose derivatives and cationic guar gum derivatives such as guar

hydroxypropyltrimethylammonium chloride. (meth)acrylamide, alkyl and dialkyl (meth)acrylamides, alkyl (meth)acrylate, vinyl caprolactone and vinyl pyrrolidine, Dimethyldiallylammonium chloride, Polyquaternium 6 and Polyquaternium 7, quaternary ammonium salts such as quaternary ammonium salts include benzyl triethyl ammonium chloride, cetyl trimethylammonium chloride (cetrimonium chloride, CTAC), behentrimonium chloride (BTAC) or cetylpyridinium chloride or mixtures thereof.

Suspending agents increases the viscosity of the dispersion medium and slow down the sedimentation speed of particles it helps to prevent caking at the bottom of the container. Personal care compositions may also include suspending agents are such as but not limited to polyacrylic acids, cross-linked polymers of acrylic acid, copolymers of acrylic acid with a hydrophobic monomer, copolymers of carboxylic acid-containing monomers and acrylic esters, crosslinked copolymers of acrylic acid and acrylate esters, heteropolysaccharide gums and crystalline long chain acyl derivatives. The long chain acyl derivative such as ethylene glycol stearate, alkanolamides of fatty acids. Ethylene glycol distearate and polyethylene glycol 3 Polyacrylic acid traded under the name of Carbopol such as Carbopol 420, Carbopol 488 or Carbopol 493. Polymers of acrylic acid cross-linked with a polyfunctional agent such as Carbopol 910, Carbopol 934, Carbopol 941 and Carbopol 980. Carboxylic acid containing monomer and acrylic acid esters such as Carbopol 1342. Cross-linked polymers of acrylic acid and acrylate esters are Pemulen TR1 or Pemulen TR2 and heteropolysaccharide gum such as xanthan gum or mixtures thereof.

Silicone polymers composed of repeating units of siloxane can be used as a conditioning agent. They are used in various personal care formulations such as shampoos, hair conditioners and styling products, moisturisers, skin protectants and antiperspirants and hair. Personal care compositions may also include silicones such as but not limited to polydiorganosiloxanes silicone oil comprises dimethicone, dimethiconol, cyclopentasiloxane, phenyl trimethicone, amodimethicone, cyclomethicone or mixtures thereof.

A humectant has ability to retain moisture and it can be used as a moisturising agent in various personal care compositions such as shampoos and lotions, Personal care

compositions may include humectants which reduces the water of evaporation rate from the hair and skin. Humectants used in personal care compositions include but not limited polyols such as glycerin, sorbitol, propylene glycol, butylene glycol, hexylene glycol, ethoxylated glucose, 1, 2-hexanediol, hexanetriol, dipropylene glycol, erythritol, trehalose, diglycerin, xylitol, maltitol, maltose, glucose, fructose, sodium chondroitinsulfate, sodium hyaluronate, sodium adenosine phosphate, sodium lactate, pyrrolidone carbonate, glucosamine, glucam P20, cyclodextrin or mixtures thereof.

Preservatives can be added in the personal care compositions to prevent decomposition of products due to microbes or chemical changes. Personal care compositions may also include but not limited to preservatives selected from the group consisting of pentylene glycol, caprylyl glycol, butylene glycol, hexylene glycol, decylene glycol, 1,2-hexanediol, Kathon CG , potassium sorbate, glyceryl ester including glyceryl caprylate and sodium benzoate or mixtures thereof.

High melting points compounds are higher molecular weight fatty acid esters and alcohols which can be added into personal care formulations for solid consistency of product and softening of the skin. Personal care compositions may also include but not limited to high melting point fatty compound selected from the group consisting of stearyl alcohol, cetyl alcohol, brassica alcohol and behenyl alcohol or glycerides, phospholipids and sterols or mixtures thereof.

Personal care compositions may include pH adjusting agents, such as but not limited to citric acid, sodium citrate, succinic acid, phosphoric acid, sodium hydroxide, sodium carbonate, sodium bicarbonate, potassium acetate, sodium acetate, ammonium chloride, ammonium acetate or mixtures thereof.

Personal care compositions may also include one or more of cosmetically acceptable solvents include deionized water, vegetable or mineral oils, vinegar, methyl acetate, ethyl acetate, acetone, isopropyl myristate, tetrachloroethylene, toluene and alcohols such as 1,3-propanediol, butylene glycol, dipropylene glycol, triethyl citrate, diethyl adipate, isopropyl

alcohol and propylene glycol, ethanol, methanol, liquefied petroleum gas, diethyl Phthalate or mixtures thereof.

Personal care compositions may comprise one or more skin and hair benefiting ingredients such as panthenyl ethyl ether panthenol, proteins, hydrolysed proteins (hydrolysed keratin or hydrolysed collagen), nutrients, antioxidants such as coenzyme Q10, carotenoids, resveratrol and polyphenols etc. vitamins such as vitamin A, vitamin B3, vitamin B5, vitamin C, vitamin B12, vitamin E, vitamin K etc. emollients, such as trimethyl pentanol hydroxyethyl ether, glyceryl caprylate caprate, PPG-3 myristyl ether, polypropylene glycol and derivatives. Sunscreen agents such as titanium dioxide, zinc oxide, diethylamino hydroxybenzoyl hexyl benzoate, octocrylene, ensulizole and enzacamene etc. Anti-aging actives such as lactic Acid, hyaluronic acid, retinol and niacinamide etc. Essential oils, anti-malodour agents including aluminium anti-perspirant salts, pharmaceutical agents, pigments, natural hair nutrients such as botanicals, fruit extracts, sugar derivatives and amino acids or mixtures thereof.

Personal care compositions may comprise one or more additives such as fragrance, profragrances, pearlescers or opacifiers, chelating agents such as disodium ethylenediaminetetraacetic acid (EDTA), tetrasodium EDTA and sodium phytate and viscosity modifiers such as sodium chloride, potassium chloride, clay, etc.

The following non-limiting and illustrative embodiments are hereby disclosed:

Embodiment 1: Antimicrobial compound of formula (I), (II), (III), (IV), (V), (VI), (VIII), (X), or (XI) or a mixture of two or more compounds thereof, for use as a medicament, wherein the compounds of formula (I) to (XI) have the following IUPAC names

Compounds	IUPAC name
Compound of formula (I)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one

Compound of formula (II)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol
Compound of formula (III)	4-(4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (IV)	4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (V)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-one
Compound of formula (VI)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-ol
Compound of formula (VII)	4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (VIII)	Combination of 1. 2',5,5-trimethyl-4,4a,5,6,7,8-hexahydro-3H-spiro[naphthalene-2,5'-[1,3]dioxane], 2. 2',5,5-trimethyl-3,4,4a,5,6,7-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane], and 3. 2',5,5-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (IX)	2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (X)	2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (XI)	8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]

5

Embodiment 2: Antimicrobial composition comprising

- 0.01 weight percent to 90 weight percent of the antimicrobial compound(s) according to claim 1, and
- 10 weight percent to 99.99 weight percent of cosmetically acceptable ingredient(s)

wherein the sum of the antimicrobial compound(s), and cosmetically acceptable ingredient(s) is at least 90 weight percent of the composition, or 100 weight percent of the composition.

Embodiment 3: Antimicrobial composition according to embodiment 2 wherein the cosmetically acceptable ingredient(s) is selected amongst anionic surfactants, nonionic surfactants, amphoteric/zwitterionic surfactants, cationic surfactants, cationic polymers, conditioning agents, suspending agents, silicone polymers, humectants, preservatives, high melting point fatty compounds, pH adjusting agents, emulsifiers, additives, skin and hair benefiting ingredients solvents and/or a mixture of two or more carriers thereof.

Embodiment 4: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 and 3 for use as antibacterial and antifungal treatment.

Embodiment 5: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 and 3 for use in the treatment of malodour, dandruff and/or pathogenic microorganisms.

Embodiment 6: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 and 3 for use in the treatment of *Malassezia furfur*, *Corynebacterium xerosis*, *Staphylococcus epidermidis* and/or *Staphylococcus aureus*.

Embodiment 7: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I), (II), (III), (VI), (VIII), or a mixture of compounds of formula (I) and formula (II), for use in the treatment of *Malassezia furfur*.

Embodiment 8: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I), (II), (VI), (VIII), (X), or (XI), or wherein the compound of the composition is the compound formula (I) for use in the treatment of *Corynebacterium xerosis*.

Embodiment 9: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I) or (VIII), or wherein the compound of the composition is the compound formula (I) for use in the treatment of *Staphylococcus epidermidis*.

Embodiment 10: Antimicrobial compound according to embodiment 1 or antimicrobial composition according to any one of embodiments 2 to 6 wherein the compounds are selected from Antimicrobial compound of formula (I) for use in the treatment of *Staphylococcus aureus*.

Embodiment 11: Antimicrobial compound or antimicrobial composition according to any one of the preceding embodiments for use in a rinse-off and/or wash-off personal care formulation for the treatment of human scalp or human skin or underarms.

Embodiment 12: Personal care composition comprising an antimicrobial compound or antimicrobial composition according to any one of the preceding embodiments for use as shampoo, hair conditioner, hair tonic, hair oil, hair serum, hair gel, cream rinse, body wash, hand wash, bubble bath, bath oil, facial cleanser, cleansing mask, cleansing milk, micellar water, make-up remover, cleansing wipes, perfume, talc, deodorants, soaps, shaving soaps, shaving foams, cleansing foams, face mask, face cream, hand cream, body lotion and roll-on.

Embodiment 13: Process for decreasing the level of microorganisms like *Malassezia furfur*, *Corynebacterium xerosis*, *Staphylococcus epidermidis*, and/or *Staphylococcus aureus* on a

surface by treating said surface with a personal care composition according to embodiment 12.

The personal care compositions use in this invention are used for the benefits of hair and skin including wash-off, rinse-off or leave-on formulations such as shampoos, conditioners, creams, lotions, gels, serums, mousses or oils. Some examples of personal care compositions are as follows

Chemical name/ IUPAC name of commonly used ingredients used in this invention

Sr. No.	Ingredients	Chemical name/ IUPAC name
1	Glycerin	Propane-1,2,3-triol
2	Sodium Lauroyl Sarcosinate	N-lauroylsarcosine sodium salt
3	Cocamidopropyl betaine	2-[3-(dodecanoylamino)propyl-dimethylazaniumyl]acetate
4	Glyceryl Caprylate caprate	Decanoic acid, mixed monoesters with glycerol and octanoic acid
5	Crodazosoft DBQ	Quaternium-91 (and) Cetrimonium Methosulfate (and) Cetearyl Alcohol
6	Cetosteryl Alcohol	Palmityl alcohol and 1-hexadecanol
7	Arlacel 165	Glyceryl Stearate
8	Tinoguard TT	Pentaerythrityl Tetra-Di-t-Butyl Hydroxyhydrocinnamate
9	Cyclopentasiloxane	Decamethylcyclopentasiloxane
10	Dimethicone	Polydimethylsiloxane
11	Disodium EDTA	Disodium ethylenediaminetetraacetate
12	Phenoxyethanol	2-Phenoxyethan-1-ol
13	Behentrimonium Methosulfate	1,3- Butylene Glycol

14	Geranium CTAC	Cetrimonium chloride
15	Xiameter of CE 1785	Dimethicone (and) Dimethiconol
16	Vitamin E	d-alpha-tocopherol
17	Phenyl Trimethicone	Trimethyl-[phenyl-bis(trimethylsilyloxy)silyl]oxysilane
18	Cyclomethicone	Cyclopentasiloxane
19	Isopropyl myristate	Propan-2-yl tetradecanoate
20	Diethyl Phthalate	1,2-benzenedicarboxylic acid
21	Propylene Glycol	Propane-1,2-diol

Antimicrobial studies

Minimum Inhibitory Concentration (MIC) study

Minimum Inhibitory Concentration of compounds of formulae (I) to (XI) compared to Climbazole and Triclosan were tested against pathogenic organisms *Malassezia furfur, Corynebacterium xerosis, Staphylococcus epidermidis,* and *Staphylococcus aureus.*

MIC study protocol is as follow

- Test compounds diluted in DMSO and MIC was determined against *Malassezia furfur, Corynebacterium xerosis, Staphylococcus epidermidis,* and *Staphylococcus aureus*
- Microorganisms maintained on potato dextrose agar slant and soybean casein digest agar slant were revived by inoculating in broth followed by incubation at 25^0C for 2-3 days
- This culture was then revived in fresh broth and incubated for 48h
- Series of test tubes were made with test sample concentration starting from 100mg/ml
- 1ml of the broth culture was added to get the final cell concentration to get 10^5-10^6 cfu/ml and final concentration of the sample as 50 mg/ml.

- Further 20 dilutions were made and further all tubes were incubated at 30^0C for 72 hrs for fungus growth
- After incubation, the tubes were monitored for visual turbidity.
- MIC of the sample was determined as the lowest concentration at which no turbidity and microbial growth was observed.

Results of anti-microbial studies

Sr. No.	Compound	Organisms & MIC (mg/ml)			
		M. furfur	***C. xerosis***	***S.epidermidis***	***S. aureus***
1	Climbazole	0.391	Not tested	Not tested	Not tested
2	Triclosan	Not tested	0.097	0.001	0.001
3	Compound formula (I)	0.024	0.024	0.098	0.098
4	Compound formula (II)	0.024	0.00076	NA	NA
5	Compound formula (III)	0.195	NA	NA	NA
6	Compound formula (IV)	NA	NA	NA	NA
7	Compound formula (V)	NA	NA	NA	NA
8	Compound formula (VI)	0.005	0.003	NA	NA
9	Compound formula (VII)	NA	NA	NA	NA
10	Compound formula (VIII)	0.024	0.024	0.781	NA
11	Compound formula (IX)	NA	NA	NA	NA
12	Compound formula (X)	NA	0.078	NA	NA
13	Compound formula (XI)	NA	0.156	NA	NA
14	Composition (Mixture of Compound formula (I) and Diethyl adipate (1:1))	0.006	0.012	0.001	NA

15	Mixture of compound formula (I) and compound formula (II) (1:1)	0.391	NA	NA	NA

In the Table, "-" means no activity detected; "NA" means "not available", i.e. the detailed analysis have not been obtained yet.

The MIC analysis indicates that the Compound formulae (I) to (XI) and mixtures thereof exhibited antimicrobial activities against various microbes at sub-mg/ml dosages. Therefore, as per this invention, compositions containing Compound formulae (I) to (XI) and mixtures thereof can be used as antimicrobial formulations.

Examples (compositions)

Examples 1, Example 2 and Comparative Example 3:

Ingredients	**Category**	**Example 1**	**Example 2**	**Comparative Example 3**
		Shampoo formulation as per this invention	**Shampoo formulation as per this invention**	**Shampoo formulation using anti-dandruff agent**
		%w/w	**%w/w**	**%w/w**
Compound of formula (I)	Active	1	-	-
Mixture of compound formula (I) and compound formula (II) (1:1)	Active	-	1	-
Climbazole	Active	-	-	1
Glycerin	Humectant	3.5	3.5	3.5
Sodium Lauroyl Sarcosinate	Anionic Surfactant	12	12	12

Cocamidopropyl betaine	Amphoteric surfactant	30	30	30
Glyceryl Caprylate caprate	Emollients	2.5	2.5	2.5
Disodium EDTA	Chelating agent	0.1	0.1	0.1
Phenoxyethanol	Preservative	1.5	1.5	1.5
Sodium Chloride	Viscosity modifier	0.1	0.1	0.1
Deionised Water	Solvent	49.8	49.8	49.8

The numerical values given are percentages by weight based on 100% pure substance.

Time kill study (ASTM E2315)

Time kill of compounds of formula (I) and Mixture of compound formula (I) and compound formula (II) (1:1) tested against pathogenic organisms *Malassezia furfur* and reference anti-dandruff compound is Climbazole

Time kill study protocol is as follow

- In the time kill experiment, fungicidal activity of the test compounds and reference anti-dandruff compound was determined against *M.furfur*
- Test compound of formula (I) and Mixture of compounds and reference anti-dandruff compound mixed at a dosage of 1 w/w% both in shampoo base as a representative of wash off product (Example 1, example 2 and comparative example 3)
- Test compound of formula (I) and Mixture of compounds and reference anti-dandruff compound diluted with water at 1:1 ratio
- The inoculum suspension was prepared to achieve a minimum of 10^5-10^6 cfu/ml microbial population
- The test sample were mixed with appropriate inoculum suspension and uniform mixing was maintained to disperse the inoculum suspension

- 1ml aliquot was removed from the sample/inoculum container after the 1 min contact time and neutralization
- Viable organisms were recovered from appropriate dilutions by culturing in duplicate by use of pour plating technique and plates were incubated
- Percent reduction was calculated by comparing viable organisms at the beginning and at the end of the contact time (2 min)

Test compound of formula (I) mixed in shampoo base (Example 1), Mixture of compounds mixed in shampoo base (Example 2) and reference anti-dandruff compound mixed in shampoo base (Comparative example 3) . The test compound of formula (I) and Mixture of compounds showed time kill 99.26 % and 99.42 % respectively against *M.furfur* and the time kill of anti-dandruff benchmark climbazole is 99.47 % at same concentration.

This invention illustrates accordingly the antimicrobial activities of Compound formulae (I), (II), (III), (VI), (VIII), (X), (XI), Mixture of compound formula (I) and (II) (1:1) and composition containing compound (I) thereof, against various microbes such as dandruff-causing, malodour-causing, and pathogenic microorganisms by significantly reducing the population of such microorganisms. It particularly relates to antimicrobial compositions for use in personal care formulations.

Claims

1. Antimicrobial compound of formula (I), (II), (III), (IV), (V), (VI), (VIII), (X), or (XI) or a mixture of two or more compounds thereof, for use as a medicament,
wherein the compounds of formula (I) to (XI) have the following IUPAC names

Compounds	IUPAC name
Compound of formula (I)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-one
Compound of formula (II)	4-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)pent-3-en-2-ol
Compound of formula (III)	4-(4-methoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (IV)	4-(4-butoxypent-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (V)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-one
Compound of formula (VI)	5-(1,7a-dimethyloctahydro-4H-1,4-methanoinden-4-yl)hex-4-en-3-ol
Compound of formula (VII)	4-(4-methoxyhex-2-en-2-yl)-1,7a-dimethyloctahydro-1H-1,4-methanoindene
Compound of formula (VIII)	Combination of 1. 2',5,5-trimethyl-4,4a,5,6,7,8-hexahydro-3H-spiro[naphthalene-2,5'-[1,3]dioxane], 2. 2',5,5-trimethyl-3,4,4a,5,6,7-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane], and 3. 2',5,5-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]

Compound of formula (IX)	2'-ethyl-2',8,8-trimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (X)	2',2'-diethyl-8,8-dimethyl-3,4,5,6,7,8-hexahydro-1H-spiro[naphthalene-2,5'-[1,3]dioxane]
Compound of formula (XI)	8",8"-dimethyl-3",4",5",6",7",8"-hexahydro-1"H-dispiro[cyclohexane-1,2'-[1,3]dioxane-5',2"-naphthalene]

2. Antimicrobial composition for use as a medicament comprising

- 0.01 weight percent to 90 weight percent of the antimicrobial compound(s) according to claim 1, and
- 10 weight percent to 99.99 weight percent of cosmetically acceptable ingredient(s)

wherein the sum of the antimicrobial compound(s), and cosmetically acceptable ingredient(s) is at least 90 weight percent of the composition, or 100 weight percent of the composition.

3. Antimicrobial composition according to claim 2 wherein the cosmetically acceptable ingredient(s) is selected amongst anionic surfactants, nonionic surfactants, amphoteric/zwitterionic surfactants, cationic surfactants, cationic polymers, conditioning agents, suspending agents, silicone polymers, humectants, preservatives, high melting point fatty compounds, pH adjusting agents, emulsifiers, additives, skin and hair benefiting ingredients solvents and/or a mixture of two or more carriers thereof.

4. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 and 3 for use as antibacterial or antifungal medicament.

5. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 and 3 for use as a medicament in a method for the treatment of malodour, dandruff and/or pathogenic microorganisms.

6. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 and 3 for use as a medicament in a method for the treatment of dandruff due to the presence of *Malassezia furfur*, or for the treatment of malodour caused by the presence of *Corynebacterium xerosis*, *Staphylococcus epidermidis* and/or *Staphylococcus aureus*.

7. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I), (II), (III), (VI), (VIII), or a mixture of compounds of formula (I) and formula (II), for use as a medicament in a method for the treatment of dandruff due to the presence of *Malassezia furfur*.

8. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I), (II), (VI), (VIII), (X), or (XI), or wherein the compound of the composition is the compound formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Corynebacterium xerosis*.

9. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 to 6 wherein the compounds are selected from Antimicrobial compounds of formula (I) or (VIII), or wherein the compound of the composition is the compound formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Staphylococcus epidermidis*.

10. Antimicrobial compound according to claim 1 or antimicrobial composition according to any one of claims 2 to 6 wherein the compounds are selected from Antimicrobial compound of formula (I) for use as a medicament in a method for the treatment of malodour caused by the presence of *Staphylococcus aureus*.

11. Antimicrobial compound or antimicrobial composition according to any one of the preceding claims formulated as a rinse-off and/or wash-off personal care formulation for the

treatment of human scalp or human skin or underarms for use as a medicament in a method for the treatment of malodour, dandruff and/or pathogenic microorganisms.

12. Personal care composition comprising an antimicrobial compound or antimicrobial composition according to any one of the preceding claims for use as a medicament, wherein the personal care composition is in the form of a shampoo, hair conditioner, hair tonic, hair oil, hair serum, hair gel, cream rinse, body wash, hand wash, bubble bath, bath oil, facial cleanser, cleansing mask, cleansing milk, micellar water, make-up remover, cleansing wipes, perfume, talc, deodorants, soaps, shaving soaps, shaving foams, cleansing foams, face mask, face cream, hand cream, body lotion or roll-on.

13. Process for decreasing the level of microorganisms like *Malassezia furfur*, *Corynebacterium xerosis*, *Staphylococcus epidermidis*, and/or *Staphylococcus aureus* on a surface by treating said surface with a personal care composition according to claim 12.