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(71) Applicant (for all designated States except US): **SYMRISE GMBH & CO. KG** [DE/DE]; Mühlenfeldstrasse 1, 37603 Holzminden (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SCHMAUS, Gerhard** [DE/DE]; Herrenburgstrasse 29, 37671 Hötter (DE).
LANGE, Sabine [DE/DE]; Danzigerstrasse 20, 37603 Holzminden (DE).

(74) Agents: **STILKENBÖHMER, Uwe** et al.; c/o Eisenführ, Speiser & Partner, P.O. Box 10 60 78, 28060 Bremen (DE).

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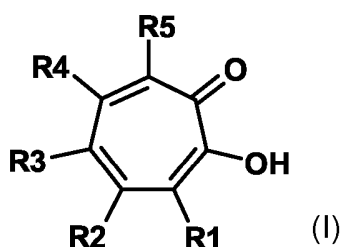
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(54) Title: SYNERGISTIC MIXTURES OF C6- TO C12-ALKANEDIOLS AND TROPOLONE (DERIVATIVES)



(57) Abstract: Antimicrobial mixtures comprising or consisting of: (a) one or more branched or unbranched alkanediols having 6-12 carbon atoms, (b) one, two or more compounds chosen from the group consisting of the tropolones of the formula (I) wherein the substituents R1, R2, R3, R4 and R5 independently of one another have the following meaning: H; linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms; OH; OR6, wherein R6 is a linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms; COOH; COOR7, wherein R7 is a linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms; NO₂, NH₂, F, Cl, Br, I, are described.



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Symrise GmbH & Co. KG
Mühlenfeldstraße 1, 37603 Holzminden

Synergistic mixtures of C6- to C12-alkanediols and
tropolone (derivatives)

The present invention relates to the field of antimicrobial active compounds, and in particular certain mixtures, formulations and foodstuffs comprising at least one C6- to C12-alkanediol and at least one tropolone of the general formula (I) and to products comprising such mixtures in an antimicrobially active amount.

- 5 In the cosmetics and pharmaceutical and in the foodstuffs industry there is a constant need for agents having antimicrobial properties, in particular for the preservation of products which are otherwise perishable (such as e.g. cosmetics, pharmaceutical products or foodstuffs), but also for direct cosmetic or therapeutic treatment of microorganisms which can have an adverse influence on the human
- 10 or animal body. Reference may be made by way of example to microorganisms which can cause body odour, acne, mycoses or the like.

In the technical fields referred to a large number of antimicrobial active compounds are indeed already employed, but alternatives nevertheless continue to be sought, in order to be able to perform targeted specific treatments and/or

15 reduce side effects. In this context, however, in the search for alternative agents

having an antimicrobial and in particular preserving action it is to be noted that the substances used in the cosmetics, pharmaceutical and/or foodstuffs field must be

- toxicologically acceptable,
- 5 - readily tolerated by the skin,
- stable (in particular in the conventional cosmetic and/or pharmaceutical formulations),
- largely and preferably completely odourless and
- inexpensive to prepare (i.e. employing standard processes and/or starting
10 from standard precursors).

The search for suitable (active) substances which have one or more of the properties mentioned to an adequate extent is made difficult for the person skilled in the art in that there is no clear dependency between the chemical structure of a substance on the one hand and its biological activity against certain
15 microorganisms (germs) and its stability on the other hand. Furthermore, there is no predictable connection between the antimicrobial action, the toxicological acceptability, the skin tolerability and the stability of a substance.

According to a first aspect, the invention relates to an antimicrobial mixture comprising or consisting of:

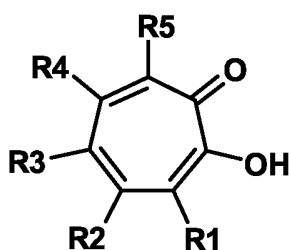
- 20 (a) one or more branched or unbranched alkanediols having 6-12 carbon atoms, preferably one or more branched or unbranched 1,2-alkanediols having 6-12 carbon atoms,
and particularly preferably
1,2-hexanediol,
25 1,2-octanediol or
1,2-decanediol or
a mixture of 1,2-hexanediol and 1,2-octanediol or

a mixture of 1,2-hexanediol and 1,2-decanediol or

a mixture of 1,2-octanediol and 1,2-decanediol or

a mixture of 1,2-hexanediol, 1,2-octanediol and 1,2-decanediol,

- (b) one, two or more compounds chosen from the group consisting of the
5 tropolones of the formula (I)



wherein the substituents R1, R2, R3, R4 and R5 independently of one another have the following meaning:

- 10 H;

linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms;

OH;

- OR6, wherein R6 is a linear or branched, saturated or unsaturated, aliphatic
15 hydrocarbon radical having up to 30 C atoms;

COOH;

COOR7, wherein R7 is a linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms;

NO₂,

NH₂,

F, Cl, Br, I.

The contents of the alkanediols and tropolones of the formula (I) in the mixture here are preferably adjusted such that their antimicrobial action is intensified synergistically.

Alternatively or in addition to the particularly preferred 1,2-alkanediols, it is also possible to employ 1,6-hexanediol, 2-methylpentane-2,4-diol, 2,5-hexanediol, 3,6-octanediol, 2-ethyl-1,3-hexanediol, 1,3-octanediol, 1,3-decanediol and mixtures thereof with very good success in or as constituent (a).

Compounds which are preferred for use as constituent (b) in antimicrobial mixtures according to the invention are:

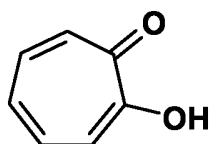
tropolone (formula (I): R₁, R₂, R₃, R₄, R₅ = H),

alpha-thujaplicin ((formula (I): R₁ = iso-propyl, R₂, R₃, R₄, R₅ = H),

beta-thujaplicin (formula (I): R₂ = iso-propyl, R₁, R₃, R₄, R₅ = H)

gamma-thujaplicin (formula (I): R₃ = iso-propyl, R₁, R₂, R₄, R₅ = H) and mixtures of these compounds of the formula (I).

The structural formula of the compound tropolone (CAS No.: 533-75-5; 2,4,6-cycloheptatrien-1-one, 2-hydroxy), which is particularly preferred for use in a mixture according to the invention, is:



The invention is based on the surprising finding that the mixtures according to the invention show a synergistically intensified antimicrobial effect at least against selected germs, in particular against *Aspergillus niger*, a mould which can be combated only with great difficulty.

In particular, it has been found that the mixtures according to the invention can be used outstandingly as an antimicrobial active compound mixture, in particular for preserving otherwise perishable articles (see above).

Although persons skilled in the art have already addressed the antimicrobial properties of alkanediols and of tropolone and tropolone derivatives extensively, there has hitherto been no indication that the mixtures according to the invention of such compounds have a significantly improved antimicrobial action (at least against selected germs) in the individual case.

The antimicrobial action of tropolone and tropolone derivatives is known e.g. from Antimicrob. Agents Chemother. vol. 7(5), 500-506 (1975). However, studies of a synergistically intensified activity in combination with alkanediols against *Aspergillus niger* are not disclosed in any of these publications.

The antimicrobial action of polyols, in particular of aliphatic 1,2 -diols and combinations of 1,2-diols with further antimicrobially active substances, is described in various documents. JP5191327, JP11322591, EP1206933 and WO 03/069994 may be mentioned here by way of example. However, studies of a synergistically intensified activity against *Aspergillus niger* in combination with tropolone or a tropolone derivative are not disclosed in any of these publications.

Polyols, and in particular 1,2-alkanediols, usually have only a deficient action against moulds such as *Aspergillus niger*. In respect of individual polyols or mixtures of polyols, a gap in the activity on moulds (e.g. the "problem germ" *Aspergillus niger*) is thus to be recorded. High use concentrations of individual polyols or of mixtures of polyols have therefore hitherto been necessary for complete inhibition of moulds.

JP2001278728 describes the use of tropolone derivatives in combination with polyols, such as dipropylene glycol, 1,3-butylene glycol and 1,2-pentanediol, in antimicrobial cosmetics. On the other hand, alkanediols having 6-12 carbon atoms are not described. A synergistic intensification in activity in the combination of a tropolone derivative with a branched or unbranched alkanediol having 6-12 carbon atoms is also not disclosed.

It was therefore particularly surprising that the mixtures according to the invention show a highly synergistic activity, and in the treatment of *Aspergillus niger* are significantly superior to

- individually dosed tropolones of the formula (I) and mixtures of tropolones of the formula (I) or
- individually dosed branched or unbranched alkanediols having 6-12 carbon atoms, in particular branched or unbranched 1,2-alkanediols having 6-12 carbon atoms, and chosen from this group in particular 1,2-hexanediol, 1,2-octanediol and 1,2-decanediol

at the same concentration, in particular in respect of the reduction in germ count and the speed of the reduction in germ count. In particular, in the individual case a CFU value (CFU = number of colony-forming units) of 0 was achieved only with the said mixtures according to the invention.

On the basis of the particularly significant intensification in the action of their constituents, mixtures according to the invention are suitable in particular for combating *Aspergillus niger* even at a low dosage of the mixture according to the invention.

For the preparation of an effective mixture according to the invention which causes a complete reduction in the *Aspergillus niger* germ count, it is sufficient to mix one mixture constituent (a) comprising one or more branched or unbranched alkanediols having 6-12 carbon atoms, preferably at least one or more branched or unbranched 1,2-alkanediols having 6-12 carbon atoms, and from this group particularly preferably 1,2-hexanediol, 1,2-octanediol, 1,2-decanediol and mixtures thereof, with a small amount of constituent (b), i.e. one, two or more tropolones of the formula (I), for example an amount in the range of 0.001 - 10 wt.%, for example only 0.5 - 4 wt.%, based on the amount of constituent (a). If an amount of 0.3 wt.% 1,2-hexanediol and/or 1,2-octanediol and/or 1,2-decanediol is employed, this corresponds e.g. to an amount of tropolone(s) of just about 0.01 wt.%, in each case based on the total weight of the end product.

Based on the total weight of constituents (a) and (b) to be employed according to the invention, the content of constituent (a) is in the range of from 80 to 99.9 wt.%, but preferably in the range of 94 - 99 wt.%.

The antimicrobial mixtures according to the invention are suitable for preservation
5 and antimicrobial treatment of perishable products, such as e.g. cosmetic products, pharmaceutical products or foodstuffs. In this context, the perishable product is brought into contact with an antimicrobially active amount, preferably an amount which is active against *Aspergillus niger*, of a mixture according to the invention. On the basis of their synergistically intensified antimicrobial activity,
10 however, the mixtures according to the invention can also be employed

- (a) for the cosmetic treatment of microorganisms which cause body odour,
- (b) for the cosmetic treatment of microorganisms which cause acne,
- (c) for the cosmetic treatment of microorganisms which cause
15 mycoses and
- (d) for the treatment of microorganisms on or in inanimate matter.

The mixtures according to the invention display their synergistically intensified antimicrobial action against a large number of Gram-positive bacteria, Gram-negative bacteria, moulds and yeasts. A particularly good action exists against
20 Gram-negative bacteria, such as *Escherichia coli* and *Pseudomonas aeruginosa*, against yeasts, such as *Candida albicans* and precisely - as already mentioned - against fungi, such as *Aspergillus niger*. The very good activity of the mixtures according to the invention against *Aspergillus niger*, a mould which can be combated only with great difficulty, is to be regarded as particularly
25 advantageous here.

The present invention also relates to the use of a mixture according to the invention, that is to say a mixture comprising or consisting of:

- (a) one or more branched or unbranched alkanediols having 6-12 carbon atoms, preferably one or more branched or unbranched 1,2-alkanediols having 6-12 carbon atoms, and chosen from this group particularly preferably 1,2-hexanediol, 1,2-octanediol and 1,2-decanediol
- 5 (b) one, two or more compounds chosen from the group consisting of tropolones of the formula (I), with the abovementioned meanings of the substituents, in particular the compounds described above as preferred,

as an antimicrobial active compound mixture.

The present invention furthermore relates to corresponding methods for the
10 cosmetic and/or therapeutic treatment of germs, and in particular especially of (a) microorganisms which cause body odour, (b) microorganisms which cause acne and/or (c) microorganisms which cause mycoses, comprising topical application of an antimicrobially active amount of a mixture according to the invention, the contents of the said diols in the mixture preferably being adjusted such that their
15 antimicrobial action is synergistically intensified.

Preferred embodiments of the methods according to the invention correspond to the preferred embodiments of the use according to the invention which are explained above.

The human skin is populated by a large number of various microorganisms,
20 which include the microorganisms already mentioned above, as well as others. Most of these microorganisms are not pathogenic and are irrelevant to the physiological state of the skin and to the odour thereof. On the other hand, others can influence the healthy state of the skin decisively.

As our own studies have now shown, the synergistically active mixtures
25 according to the invention have a good action not only against the germs already named above, but also against *Staphylococcus epidermidis*, *Corynebacterium xerosis*, *Brevibacterium epidermidis*, *Propionibacterium acnes* and against *Trichophyton* and *Epidermophyton* species, so that they can also be employed as agents for the treatment of (combating) underarm and foot odour or body odour

generally, as agents for combating acne, as antidandruff agents and for the treatment of mycoses (in particular dermatomycoses).

In the context of the present text, "treatment" is understood here as meaning any form of influencing of the microorganisms in question in which the multiplication
5 of these microorganisms is inhibited and/or the microorganisms are killed.

The use concentration of a mixture according to the invention (which is preferably in a preferred embodiment) when used as a preservative or antimicrobial active compound in a foodstuff or a cosmetic or pharmaceutical formulation is preferably in the range of from 0.01 to 10 wt.%, but particularly preferably in the
10 range of from 0.05 to 5 wt.%, in each case based on the total weight of the foodstuff or the formulation. The foodstuff and formulation additionally comprise conventional further constituents, in this context see below. The particular content of constituents (a) and/or (b) to be used according to the invention in mixtures according to the invention can be below the amount regarded as
15 antimicrobially active in itself if the total amount of these substances which is present is sufficiently high to achieve an antimicrobial action of the total mixture. This applies in particular to the action against *Aspergillus niger*.

In a preferred method according to the invention for the cosmetic and/or therapeutic treatment of (a) microorganisms which cause body odour, (b)
20 microorganisms which cause acne and/or (c) microorganisms which cause mycoses, the use concentration of the synergistically active mixtures according to the invention is also in the range between 0.01 and 10 wt.%, and particularly preferably in the range between 0.05 and 5 wt.%, in each case based on the total weight of the cosmetic or pharmaceutical product which comprises the mixture.

25 The synergistically active mixtures can be employed here (a) prophylactically or (b) as required.

The concentration of the amount of active compound to be applied e.g. daily varies and depends on the physiological state of the subject and individual-specific parameters, such as age or body weight. The synergistically active

mixtures according to the invention can be employed either by themselves or in combination with further antimicrobially active substances.

In the context of the present text, it is to be pointed out that the 1,2-alkanediols to be employed according to the invention can be in the form of either the
5 corresponding enantiomer of 2S configuration or the enantiomer of 2R configuration and in the form of any desired mixtures of these enantiomers of 2S and 2R configuration. For commercial reasons, it is indeed particularly advantageous to employ, for combating microorganisms, mixtures of racemates of the particular 1,2-alkanediols to be employed according to the invention, since
10 these are particularly readily accessible by synthesis, but the pure enantiomers or non-racemic mixtures of these enantiomers are likewise suitable for the purposes according to the invention.

Further uses/methods and mixtures/compositions according to the invention can be found in the following statements and the attached patent claims.

15 Compositions which comprise a mixture according to the invention are, especially if they are employed against germs which cause body odour, as a rule applied topically in the form of solutions, creams, lotions, gels, sprays or the like. For other purposes, an oral (tablets, capsules, powders, drops), intravenous, intraocular, intraperitoneal or intramuscular administration or an administration in
20 the form of an impregnated dressing is appropriate in some cases.

The mixtures according to the invention can be incorporated without difficulties into the usual cosmetic and/or dermatological formulations, such as, inter alia, pump sprays, aerosol sprays, creams, ointments, tinctures, lotions, nail care products (e.g. nail varnishes, nail varnish removers, nail balsams) and the like. It
25 is also possible here, and in some cases advantageous, to combine the synergistic mixtures according to the invention with further active compounds, for example with other antimicrobially, antimycotically or antivirally active substances. The cosmetic and/or dermatological/keratological formulations comprising the synergistic mixtures according to the invention can otherwise
30 have the conventional composition here and serve for the treatment of skin and/or hair in the sense of a dermatological treatment or a treatment in the sense

of care cosmetics. However, they can also be employed in make-up products in decorative cosmetics.

If the mixtures according to the invention are employed as active compounds for preserving organic material, a further or several further preservatives can advantageously additionally be employed. Preservatives which are preferably chosen here are those such as benzoic acid, its esters and salts, propionic acid and its salts, salicylic acid and its salts, 2,4-hexadienoic acid (sorbic acid) and its salts, formaldehyde and paraformaldehyde, 2-hydroxybiphenyl ether and its salts, 2-zinc-sulfidopyridine N-oxide, inorganic sulfites and bisulfites, sodium iodate, chlorobutanol, 4-ethylmercury-(II)-5-amino-1,3-bis(2-hydroxybenzoic acid), its salts and esters, dehydracetic acid, formic acid, 1,6-bis(4-amidino-2-bromophenoxy)-n-hexane and its salts, the sodium salt of ethylmercury-(II)-thiosalicylic acid, phenylmercury and its salts, 10-undecylenic acid and its salts, 5-amino-1,3-bis(2-ethylhexyl)-5-methyl-hexahydropyrimidine, 5-bromo-5-nitro-1,3-dioxane, 2-bromo-2-nitro-1,3-propanediol, 2,4-dichlorobenzyl alcohol, N-(4-chlorophenyl)-N'-(3,4-dichlorophenyl)-urea, 4-chloro-m-cresol, 2,4,4'-trichloro-2'-hydroxy-diphenyl ether, 4-chloro-3,5-dimethylphenol, 1,1'-methylene-bis(3-(1-hydroxymethyl-2,4-dioximidazolidin-5-yl)urea), poly-(hexamethylenediguanide) hydrochloride, 2-phenoxyethanol, hexamethylenetetramine, 1-(3-chloroallyl)-3,5,7-triaza-1-azonia-adamantane chloride, 1-(4-chlorophenoxy)-1-(1H-imidazol-1-yl)-3,3-dimethyl-2-butanone, 1,3-bis-(hydroxymethyl)-5,5-dimethyl-2,4-imidazolidinedione, benzyl alcohol, Octopirox, 1,2-dibromo-2,4-dicyanobutane, 2,2'-methylene-bis(6-bromo-4-chlorophenol), bromochlorophene, mixture of 5-chloro-2-methyl-3(2H)-isothiazolinone and 2-methyl-3(2H)-isothiazolinone with magnesium chloride and magnesium nitrate, 2-benzyl-4-chlorophenol, 2-chloroacetamide, chlorhexidine, chlorhexidine acetate, chlorhexidine gluconate, chlorhexidine hydrochloride, 1-phenoxy-propan-2-ol, N-alkyl(C₁₂-C₂₂)trimethylammonium bromide and chloride, 4,4-dimethyl-1,3-oxazolidine, N-hydroxymethyl-N-(1,3-di(hydroxymethyl)-2,5-dioximidazolidin-4-yl)-N'-hydroxy-methylurea, 1,6-bis(4-amidino-phenoxy)-n-hexane and its salts, glutaraldehyde, 5-ethyl-1-aza-3,7-dioxabicyclo(3.3.0)octane, 3-(4-chlorophenoxy)-1,2-propanediol, hyamines, alkyl-(C₈-C₁₈)-dimethyl-benzyl-ammonium chloride, alkyl-(C₈-C₁₈)-dimethyl-benzylammonium bromide, alkyl-(C₈-C₁₈)-dimethyl-benzyl-ammonium

saccharinate, benzyl hemiformal, 3-iodo-2-propynyl butylcarbamate, sodium hydroxymethyl-aminoacetate or sodium hydroxymethyl-aminoacetate.

If the mixtures according to the invention are to be employed chiefly for inhibition of the growth of undesirable microorganisms on or in animal organisms, a combination with further antibacterial or antimycotic active substances is also advantageous here in some cases. In this respect, further active compounds which are worth mentioning, in addition to the large group of conventional antibiotics, are, in particular, the products relevant for cosmetics, such as triclosan, climbazole, octoxyglycerol, Octopirox (1-hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2(1H)-pyridone, 2-aminoethanol), chitosan, farnesol, glycerol monolaurate or combinations of the substances mentioned, which are employed, inter alia, against underarm odour, foot odour or dandruff formation.

The mixtures according to the invention can advantageously be combined, in particular in cosmetic formulations, with further conventional constituents, such as, for example:

Further preservatives, further antimicrobial agents, such as e.g. further antibacterial agents or fungicides, abrasives, antiacne agents, agents against ageing of the skin, anticellulitis agents, antidandruff agents, antiinflammatory agents, irritation-preventing agents, irritation-inhibiting agents, antioxidants, astringents, perspiration-inhibiting agents, antiseptic agents, antistatics, binders, buffers, carrier materials, chelating agents, cell stimulants, cleansing agents, care agents, depilatory agents, surface-active substances, deodorizing agents, antiperspirants, softeners, emulsifiers, enzymes, essential oils, fibres, film-forming agents, fixatives, foam-forming agents, foam stabilizers, substances for preventing foaming, foam boosters, gelling agents, gel-forming agents, hair care agents, hair-setting agents, hair-straightening agents, moisture-donating agents, moisturizing substance, moisture-retaining substances, bleaching agents, strengthening agents, stain-removing agents, optically brightening agents, impregnating agents, dirt-repellent agents, friction-reducing agents, lubricants, moisturizing creams, ointments, opacifying agents, plasticizing agents, covering agents, polish, gloss agents, polymers, powders, proteins, re-oiling agents, abrading agents, silicones, skin-soothing agents, skin-cleansing agents, skin care

agents, skin-healing agents, skin-lightening agents, skin-protecting agents, skin-softening agents, cooling agents, skin-cooling agents, warming agents, skin-warming agents, stabilizers, UV-absorbing agents, UV filters, detergents, fabric conditioning agents, suspending agents, skin-tanning agents, thickeners,
5 vitamins, oils, waxes, fats, phospholipids, saturated fatty acids, mono- or polyunsaturated fatty acids, α -hydroxy acids, polyhydroxy-fatty acids, liquefiers, dyestuffs, colour-protecting agents, pigments, anticorrosives, aromas, flavouring substances, odoriferous substances, polyols, surfactants, electrolytes, organic solvents or silicone derivatives.

10 The mixtures according to the invention can moreover also particularly advantageously be employed in combination with perspiration-inhibiting active compounds (antiperspirants) for combating body odour. Perspiration-inhibiting active compounds which can be employed are, above all, aluminium salts, such as aluminium chloride, aluminium hydrochloride, nitrate, sulfate, acetate etc. In
15 addition, however, the use of compounds of zinc, magnesium and zirconium may also be advantageous. For use in cosmetic and dermatological antiperspirants, the aluminium salts and - to a somewhat lesser extent - aluminium/zirconium salt combinations have essentially proved suitable. The aluminium hydroxychlorides which are partly neutralized and therefore tolerated better by the skin, but not
20 quite so active, are additionally worth mentioning.

If the mixtures according to the invention are to be employed for antimicrobial treatment of a surface (e.g. of a human or animal body), a combination with (metal) chelators is advantageous in some cases. (Metal) chelators which are preferably to be employed here are, inter alia, α -hydroxy fatty acids, phytic acid,
25 lactoferrin, α -hydroxy acids, such as, inter alia, citric acid, lactic acid and malic acid, and humic acids, bile acids, bile extracts, bilirubin, biliverdin or EDTA, EGTA and derivatives thereof.

It is moreover to be mentioned that the tropolones of the formula (I), in particular tropolone and the abovementioned thujaplicins, are (metal) chelators and are
30 also very particularly suitable in this respect for use in cosmetic and dermatological formulations.

For use, the cosmetic and/or dermatologically active mixtures according to the invention are applied to the skin and/or hair in a sufficient amount in the conventional manner for cosmetics and dermatics. In this context, cosmetic and dermatological formulations which comprise a mixture according to the invention and additionally act as sunscreen compositions offer particular advantages. These formulations advantageously comprise at least one UVA filter and/or at least one UVB filter and/or at least one inorganic pigment. In this context, the formulations can be in various forms such as are conventionally employed e.g. for sunscreen formulations. They can be e.g. a solution, an emulsion of the water-in-oil (W/O) type or of the oil-in-water (O/W) type or a multiple emulsion, for example of the water-in-oil-in-water (W/O/W) type, a gel, a hydrodispersion, a solid stick or also an aerosol.

As mentioned, formulations which comprise a mixture according to the invention can advantageously be combined with substances which absorb UV radiation, the total amount of the filter substances being e.g. 0.01 wt.% to 40 wt.%, preferably 0.1 % to 10 wt.%, in particular 1.0 to 5.0 wt.%, based on the total weight of the formulations, in order to provide cosmetic formulations which protect the hair or skin from ultraviolet radiation.

A high content of care substances is regularly advantageous in formulations for topical prophylactic or cosmetic treatment of the skin comprising mixtures according to the invention. According to a preferred embodiment, the compositions comprise one or more animal and/or plant fats and oils having care properties, such as olive oil, sunflower oil, refined soya oil, palm oil, sesame oil, rapeseed oil, almond oil, borage oil, evening primrose oil, coconut oil, shea butter, jojoba oil, sperm oil, beef tallow, neat's foot oil and lard, and optionally further care constituents, such as, for example, fatty alcohols having 8-30 C atoms.

Care substances which can be combined in an outstanding manner with the synergistic mixtures according to the invention moreover also include

- ceramides, where ceramides are understood as meaning N-acylsphingosins (fatty acid amides of sphingosin) or synthetic analogues of

such lipids (so-called pseudo-ceramides), which significantly improve the water retention capacity of the stratum corneum.

- phospholipids, for example soya lecithin, egg lecithin and cephalins
- vaseline, paraffin oils and silicone oils; the latter include, inter alia, dialkyl-
5 and alkylarylsiloxanes, such as dimethylpolysiloxane and methylphenylpolysiloxane, as well as alkoxylated and quaternized derivatives thereof.

Cosmetic formulations which comprise mixtures according to the invention can also comprise antioxidants, it being possible for all the antioxidants which are
10 suitable or usual for cosmetic and/or dermatological uses to be used.

Cosmetic formulations which comprise mixtures according to the invention can also comprise vitamins and vitamin precursors, it being possible for all the vitamins and vitamin precursors which are suitable or usual for cosmetic and/or dermatological uses to be used. There are worth mentioning here, in particular,
15 vitamins and vitamin precursors such as tocopherols, vitamin A, niacic acid and niacinamide, further vitamins of the B complex, in particular biotin, and vitamin C and panthenol and derivatives thereof, in particular the esters and ethers of panthenol and cationically derivatized panthenols, such as e.g. panthenol triacetate, panthenol monoethyl ether and the monoacetate thereof and cationic
20 panthenol derivatives.

Cosmetic formulations which comprise mixtures according to the invention can also comprise antiinflammatory or redness- or itching-alleviating active compounds. All the antiinflammatory or redness- and itching-alleviating active compounds which are suitable or usual for cosmetic and/or dermatological uses
25 can be used here.

Cosmetic formulations which comprise mixtures according to the invention can also comprise active compounds having a skin-lightening or skin-tanning action. According to the invention, all the skin-lightening or skin-tanning active

compounds which are suitable or usual for cosmetic and/or dermatological uses can be used here.

Cosmetic formulations which comprise mixtures according to the invention can also comprise anionic, cationic, nonionic and/or amphoteric surfactants, especially if crystalline or microcrystalline solids, for example inorganic micropigments, are to be incorporated into the formulations.

The invention is explained in more detail in the following with the aid of an example. Unless stated otherwise, the data relate to the weight.

Example: Comparison of adequate preservation of cosmetic formulations comprising a mixture of 1,2-hexanediol and 1,2-octanediol (product A, not according to the invention), tropolone (product B, not according to the invention) and a mixture of 1,2-hexanediol, 1,2-octanediol and tropolone (product C, according to the invention)

Testing for adequate preservation was carried out in accordance with the European Pharmacopoeia.

Testing thus comprises contamination of the formulation, if possible in its final condition, with a prescribed inoculum of suitable microorganisms, storage of the inoculated formulation at a certain temperature, removal of samples from the container at certain intervals of time and determination of the number of microorganisms in the samples removed in this way. The preserving properties are adequate if, under the conditions of the test, a clear reduction or, where appropriate, no increase in the germ count results in the inoculated formulations after the prescribed times at the prescribed temperatures. Experimental details of the test procedure are described in the European Pharmacopoeia (ISBN 3-7692-2768-9; Supplement 2001 to the 3rd Edition, page 421-422, chapter 5.1.3).

Test germs:

The following microorganism strains were used for the tests for adequate preservation:

A: *Escherichia coli* ATCC 8739

5 B: *Pseudomonas aeruginosa* ATCC 9027

C: *Staphylococcus aureus* ATCC 6538

D: *Candida albicans* ATCC 10231

E: *Aspergillus niger* ATCC 16404

10 The initial germ count (CFU/g; "0 value") was in the range of from 250,000 to 320,000 in the various test series.

Formulation:

For the tests for adequate preservation, a defined amount of the active compound combination according to the invention (product C) was incorporated into an O/W emulsion. For comparison purposes, the comparison products
15 (product A and B) were incorporated into separate O/W emulsions.

Formulations with products A, B and C:

Table 1:

			Wt.%	Wt.%	Wt.%
Phase A	INCI name	Manufacturer	with "A"	with "B"	with "C"
Dracorin CE 614035	Glyceryl Stearate Citrate	Symrise	4.0	4.0	4.0
PCL Solid 660086	Stearyl Heptanoate, Stearyl Caprylate	Symrise	3.0	3.0	3.0
Paraffin oil °E	Paraffinum Liquidum	Parafluid	7.0	7.0	7.0
Lanette 18	Stearyl Alcohol	Cognis	1.5	1.5	1.5
Dracorin GMS 647834	Glyceryl Stearate	Symrise	1.5	1.5	1.5
Dow Corning 200 fluid	Dimethicone	Dow Corning	2.0	2.0	2.0
Phase B					
Water, demineralized	Water (Aqua)		to 100	to 100	to 100
Carbopol ETD 2050 Polymer	Carbomer	Noveon	0.15	0.15	0.15
1,2-Hexanediol	1,2-Hexanediol	Symrise	0.25	-	0.15
Caprylyl Glycol	Caprylyl Glycol	Symrise	0.25	-	0.15

Tropolone		Symrise	-	0.01	0.01
Phase C					
Neutralizer AMP-95	Amino Methylpropanol	Dow/Angus	0.1	0.1	0.1
Total:			100.0	100.0	100.0

pH: 5.5

Result:

The results of the preservative stress tests for *Aspergillus niger* for the active compound combinations investigated, comprising the mixture according to the invention (product C) or the comparison systems (products A and B) are compared in Table 2. The synergistic effect of the mixture according to the invention (product C) manifests itself here above all in the residual germ counts for *Aspergillus niger* which remain after 28 days. As can be seen from the table, it was possible to reduce the germ count of *Aspergillus niger*, a germ which is particularly problematic in respect of preservation of industrial products, to 0 within 28 days by using the mixture according to the invention. In contrast, the active compound tested in product A in a dosage of 0.5 wt.% for comparison purposes (1,2-hexanediol + 1,2-octanediol; amounts ratio 1:1; w/w) rendered possible no such significant reduction in the number of colony-forming units (CFU), which also applies to product B (tropolone). This test series thus shows by way of example that active compound mixtures according to the invention have an action which is improved again synergistically compared with product A (mixture comprising 1,2-hexanediol and 1,2-octanediol; ratio of amounts 1:1; w/w).

Outstanding results which confirm the superiority of product C according to the invention were likewise obtained in respect of the further test germs.

Table 2: Testing for adequate preservation for product A, an active compound combination comprising 1,2-hexanediol and 1,2-octanediol in the amounts ratio of 1:1 (w/w), for product B (tropolone, formula (I): R1-R5 = H) and for product C, the mixture according to the invention comprising 1,2-hexanediol, 1,2-octanediol and tropolone

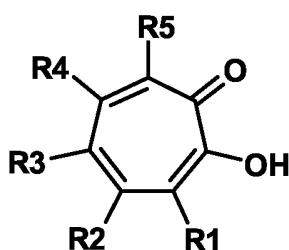
Days	0.5 % product A (1,2-hexanediol plus 1,2-octanediol; 1:1 w/w) <i>Aspergillus niger</i> [CFU/ml]	0.1 % product B (tropolone) <i>Aspergillus niger</i> [CFU/ml]	0.31% product C (0.3 % 1,2-hexanediol plus 1,2-octanediol; 1:1 w/w and 0.01 % tropolone) <i>Aspergillus niger</i> [CFU/ml]
0	280,000	280,000	280,000
2	80,000	72,000	300
7	68,000	2,000	0
14	40,000	4,800	0
28	30,000	100	0

Claims

1. Antimicrobial mixture comprising or consisting of:

(a) one or more branched or unbranched alkanediols having 6-12 carbon atoms,

(b) one, two or more compounds chosen from the group consisting of the
5 tropolones of the formula (I)



wherein the substituents R1, R2, R3, R4 and R5 independently of one another have the following meaning:

10 H;

linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms;

OH;

OR6, wherein R6 is a linear or branched, saturated or unsaturated, aliphatic
15 hydrocarbon radical having up to 30 C atoms;

COOH;

COOR7, wherein R7 is a linear or branched, saturated or unsaturated, aliphatic hydrocarbon radical having up to 30 C atoms;

NO₂,

NH₂,

F, Cl, Br, I.

2. Antimicrobial mixture according to claim 1, wherein one or more branched
5 or unbranched 1,2-alkanediols having 6-12 carbon atoms are employed as
constituent (a).

3. Antimicrobial mixture according to claim 1 or 2, wherein
1,2-hexanediol,
1,2-octanediol or
10 1,2-decanediol or
a mixture of 1,2-hexanediol and 1,2-octanediol or
a mixture of 1,2-hexanediol and 1,2-decanediol or
a mixture of 1,2-octanediol and 1,2-decanediol or
a mixture of 1,2-hexanediol, 1,2-octanediol and 1,2-decanediol
15 is employed as constituent (a).

4. Antimicrobial mixture according to one of claims 1, 2 or 3, wherein
tropolone (formula (I): R1, R2, R3, R4, R5 = H),
alpha-thujaplicin (formula (I): R1 = iso-Propyl, R2, R3, R4, R5 = H),
beta-thujaplicin (formula (I): R2 = iso-propyl, R1, R3, R4, R5 = H)
20 gamma-thujaplicin (formula (I): R3 = iso-propyl, R1, R2, R4, R5 = H)
or a mixture of these compounds of the formula (I)
is employed as constituent (b).

5. Antimicrobial mixture according to one of claims 1-4, comprising an amount
of constituent (b) in the range of 0.001 - 10 wt.%, based on the amount of
25 constituent (a).

6. Cosmetic or pharmaceutical formulation or foodstuff comprising
- an antimicrobial mixture comprising or consisting of constituents (a) and (b) according to one of claims 1 to 5 and
 - further conventional constituents
- 5 the total amount of constituents (a) and (b) being in the range of from 0.01 to 10 wt.%, based on the total weight of the formulation or of the foodstuff.
7. Antimicrobial mixture according to one of claims 1 to 5 or formulation or foodstuff according to claim 6, wherein the amount of constituent (a) and/or the amount of constituent (b) in each case considered in itself is not antimicrobially
- 10 active, but the total amount of constituents (a) and (b) is antimicrobially active.
8. Use of an antimicrobial mixture according to one of claims 1 to 5 or according to claim 7 as an antimicrobial active compound mixture.
9. Method for the preservation or antimicrobial treatment of a perishable product, with the following step:
- 15 - bringing of the perishable product into contact with an antimicrobially active amount, preferably an amount which is active against *Aspergillus niger*, of a mixture according to one of claims 1 to 5 or according to claim 7.
10. Method for the cosmetic and/or therapeutic treatment of
- (i) microorganisms which cause body odour,
 - 20 (i) microorganisms which cause acne and/or
 - (i) microorganisms which cause mycoses,
- comprising topical application of an antimicrobially active amount of a mixture according to one of claims 1 to 5 or according to claim 7.