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(54) Title: TOPICAL COLOURING COMPOSITION

(57) Abstract: Hair colourant formulations fall into three main categories designated permanent, semi-permanent and temporary. Permanent hair colourant formulations are oxidative dye systems and generally contain paraphenylenediamine (PPD) and resorcinol, both of which have been shown to cause sensitisation and mutagenicity. Furthermore, severe oxidising conditions are required which in themselves cause skin irritation and sensitization as well as hair fibre damage. The inventive composition addresses the aforementioned disadvantages by providing a topical colour composition comprising: (a) Quercetin; and (b) A laccase, wherein the composition has a pH of 4.5 to 7.0, preferably less than or equal to 6.0.



TOPICAL COLOURING COMPOSITION

5 A topical colour composition is disclosed, the composition comprising the flavonol quercetin, and a laccase, wherein the composition has a pH of 4.5 to 7.0, preferably less than or equal to 6.0. Optionally the topical colour composition includes metal ions, for example iron or copper, which are able to generate a range of colours for dyeing hair through coordination chemistry with quercetin, or reaction products thereof with the enzyme.

10 Hair colourant formulations fall into three main categories designated permanent, semi-permanent and temporary. They vary in their degree of wash-fastness where permanent hair colourant formulations last 30-40 shampoo cycles (4-6 weeks) and temporary systems are rinsed out during the first wash. Permanent hair colourant formulations are oxidative dye systems and generally contain paraphenylene
15 diamine (PPD) and resorcinol, both of which have been shown to cause sensitisation and mutagenicity. Furthermore the severe oxidising conditions required (hydrogen peroxide concentrations of 3 % or more and a pH of 8.5 or higher for time periods of 20 minutes or more) in themselves can cause skin irritation and sensitization for some individuals as well as hair fibre damage. In addition, permanent hair colourant
20 formulations also contain ammonia, used to swell the hair and lift the cuticle scales to allow penetration of dye precursors, which gives off a strong and unpleasant odour.

25 Takada et al. (Journal of Oleo Science, 52, 10, 557-563 (2003)) discloses a hair colouring composition comprising laccase and the flavan-3-ol catechin at pH 5.

WO 99/16893 (Instituut voor Agrotechnologisch Onderzoek (ATO-DLO)) discloses an enzymatic method for the synthesis of organic dyes, comprising bringing together an oxidative enzyme, a hydrogen acceptor and a hydrogen donor wherein at least
30 the hydrogen acceptor or donor is a substrate. In particular, Example 3 discloses reactions between peroxidase, hydrogen peroxide and the flavonols myricetin or quercetin.

The invention addresses the aforementioned disadvantages by providing a hair colouring compositions which avoids the issues of safety and toxicity associated with the known synthetic oxidative systems, causes less damage by avoiding the use of high levels of hydrogen peroxide, whilst maintaining colour fastness.

5

Summary of the invention

In a first aspect of the invention, a topical colour composition is provided, the composition comprising:

(a) Quercetin; and

10 (b) A laccase,

wherein the composition has a pH of 4.5 to 7.0, preferably less than or equal to 6.0.

Preferably the topical colour composition is a hair or skin colour composition.

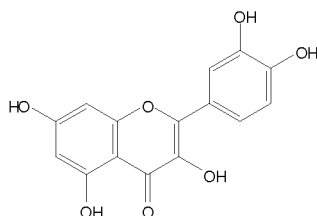
15 In a second aspect of the invention, a method of colouring hair fibres is provided, the method comprising the step of applying the hair colour composition of the first aspect of the invention to hair fibres.

In a third aspect of the invention, a method of colouring skin is provided, the method
20 comprising the step of applying the skin colour composition of the first aspect of the invention to skin.

Detailed description of the invention

As consumers will benefit from avoiding the issues around allergic skin reactions,
25 safety and toxicity of current permanent hair colourant formulations, the topical colour composition may be applied more frequently, for example daily, in the form of, for example, a shampoo or conditioner thereby addressing the problem of grey hair or natural hair colour re-growth observed during the intervals between hair dyeing treatments. Furthermore by multiple consecutive applications of the topical colour
30 composition, the consumer can also control the degree of colour desired.

The topical colour composition may comprise 0.001 – 10, preferably 0.1 - 5 % w/w (+)-quercetin.



Quercetin

The laccase is selected from those which are suited to neutral or slightly acid pH, that is to say a pH of 4.5 to 7.0, preferably a pH of less than or equal to 6.0. The advantage of this is that this more closely conforms to the pH of the skin thereby leading to lower levels of skin irritation. The laccase preferably originates from a fungal or a plant source such as those from the group consisting of the *Aspergillus*, *Botrytis*, *Ceriporiopsis*, *Cerrena*, *Chaetomium*, *Coprinus*, *Coriolus*, *Neurospora*, *Panus*, *Phanerochaete*, *Pleurotus*, *Polyporus*, *Pycnoporus* and *Trametes* genera, and *Rhus vernicifera*. The topical colour composition may comprise 0.0001 – 5, preferably 0.0001 - 1 % w/w laccase.

The topical colour composition of the first aspect may additionally comprise a metal ion suitable for coordinating to quercetin, or the product of the reaction of quercetin in the presence of laccase. The metal ion may be selected from the group consisting of iron (II), iron (III), copper (I), copper (II), and aluminium (III). The topical colour composition may comprise 0.0001 – 2, preferably 0.001 – 0.1 % w/w metal ion.

In one embodiment, the topical colour composition is a hair colour composition.

Shampoo Compositions

Shampoo compositions will nearly always comprise a cleansing surfactant component in an aqueous base.

Cleansing Surfactant

The cleansing surfactant may consist of a single surfactant, usually an anionic surfactant (to provide foam) such as sodium lauryl ether sulphate, or more commonly a mixture of sodium lauryl ether sulphate with a co-surfactant to provide mildness. The most preferred co-surfactant is cocoamidopropyl betaine.

The total amount of surfactant (including any co-surfactant, and/or any emulsifier) in a shampoo composition may be from 1 to 50., preferably from 2 to 40, more preferably from 10 to 25 % w/w. Compositions comprising more than 25 % w/w cleansing surfactant are commonly considered concentrated shampoos.

5

Examples of suitable anionic cleansing surfactants are the alkyl sulphates, alkyl ether sulphates, alkaryl sulphonates, alkanoyl isethionates, alkyl succinates, alkyl sulphosuccinates, alkyl ether sulphosuccinates, N-alkyl sarcosinates, alkyl phosphates, alkyl ether phosphates, and alkyl ether carboxylic acids and salts thereof, especially their sodium, magnesium, ammonium and mono-, di- and triethanolamine salts. The alkyl and acyl groups generally contain from 8 to 18, preferably from 10 to 16 carbon atoms and may be unsaturated. The alkyl ether sulphates, alkyl ether sulphosuccinates, alkyl ether phosphates and alkyl ether carboxylic acids and salts thereof may contain from 1 to 20 ethylene oxide or propylene oxide units per molecule.

15

Typical anionic cleansing surfactants for use in shampoo compositions of the invention include sodium oleyl succinate, ammonium lauryl sulphosuccinate, sodium lauryl sulphate, sodium lauryl ether sulphate, sodium lauryl ether sulphosuccinate, ammonium lauryl sulphate, ammonium lauryl ether sulphate, sodium dodecylbenzene sulphonate, triethanolamine dodecylbenzene sulphonate, sodium cocoyl isethionate, sodium lauryl isethionate, lauryl ether carboxylic acid and sodium N-lauryl sarcosinate.

20

Preferred anionic surfactants are the alkyl sulfates and alkyl ether sulfates. These materials have the respective formulae R_2OSO_3M and $R_1O(C_2H_4O)_xSO_3M$, wherein R_2 is alkyl or alkenyl of from 8 to 18 carbon atoms, x is an integer having a value of from about 1 to about 10, and M is a cation such as ammonium, alkanolamines, such as triethanolamine, monovalent metals, such as sodium and potassium, and polyvalent metal cations, such as magnesium, and calcium. Most preferably R_2 has 12 to 14 carbon atoms, in a linear rather than branched chain.

30

Preferred anionic cleansing surfactants are selected from sodium lauryl sulphate and sodium lauryl ether sulphate(n)EO, (where n is from 1 to 3); more preferably sodium lauryl ether sulphate(n)EO, (where n is from 1 to 3); most preferably sodium lauryl ether sulphate(n)EO where n=1.

5

Preferably the level of alkyl ether sulphate is from 0.5 to 25, more preferably from 3 to 18, most preferably from 6 to 15 % w/w of the composition.

10 The total amount of anionic cleansing surfactant in shampoo compositions of the invention generally ranges from 0.5 to 45, more preferably from 1.5 to 20 % w/w of the composition.

Nonionic Surfactant

15 Shampoo compositions of the invention may contain non-ionic surfactant. Most preferably non-ionic surfactants are present in the range 0 to 5 % w/w of the composition.

20 Nonionic surfactants that can be included in shampoo compositions of the invention include condensation products of aliphatic (C8 - C18) primary or secondary linear or branched chain alcohols or phenols with alkylene oxides, usually ethylene oxide and generally having from 6 to 30 ethylene oxide groups. Alkyl ethoxylates are particularly preferred. Most preferred are alkyl ethoxylates having the formula R-(OCH₂CH₂)_nOH, where R is an alkyl chain of C12 to C15, and n is 5 to 9.

25 Other suitable nonionic surfactants include mono- or di-alkyl alkanolamides. Examples include coco mono- or di-ethanolamide and coco mono-isopropanolamide.

30 Further nonionic surfactants which can be included in shampoo compositions of the invention are the alkyl polyglycosides (APGs). Typically, APG is one which comprises an alkyl group connected (optionally via a bridging group) to a block of one or more glycosyl groups. Preferred APGs are defined by the following formula RO - (G)_n wherein R is a branched or straight chain alkyl group which may be saturated or unsaturated and G is a saccharide group.

R may represent a mean alkyl chain length of from about C5 to about C20. Preferably R represents a mean alkyl chain length of from about C8 to about C12. Most preferably the value of R lies between about 9.5 and about 10.5. G may be selected from C5 or C6 monosaccharide residues, and is preferably a glucoside. G
5 may be selected from the group comprising glucose, xylose, lactose, fructose, mannose and derivatives thereof. Preferably G is glucose. The degree of polymerisation, n, may have a value of from about 1 to about 10 or more, preferably a value of from about 1.1 to about 2, most preferably a value of from about 1.3 to about 1.5. Suitable alkyl polyglycosides for use in the invention are commercially
10 available and include for example those materials identified as: Oramix NS10 ex Seppic; Plantaren 1200 and Plantaren 2000 ex Henkel.

Other sugar-derived nonionic surfactants which can be included in compositions of the invention include the C10-C18 N-alkyl (C1-C6) polyhydroxy fatty acid amides,
15 such as the C12-C18 N-methyl glucamides, as described for example in WO 92/06154 and US 5 194 639, and the N-alkoxy polyhydroxy fatty acid amides, such as C10-C18 N-(3-methoxypropyl) glucamide.

Amphoteric/zwitterionic Surfactant

20 Amphoteric or zwitterionic surfactant can be included in an amount ranging from 0.5 to about 8, preferably from 1 to 4 % w/w of the shampoo compositions of the invention.

Examples of amphoteric or zwitterionic surfactants include alkyl amine oxides, alkyl
25 betaines, alkyl amidopropyl betaines, alkyl sulphobetaines (sultaines), alkyl glycinate, alkyl carboxyglycinates, alkyl amphotacetates, alkyl amphopropionates, alkylamphoglycinates, alkyl amidopropyl hydroxysultaines, acyl taurates and acyl glutamates, wherein the alkyl and acyl groups have from 8 to 19 carbon atoms. Typical amphoteric and zwitterionic surfactants for use in shampoos of the invention
30 include lauryl amine oxide, cocodimethyl sulphopropyl betaine, lauryl betaine, cocamidopropyl betaine and sodium cocoamphoacetate.

A particularly preferred amphoteric or zwitterionic surfactant is cocamidopropyl betaine.

5 Mixtures of any of the foregoing amphoteric or zwitterionic surfactants may also be suitable. Preferred mixtures are those of cocamidopropyl betaine with further amphoteric or zwitterionic surfactants as described above. A preferred further amphoteric or zwitterionic surfactant is sodium cocoamphoacetate.

Suspending agents

10 Preferably an aqueous shampoo composition of the invention further comprises a suspending agent. Suitable suspending agents are selected from 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, cross-linked copolymers of acrylic acid and acrylate esters, heteropolysaccharide
15 gums and crystalline long chain acyl derivatives. The long chain acyl derivative is desirably selected from ethylene glycol stearate, alkanolamides of fatty acids having from 16 to 22 carbon atoms and mixtures thereof. Ethylene glycol distearate and polyethylene glycol 3 distearate are preferred long chain acyl derivatives, since these impart pearlescence to the composition. Polyacrylic acid is available commercially
20 as Carbopol 420, Carbopol 488 or Carbopol 493. Polymers of acrylic acid cross-linked with a polyfunctional agent may also be used; they are available commercially as Carbopol 910, Carbopol 934, Carbopol 941 and Carbopol 980. An example of a suitable copolymer of a carboxylic acid containing monomer and acrylic acid esters is Carbopol 1342. Carbopol 980 is the commonly used suspending agent though
25 there is a growing desire to find an alternative. All Carbopol (trademark) materials are available from Goodrich.

Suitable cross-linked polymers of acrylic acid and acrylate esters are Pemulen TR1 or Pemulen TR2. A suitable heteropolysaccharide gum is xanthan gum, for example
30 that available as Kelzan mu.

Mixtures of any of the above suspending agents may be used. Preferred is a mixture of cross-linked polymer of acrylic acid and crystalline long chain acyl derivative.

Suspending agent will generally be present in a shampoo composition of the invention at levels of from 0.1 to 10, preferably from 0.5 to 6, more preferably from 0.9 to 4 % w/w of the composition. Generally such suspending agents are present at around 2 % w/w of the composition.

5

Water

Shampoo compositions of the invention are generally aqueous, i.e. they have water or an aqueous solution or a lyotropic liquid crystalline phase as their major component. Suitably, the composition will comprise from 50 to 98, preferably from 10 60 to 90 % w/w of the composition.

Typically, shampoo compositions have a pH of around 5.5.

Optional Ingredients

15 The shampoo compositions of the invention might also contain the following optional ingredients: conditioning agents;

Conditioning Agents

Conditioning actives are often included in shampoo compositions. These are 20 sometimes called '2-in-1' formulations. Conditioning actives fall into three classes:

- silicones (and cationic deposition polymers to assist in silicone deposition)
- cationic surfactants
- non-silicone oils

25 Where silicones are included, the composition is likely to also contain a cationic deposition polymer for enhancing deposition of the silicone. Further, a silicone-containing composition is likely to be lamellar as opposed to isotropic. Isotropic compositions do not deposit silicone effectively.

Silicones

30 The shampoo compositions of the invention can contain emulsified droplets of a silicone conditioning agent, for enhancing conditioning performance.

Suitable silicones include polydiorganosiloxanes, in particular polydimethylsiloxanes which have the CTFA designation dimethicone. Also suitable for use compositions of the invention (particularly shampoos and conditioners) are polydimethyl siloxanes having hydroxyl end groups, which have the CTFA designation dimethiconol. Also
5 suitable for use in compositions of the invention are silicone gums having a slight degree of cross-linking, as are described for example in WO 96/31188.

Examples of suitable pre-formed emulsions include Xiameter MEM 1785 and microemulsion DC2-1865 available from Dow Corning. These are emulsions
10 /microemulsions of dimethiconol. Cross-linked silicone gums are also available in a pre-emulsified form, which is advantageous for ease of formulation.

A further preferred class of silicones for inclusion in shampoos and conditioners of the invention are amino functional silicones. By "amino functional silicone" is meant
15 a silicone containing at least one primary, secondary or tertiary amine group, or a quaternary ammonium group. Examples of suitable amino functional silicones include: polysiloxanes having the CTFA designation "amodimethicone".

Specific examples of amino functional silicones suitable for use in the invention are
20 the aminosilicone oils DC2-8220, DC2-8166 and DC2-8566 (all ex Dow Corning). The most commonly used amino silicone is sourced from Dow Corning and is coded DC7134. Pre-formed emulsions of amino functional silicone are also available from suppliers of silicone oils such as Dow Corning and General Electric. Specific examples include DC939 Cationic Emulsion and the non-ionic emulsions DC2-7224,
25 DC2-8467, DC2-8177 and DC2-8154 (all ex Dow Corning).

Suitable quaternary silicone polymers are described in EP-A-0 530 974. A preferred quaternary silicone polymer is K3474, ex Goldschmidt.

30 With some shampoos it is preferred to use a combination of amino and non amino functional silicones.

Emulsified silicones for use in the shampoo compositions of the invention will typically have an average silicone droplet size in the composition of less than 30, preferably less than 20, more preferably less than 10 micron, ideally from 0.01 to 1 micron. Silicone emulsions having an average silicone droplet size of about 0.15
5 micron are generally termed microemulsions.

Emulsified silicones for use in the conditioner compositions of the invention will typically have a size in the composition of less than 30, preferably less than 20, more preferably less than 15. Preferably the average silicone droplet is greater than 0.5
10 micron, more preferably greater than 1 micron, ideally from 2 to 8 micron.

Silicone particle size may be measured by means of a laser light scattering technique, for example using a 2600D Particle Sizer from Malvern Instruments.

15 The viscosity of the emulsified silicone itself (not the emulsion or the final hair conditioning composition) is typically at least 10,000, preferably at least 60,000, most preferably at least 500,000, ideally at least 1,000,000 cst at 25 °C. Preferably the viscosity does not exceed 10^9 cst at 25 °C for ease of formulation.

20 The total amount of silicone is preferably from 0.01 to 10, more preferably from 0.1 to 5, most preferably 0.5 to 3 % w/w of the composition of the invention.

Also suitable are emulsions of amino functional silicone oils with non ionic and/or cationic surfactant.

25

Cationic deposition polymers are used to deposit the silicone droplets to the hair surface and hence enhance performance.

Suitable cationic polymers may be homopolymers which are cationically substituted
30 or may be formed from two or more types of monomers. The weight average (Mw) molecular weight of the polymers will generally be between 100 000 and 2 million daltons. The polymers will have cationic nitrogen containing groups such as quaternary ammonium or protonated amino groups, or a mixture thereof. If the

molecular weight of the polymer is too low, then the conditioning effect is poor. If too high, then there may be problems of high extensional viscosity leading to stringiness of the composition when it is poured.

- 5 The cationic nitrogen-containing group will generally be present as a substituent on a fraction of the total monomer units of the cationic polymer. Thus when the polymer is not a homopolymer it can contain spacer non-cationic monomer units. Such polymers are described in the CTFA Cosmetic Ingredient Directory. The ratio of the cationic to non-cationic monomer units is selected to give polymers having a cationic charge density in the required range, which is generally from 0.2 to 3.0 meq/gm. The cationic charge density of the polymer is suitably determined via the Kjeldahl method as described in the US Pharmacopoeia under chemical tests for nitrogen determination.
- 10
- 15 Suitable cationic polymers include, for example, copolymers of vinyl monomers having cationic amine or quaternary ammonium functionalities with water soluble spacer monomers such as (meth)acrylamide, alkyl and dialkyl (meth)acrylamides, alkyl (meth)acrylate, vinyl caprolactone and vinyl pyrrolidine. The alkyl and dialkyl substituted monomers preferably have C1-C7 alkyl groups, more preferably C1-3
- 20 alkyl groups. Other suitable spacers include vinyl esters, vinyl alcohol, maleic anhydride, propylene glycol and ethylene glycol.

The cationic amines can be primary, secondary or tertiary amines, depending upon the particular species and the pH of the composition. In general secondary and tertiary amines, especially tertiary, are preferred.

25

Amine substituted vinyl monomers and amines can be polymerized in the amine form and then converted to ammonium by quaternization.

- 30 The cationic polymers can comprise mixtures of monomer units derived from amine- and/or quaternary ammonium-substituted monomer and/or compatible spacer monomers.

Suitable cationic polymers include, for example:

- cationic diallyl quaternary ammonium-containing polymers including, for example, dimethyldiallylammonium chloride homopolymer and copolymers of acrylamide and dimethyldiallylammonium chloride, referred to in the industry (CTFA) as Polyquaternium 6 and Polyquaternium 7, respectively;
- mineral acid salts of amino-alkyl esters of homo-and co-polymers of unsaturated carboxylic acids having from 3 to 5 carbon atoms, (as described in US 4 009 256); and
- cationic polyacrylamides (as described in WO95/22311).

10

Other cationic polymers that can be used include cationic polysaccharide polymers, such as cationic cellulose derivatives, cationic starch derivatives, and cationic guar gum derivatives.

15

Cationic polysaccharide polymers suitable for use in compositions of the invention include monomers of the formula $A-O-[R-N+(R1)(R2)(R3)X-]$ wherein A is an anhydroglucose residual group, such as a starch or cellulose anhydroglucose residual; R is an alkylene, oxyalkylene, polyoxyalkylene, or hydroxyalkylene group, or combination thereof; R1, R2 and R3 independently represent alkyl, aryl, alkylaryl, arylalkyl, alkoxyalkyl, or alkoxyaryl groups, each group containing up to about 18 carbon atoms; the total number of carbon atoms for each cationic moiety (i.e., the sum of carbon atoms in R1, R2 and R3) is preferably about 20 or less; and X is an anionic counterion.

20

25

Another type of cationic cellulose includes the polymeric quaternary ammonium salts of hydroxyethyl cellulose reacted with lauryl dimethyl ammonium-substituted epoxide, referred to in the industry (CTFA) as Polyquaternium 24. These materials are available from the Amerchol Corporation, for instance under the tradename Polymer LM-200.

30

Other suitable cationic polysaccharide polymers include quaternary nitrogen-containing cellulose ethers (e.g. as described in US 3 962 418), and copolymers of etherified cellulose and starch (e.g. as described in US 3 958 581).

A particularly suitable type of cationic polysaccharide polymer that can be used is a cationic guar gum derivative, such as guar hydroxypropyltrimethylammonium chloride (commercially available from Rhodia in their JAGUAR trademark series). Examples of such materials are JAGUAR C13S, JAGUAR C14, JAGUAR C15, JAGUAR C17 and JAGUAR C16 Jaguar CHT and JAGUAR C162.

Mixtures of any of the above cationic polymers may be used.

Cationic polymer will generally be present in a shampoo composition of the invention at levels of from 0.01 to 5, preferably from 0.05 to 1, more preferably from 0.08 to 0.5 % w/w of the weight of the compositions of the invention.

Cationic Surfactants

Cationic surfactants may be used in 2-in-1 shampoos to provide a conditioning benefit. However, since a shampoo composition is likely to also comprise anionic cleansing surfactants, the use of cationic surfactants is limited to compositions where the cationic surfactant is separated from the anionic phase by way of a stable conditioning gel phase made separately from the rest of the formulation and then incorporated afterwards.

Non-silicone Oils

These are typically hydrocarbon oils or fatty alcohols. A fatty alcohol is nearly always included in a conditioning composition and often included in 2-in-1 shampoos. Cetearyl alcohol is one of the preferred examples.

Fibre Actives

Fibre actives are provided to repair or coat the hair fibres. Examples are trehalose (a disaccharide), adipic acid (dicarboxylic acid) and gluconolactone.

Anti-dandruff Actives

There are two classes of anti-dandruff active: the azoles and the pyrithiones, both are active against the target fungi malassezia spp. The azoles include ketoconazole

and climbazole which are fat soluble actives. The pyrithiones include zinc pyrithione (ZPT) which is insoluble and delivered as a particle to the scalp.

Preferably, the antidandruff active is present at from 0.01 to 5, more preferably from 5 0.1 to 2.5 % w/w of the composition of the invention.

Hair Conditioning Compositions

The compositions of the invention may also be hair conditioning compositions (also known as conditioners). A conditioner which is to be used after a shampoo is known 10 as a 'system conditioner' whereas one which is included in a shampoo composition is known as a '2-in-1'. Hair conditioning compositions may also be left on the head, i.e. not rinsed off after application. These are known as Leave-on-Treatments (LOTs) as opposed to Rinse-off-Treatments (ROTs).

15 The main ingredients in a system conditioner are the conditioning actives described above, the main actives being a cationic surfactant (e.g. behenyltrimmonium chloride), a silicone conditioning agent (e.g. aminosilicone (DC 7134)) and a non-silicone oil, usually a fatty alcohol (e.g. cetearyl alcohol).

20 Anti-dandruff actives may also be included in hair conditioning compositions of the invention.

Cationic Surfactants

Preferably, the cationic surfactants have the formula $N+R_1R_2R_3R_4$ wherein R1, R2, 25 R3 and R4 are independently (C1 to C30) alkyl or benzyl. Preferably, one, two or three of R1, R2, R3 and R4 are independently (C4 to C30) alkyl and the other R1, R2, R3 and R4 group or groups are (C1-C6) alkyl or benzyl. More preferably, one or two of R1, R2, R3 and R4 are independently (C6 to C30) alkyl and the other R1, R2, R3 and R4 groups are (C1-C6) alkyl or benzyl groups. Optionally, the alkyl groups 30 may comprise one or more ester (-OCO- or -COO-) and/or ether (-O-) linkages within the alkyl chain. Alkyl groups may optionally be substituted with one or more hydroxyl groups. Alkyl groups may be straight chain or branched and, for alkyl groups having 3 or more carbon atoms, cyclic. The alkyl groups may be saturated or

may contain one or more carbon-carbon double bonds (e.g. oleyl). Alkyl groups are optionally ethoxylated on the alkyl chain with one or more ethyleneoxy groups.

Suitable cationic surfactants for use in conditioner compositions according to the invention include cetyltrimethylammonium chloride, behenyltrimethylammonium chloride, cetylpyridinium chloride, tetramethylammonium chloride, tetraethylammonium chloride, octyltrimethylammonium chloride, dodecyltrimethylammonium chloride, hexadecyltrimethylammonium chloride, octyldimethylbenzylammonium chloride, decyldimethylbenzylammonium chloride, stearyldimethylbenzylammonium chloride, didodecyldimethylammonium chloride, dioctadecyldimethylammonium chloride, tallowtrimethylammonium chloride, dihydrogenated tallow dimethyl ammonium chloride (eg, Arquad 2HT/75 from Akzo Nobel), cocotrimethylammonium chloride, PEG-2-oleammonium chloride and the corresponding hydroxides thereof. Further suitable cationic surfactants include those materials having the CTFA designations Quaternium-5, Quaternium-31 and Quaternium-18. Mixtures of any of the foregoing materials may also be suitable. A particularly useful cationic surfactant for use in conditioners according to the invention is cetyltrimethylammonium chloride, available commercially, for example as GENAMIN CTAC, ex Hoechst Celanese. Another particularly useful cationic surfactant for use in conditioners according to the invention is behenyltrimethylammonium chloride, available commercially, for example as GENAMIN KDMP, ex Clariant.

Another example of a class of suitable cationic surfactants for use in the invention, either alone or together with one or more other cationic surfactants, is a combination of (i) and (ii) below:

(i) an amidoamine corresponding to the general formula (I)
 $R_1CONH(CH_2)_mN(R_2)R_3$

in which R₁ is a hydrocarbyl chain having 10 or more carbon atoms, R₂ and R₃ are independently selected from hydrocarbyl chains of from 1 to 10 carbon atoms, and m is an integer from 1 to about 10; and

(ii) an acid.

As used herein, the term hydrocarbonyl chain means an alkyl or alkenyl chain. Preferred amidoamine compounds are those corresponding to formula (I) in which R1 is a hydrocarbonyl residue having from about 11 to about 24 carbon atoms, R2 and R3 are each independently hydrocarbonyl residues, preferably alkyl groups, having from 1 to about 4 carbon atoms, and m is an integer from 1 to about 4. Preferably R2 and R3 are methyl or ethyl groups. Preferably m is 2 or 3, i.e. an ethylene or propylene group.

Preferred amidoamines useful herein include stearamido-propyldimethylamine, stearamidopropyldiethylamine, stearamidoethyldiethylamine, palmitamidopropyldimethylamine, palmitamidoethyl-diethylamine, palmitamidoethyldiethylamine, behenamido-propyldimethylamine, behenamidoethyldiethylamine, behenamidoethyldiethylamine, arachidamidopropyl-dimethylamine, arachidamidopropyldiethylamine, arachid-amidoethyldiethylamine, arachidamidoethyldimethylamine, and mixtures thereof. Particularly preferred amidoamines useful herein are stearamidopropyldimethylamine, stearamidoethyldiethylamine, and mixtures thereof.

Commercially available amidoamines useful herein include: stearamidopropyldimethylamine with tradenames LEXAMINE S-13 available from Inolex (Philadelphia Pennsylvania, USA) and AMIDOAMINE MSP available from Nikko (Tokyo, Japan), stearamidoethyldiethylamine with a tradename AMIDOAMINE S available from Nikko, behenamido-propyldimethylamine with a tradename INCROMINE BB available from Croda (North Humberstone, England), and various amidoamines with tradenames SCHERCODINE series available from Scher (Clifton New Jersey, USA).

The acid may be any organic or mineral acid which is capable of protonating the amidoamine in the conditioner composition. Suitable acids useful herein include hydrochloric acid, acetic acid, tartaric acid, fumaric acid, lactic acid, malic acid, succinic acid, and mixtures thereof. Preferably, the acid is selected from the group

consisting of acetic acid, tartaric acid, hydrochloric acid, fumaric acid, lactic acid and mixtures thereof.

5 The primary role of the acid is to protonate the amidoamine in the hair treatment composition thus forming a tertiary amine salt (TAS) in-situ in the hair treatment composition. The TAS in effect is a non-permanent quaternary ammonium or pseudo-quaternary ammonium cationic surfactant. Suitably, the acid is included in a sufficient amount to protonate more than 95 mole % (20 °C) of the amidoamine present.

10

In conditioners of the invention, the level of cationic surfactant will generally range from 0.01 to 10, more preferably 0.05 to 7.5, most preferably 0.1 to 5 % by weight of the composition.

15 **Silicone Conditioning Agent**

The compositions of the invention can contain emulsified droplets of a silicone conditioning agent, for enhancing conditioning performance as previously described.

Non-silicone Oils

20 Compositions according to the present invention may also comprise a dispersed, non-volatile, water-insoluble, non-silicone oily conditioning agent. Preferably such non-silicone oily conditioning agents are present in the hair conditioning compositions of the invention. By "insoluble" is meant that the material is not soluble in water (distilled or equivalent) at a concentration of 0.1 % w/w at 25°C. Suitable
25 non-silicone oils are selected from hydrocarbon oils, fatty esters and mixtures thereof.

Straight chain hydrocarbon oils will preferably contain from about 12 to about 30 carbon atoms. Also suitable are polymeric hydrocarbons of alkenyl monomers, such
30 as C2-C6 alkenyl monomers. Specific examples of suitable hydrocarbon oils include paraffin oil, mineral oil, saturated and unsaturated dodecane, saturated and unsaturated tridecane, saturated and unsaturated tetradecane, saturated and unsaturated pentadecane, saturated and unsaturated hexadecane, and mixtures

thereof. Branched-chain isomers of these compounds, as well as of higher chain length hydrocarbons, can also be used.

5 Suitable fatty esters are characterised by having at least 10 carbon atoms, and include esters with hydrocarbyl chains derived from fatty acids or alcohols, Monocarboxylic acid esters include esters of alcohols and/or acids of the formula $R'COOR$ in which R' and R independently denote alkyl or alkenyl radicals and the sum of carbon atoms in R' and R is at least 10, preferably at least 20. Di- and trialkyl and alkenyl esters of carboxylic acids can also be used. Particularly preferred fatty
10 esters are mono-, di- and triglycerides, more specifically the mono-, di-, and tri-esters of glycerol and long chain carboxylic acids such as C1-C22 carboxylic acids. Preferred materials include cocoa butter, palm stearin, sunflower oil, soyabean oil and coconut oil.

15 The oily or fatty material is suitably present at a level of from 0.05 to 10, preferably from 0.2 to 5, more preferably from about 0.5 to 3 % w/w of the composition of the invention.

Fatty Alcohols

20 Hair conditioning compositions of the invention will typically also incorporate a fatty alcohol. The combined use of fatty alcohols and cationic surfactants in conditioning compositions is believed to be especially advantageous, because this leads to the formation of a lamellar phase, in which the cationic surfactant is dispersed.

25 Representative fatty alcohols comprise from 8 to 22 carbon atoms, more preferably 16 to 22. Fatty alcohols are typically compounds containing straight chain alkyl groups. Examples of suitable fatty alcohols include cetyl alcohol, stearyl alcohol and mixtures thereof. The use of these materials is also advantageous in that they contribute to the overall conditioning properties of compositions of the invention.

30

The level of fatty alcohol in conditioners of the invention will generally range from 0.01 to 10, preferably from 0.1 to 8, more preferably from 0.2 to 7, most preferably from 0.3 to 6 % w/w by weight of the composition. The weight ratio of cationic

surfactant to fatty alcohol is suitably from 1:1 to 1:10, preferably from 1:1.5 to 1:8, optimally from 1:2 to 1:5. If the weight ratio of cationic surfactant to fatty alcohol is too high, this can lead to eye irritancy from the composition. If it is too low, it can make the hair feel squeaky for some consumers.

5

In another embodiment, the topical colour composition of the invention is a skin colour composition.

Example

10 Materials:

Myceliphthora thermophila laccase (51003) was obtained from Novozymes A/S (Denmark)

Soy bean peroxidase (SBP) was obtained from Bio-Research Products Incorporated (SBP#510)

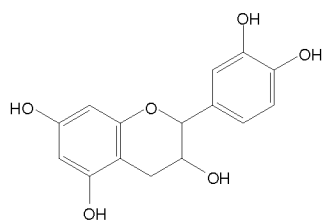
15 3 % aqueous hydrogen peroxide (H₂O₂, 323381) was obtained from Sigma-Aldrich (UK)

(+)-Catechin hydrate (C1251) was obtained from Sigma-Aldrich (UK)

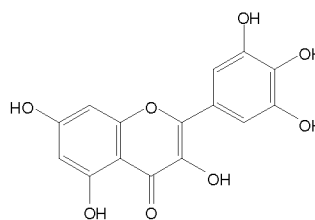
Myricetin (M6760) was obtained from Sigma-Aldrich (UK)

Quercetin dihydrate (171964) was obtained from Sigma-Aldrich (UK)

20 Natural White hair switches were obtained from International Hair Importers (New York, USA)



Catechin



Myricetin

Method:

25 Two inch / 0.25 g hair switches were washed with 1 % aqueous sodium dodecyl sulphate (SDS), followed by 10 % aqueous SDS solutions, rinsed and dried prior to use. Baseline L*a*b* colour measurements were made on all hair switches (6 per switch) prior to dyeing using a Konica Minolta Spectrophotometer CM-2600d. Hair dyeing was carried out in 15 ml Falcon tubes in a 10 ml final volume.

For SBP, hair switches were soaked in 8 ml of polyphenol in ethanol/Britton Robinson buffer (pH 6.0) for 10 minutes at room temperature. 1 ml of SBP in Britton Robinson buffer (pH 6.0) and 1 ml of 3 % aqueous hydrogen peroxide were added, such that the final concentrations were:

5

1 - 5 mM polyphenol*

5 - 28 % ethanol

10 U.ml⁻¹ SBP

0.3% hydrogen peroxide

10

* Myricetin (2 mM); catechin, quercetin (both 5 mM)

With respect to laccase, hair switches were soaked in 8 ml of polyphenol in ethanol/Britton Robinson buffer (pH 6.0) for 10 minutes at room temperature. 1 ml of laccase in Britton Robinson buffer (pH 6.0) and 1 ml of water were added, such that the final concentrations were:

15

1 - 5 mM polyphenol **

5 - 28 % ethanol

20

10 U.ml⁻¹ laccase

** Myricetin (2 mM); catechin, quercetin (both 5 mM)

25

After 10 minutes in the polyphenol/enzyme mixture, switches were rinsed in running tap water until the water ran clear. The hair switch was then dried with a hair dryer and L*a*b* colour measurements taken (6 measurements per switch). This process was repeated up to 4 times. Afterwards the hair switches were washed with 50 µl of shampoo, rinsed in water and dried. This was repeated 4 times. Shampooing was accomplished by fully wetting the switches in tap water and then applying 50 µL of shampoo was to each switch, lathering for 2 minutes before rinsing and drying. L*a*b* colour measurements were then taken to assess the amount of colour loss after each shampoo treatment.

30

ΔE^* values were calculated according to the equation below:

$$\Delta E = \sqrt{(L^*_B - L^*_D)^2 + (a^*_B - a^*_D)^2 + (b^*_B - b^*_D)^2}$$

5 Where B = background/baseline and D = dyed;

L^* = lightness (where 0 = black and 100 = diffuse white);

a^* = green/red (negative values indicate green and positive values indicate red); and

b^* = blue/yellow (negative values indicate blue and positive values indicate yellow)

10 Results:

The results are summarised below in Table 1. L^* , a^* and b^* values were observed to remain substantially constant after each shampoo cycle.

15 Table 1: ΔE^* , L^* , a^* and b^* values after four treatments for enzymatically catalysed oxidation of catechin, myricetin and quercetin on white hair switches (n = 6).

| Laccase | Four treatments | | | |
|------------|-----------------|---------------|--------------|--------------|
| | ΔE^* | ΔL^* | Δa^* | Δb^* |
| Quercetin | 17.93 ± 1.31 | -3.42 ± 1.11 | -3.28 ± 0.31 | 17.26 ± 1.40 |
| Catechin | 11.64 ± 1.87 | -5.55 ± 1.42 | 5.87 ± 0.98 | 8.32 ± 1.26 |
| Peroxidase | Four treatments | | | |
| | ΔE^* | ΔL^* | Δa^* | Δb^* |
| Quercetin | 8.44 ± 2.00 | -3.55 ± 1.13 | -1.20 ± 0.18 | 7.48 ± 2.08 |
| Myricetin | 17.16 ± 1.45 | -13.48 ± 1.15 | 8.87 ± 0.64 | 5.81 ± 0.95 |

20 Quercetin in combination with laccase provides a yellower hue (positive Δb^*) than the catechin/laccase combination. In combination with laccase, quercetin also provides a yellower hue than the equivalent combination with peroxidase/hydrogen peroxide, or with another flavonol myricetin when combined with peroxidase/hydrogen peroxide. Colour fastness after shampoo treatment was observed in all cases.

Claims

1. A topical colour composition comprising:
 - (a) Quercetin; and
 - 5 (b) A laccase,wherein the composition has a pH of 4.5 to 7.0, preferably less than or equal to 6.0.
- 10 2. A topical colour composition according to claim 1, wherein the laccase originates from a fungal or a plant source such as those from the group consisting of the *Aspergillus*, *Botrytis*, *Ceriporiopsis*, *Cerrena*, *Chaetomium*, *Coprinus*, *Coriolus*, *Neurospora*, *Panus*, *Phanerochaete*, *Pleurotus*, *Polyporus*, *Pycnoporus* and *Trametes* genera, and *Rhus vernicifera*.
- 15 3. A topical colour composition according to claim 1 or claim 2, wherein the hair colour composition comprises 0.001 – 10, preferably 0.1 - 5 % w/w (+)-quercetin.
- 20 4. A topical colour composition according to any one of the preceding claims, wherein the hair colour composition comprises 0.0001 – 5, preferably 0.0001 - 1 % w/w laccase.
- 25 5. A topical colour composition according to any one of the preceding claims additionally comprising a metal ion suitable for coordinating to quercetin, or the product of the reaction of quercetin in the presence of the laccase.
- 30 6. A topical colour composition according to claim 5, wherein the metal ion is selected from the group consisting of iron (II), iron (III), copper (I), copper (II), copper (III) and aluminium (III).
7. A topical colour composition according to claim 5 or claim 6, wherein the hair colour composition comprises 0.0001 – 2, preferably 0.001 – 0.1 % w/w metal ion.

8. A topical colour composition according to any one of the preceding claims wherein the topical colour composition is a hair or skin colour composition.
9. A method of colouring hair fibres, the method comprising the step of applying
5 the hair colour composition according to claim 8 to hair fibres.
10. A method of colouring skin, the method comprising the step of applying the skin colour composition according to claim 8 to skin.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/052166

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61Q5/10 A61K8/49 A61K8/66 A61Q1/02 A61Q1/12
 ADD.
 According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 A61Q A61K

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 EPO-Internal, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| X,P | WO 2013/189966 A2 (UNILEVER PLC [GB]; UNILEVER NV [NL]; CONOPCO INC DBA UNILEVER [US]) 27 December 2013 (2013-12-27) the whole document | 1-10 |
| X | DE 102 59 199 A1 (HENKEL KGAA [DE]) 24 June 2004 (2004-06-24) | 1-4 |
| Y | page 18, paragraph 89 - paragraph 91 | 5-7 |
| Y | WO 01/45654 A1 (HENKEL KGAA [DE]; SCHULZE ZUR WIESCHE ERIK [DE]; HOLLENBERG DETLEF [DE]) 28 June 2001 (2001-06-28) page 21 | 5-7 |
| A | WO 97/37633 A1 (NOVO NORDISK AS [DK]; SOERENSEN NIELS HENRIK [DK]) 16 October 1997 (1997-10-16) claim 1 | 1-10 |
| | ----- -/-- | |

Further documents are listed in the continuation of Box C.

See patent family annex.

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| Date of the actual completion of the international search 8 April 2014 | Date of mailing of the international search report 17/04/2014 |
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| Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016 | Authorized officer Bader, Karl Günther |
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/052166

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | US 5 770 418 A (YAVER DEBBIE SUE [US] ET AL) 23 June 1998 (1998-06-23) the whole document ----- | 1-10 |
| Y | TAKADA K ET AL: "INFLUENCE OF OXIDATIVE AND/OR REDUCTIVE TREATMENT PON HUMAN HAIR (III): OXIDATIVE REACTION OF POLYPHENOL OXIDASE (LACCASE) TO HAIR DYEING", JOURNAL OF OLEO SCIENCE, JAPAN OIL CHEMISTS SOCIETY, TOKYO, JP, vol. 52, no. 10, 20 March 2001 (2001-03-20), pages 557-563, XP002637133, ISSN: 1345-8957, DOI: 10.5650/JOS.52.557 the whole document ----- | 1-10 |
| Y | WO 99/16893 A2 (INST VOOR AGROTECH ONDERZOEK [NL]; HUIZING HINDRIK JAN [NL]; DIJK CEES) 8 April 1999 (1999-04-08) cited in the application the whole document ----- | 1-10 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2014/052166

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|--|------------------|-------------------------|-----------------------------|
| WO 2013189966 | A2 | 27-12-2013 | NONE |
| ----- | | | |
| DE 10259199 | A1 | 24-06-2004 | NONE |
| ----- | | | |
| WO 0145654 | A1 | 28-06-2001 | AU 3012601 A 03-07-2001 |
| | | | CN 1516572 A 28-07-2004 |
| | | | EP 1239816 A1 18-09-2002 |
| | | | JP 2004500361 A 08-01-2004 |
| | | | US 2002194684 A1 26-12-2002 |
| | | | WO 0145654 A1 28-06-2001 |
| ----- | | | |
| WO 9737633 | A1 | 16-10-1997 | AU 2504097 A 29-10-1997 |
| | | | CA 2250832 A1 16-10-1997 |
| | | | CN 1216914 A 19-05-1999 |
| | | | DE 69708276 D1 20-12-2001 |
| | | | EP 0891182 A1 20-01-1999 |
| | | | JP 2000510823 A 22-08-2000 |
| | | | US 6001134 A 14-12-1999 |
| | | | WO 9737633 A1 16-10-1997 |
| ----- | | | |
| US 5770418 | A | 23-06-1998 | CN 1328073 A 26-12-2001 |
| | | | CN 1772907 A 17-05-2006 |
| | | | CN 1782081 A 07-06-2006 |
| | | | CN 1782082 A 07-06-2006 |
| | | | CN 1982443 A 20-06-2007 |
| | | | US 5770418 A 23-06-1998 |
| ----- | | | |
| WO 9916893 | A2 | 08-04-1999 | AU 9367198 A 23-04-1999 |
| | | | NL 1007158 C2 30-03-1999 |
| | | | WO 9916893 A2 08-04-1999 |
| ----- | | | |