

(12) STANDARD PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. **AU 2006225152 B2**

- (54) Title
Hair and/or scalp care compositions incorporating flavonoid compounds
- (51) International Patent Classification(s)
A61K 8/49 (2006.01) **A61Q 5/00** (2006.01)
- (21) Application No: **2006225152** (22) Date of Filing: **2006.02.27**
- (87) WIPO No: **WO06/097191**
- (30) Priority Data
- (31) Number (32) Date (33) Country
05251510.3 **2005.03.12** **EP**
- (43) Publication Date: **2006.09.21**
(44) Accepted Journal Date: **2009.10.08**
- (71) Applicant(s)
Unilever PLC
- (72) Inventor(s)
Meldrum, Helen;Chugh, Jasveen;Bhogal, Ranjit
- (74) Agent / Attorney
Davies Collison Cave, 255 Elizabeth Street, Sydney, NSW, 2000
- (56) Related Art
US 2001/0012853 A1 (BISETT) 09 August 2009
Ghisalberti, E et al. Cellular and Molecular Life Sciences. 1978. Vol.34(2):157-158
US 6,482,442 B1 (DADO) 19 November 2002
Lejeune, B. et al. Parfums, Cosmetiques, Aromes. No. 56: 65-68. 1984

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
21 September 2006 (21.09.2006)

PCT

(10) International Publication Number
WO 2006/097191 A1

(51) International Patent Classification:

A61K 8/49 (2006.01) A61Q 5/00 (2006.01)

(21) International Application Number:

PCT/EP2006/001823

(22) International Filing Date:

27 February 2006 (27.02.2006)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

05251510.3 12 March 2005 (12.03.2005) EP

(71) Applicant (for AE, AG, AU, BB, BW, BZ, CA, CY, EG, GB, GD, GH, GM, IE, IL, KE, KN, LC, LK, LS, MN, MW, NA, NG, NZ, OM, PG, SC, SD, SG, SL, SZ, TT, TZ, UG, VC, ZA, ZM, ZW only): **UNILEVER PLC** [GB/GB]; Unilever House, Blackfriars, London Greater London EC4P 4BQ (GB).

(71) Applicant (for AL, AM, AT, AZ, BA, BE, BF, BG, BJ, BR, BY, CF, CG, CH, CI, CM, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FR, GA, GE, GN, GQ, GR, GW, HR, HU, ID, IS, IT, JP, KG, KM, KP, KR, KZ, LR, LT, LU, LV, LY, MA, MC, MD, MG, MK, ML, MR, MX, MZ, NE, NI, NL, NO, PH, PL, PT, RO, RU, SE, SI, SK, SM, SN, SY, TD, TG, TJ, TM, TN, TR, UA, UZ, VN, YU only): **UNILEVER NV** [NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL).

(71) Applicant (for IN only): **HINDUSTAN LEVER LIMITED** [IN/IN]; Hindustan Lever House, 165/166 Backbay Reclamation, Maharashtra, Mumbai 400 020 (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BHOGAL, Ranjit**

[GB/GB]; Unilever R & D Colworth, Sharnbrook, Bedford Bedfordshire MK44 1LQ (GB). **CHUGH, Jasveen** [GB/GB]; 5 Canterbury Close, Chigwell, Essex IG7 6HG (GB). **MELDRUM, Helen** [GB/US]; Conopco Inc. d/b/a UNILEVER, 40 Merritt Boulevard, Trumbull, Connecticut 06611 (US).

(74) Agents: **TANSLEY, Sally, Elizabeth** et al.; Unilever Patent Group, Colworth House, Sharnbrook, Bedford Bedfordshire MK44 1LQ (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

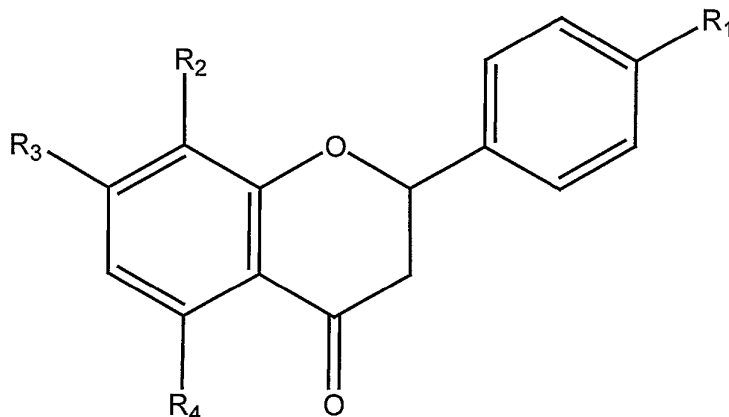
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HAIR AND/OR SCALP CARE COMPOSITIONS INCORPORATING FLAVONOID COMPOUNDS



(I)

(57) Abstract: The invention provides a hair and/or scalp care composition comprising a flavonoid compound of general formula (I) in which: R₁, R₃ and R₄ are each, independently, -H, -F, -Cl, -Br, -I, -OH, lower alkyl (e.g. C₁₋₆ alkyl) or lower alkoxy (e.g. C₁₋₆ alkoxy); and R₂ is -H or an alkenyl group.

- 1 -

HAIR AND/OR SCALP CARE COMPOSITIONS INCORPORATING FLAVONOID
COMPOUNDS

This invention relates to hair and/or scalp care
5 compositions incorporating certain selected flavonoid
compounds. The invention also relates to the use of these
flavonoid compounds for the treatment and/or prevention of
inflammatory skin conditions such as the scalp skin itching
and flaking associated with dandruff.

10

Background

It is widely believed that *Malassezia* yeasts, such as
Malassezia furfur, are the main cause of dandruff. However,
15 it is unclear why some people suffer from this condition
while others do not. What is known is that increasing the
level of *Malassezia* on the scalp does not automatically lead
to dandruff. This suggests that *Malassezia* is necessary but
not sufficient to cause the condition.

20

Recent studies have demonstrated that dandruff is associated
with changes in scalp skin condition. Dandruff scalp skin
has been shown to have decreased levels of stratum corneum
lipids such as ceramides, an increased susceptibility to
25 application of topical histamine and a perturbed balance in
the levels of inflammatory cytokine markers in the stratum
corneum. These findings clearly demonstrate that dandruff is
associated with changes in scalp skin condition and that
dandruff is multifactorial. It is believed that the
30 weakened scalp skin barrier and perturbed condition of the
scalp skin renders an individual susceptible to challenge by
factors such as *Malassezia*.

- 2 -

The main, if not only, intervention strategy used on the market currently for the treatment of dandruff is the topical application of antifungals such as zinc pyrithione (ZnPTO), octopirox and ketoconazole which are normally delivered from a shampoo. These antifungal agents remove (or at least reduce the level of) the *Malassezia* from the scalp, and provide effective treatment of the dandruff condition.

10

Although clinically proven to be effective in treating the clinical symptoms of dandruff over a two to four week period, there remains a need to treat the main symptoms of dandruff more effectively and rapidly. The main symptoms of dandruff are visible skin flakes in the hair and on the shoulders and scalp itch. Scalp itch is perceived as being a particular problem in certain parts of the world, for example it is the main symptom of dandruff in China, South-East Asia and India.

20

As well as treating the clinical signs of dandruff, therefore, there remains a need for providing rapid relief from scalp itch for dandruff sufferers.

25

WO04/00085 describes how cannabinoid receptor (CBR) activators may be useful in hair treatment compositions for the treatment and/or prevention of symptoms of dandruff such as scalp skin itching and flaking.

30

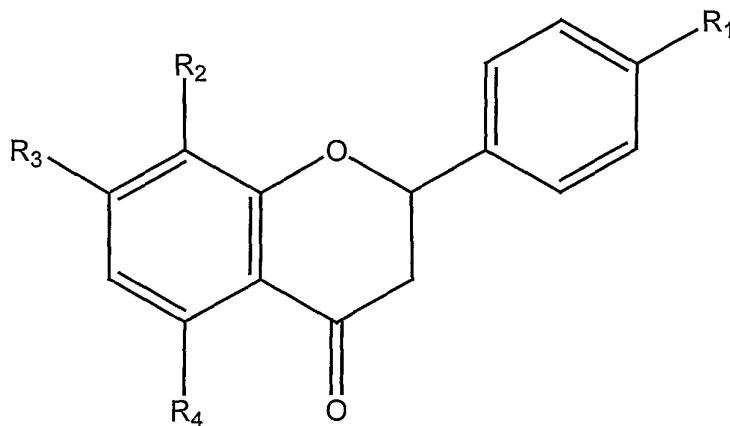
The present inventors have found that certain selected flavonoid compounds are capable of acting as CBR activators, and therefore may be used for the treatment and/or

prevention of symptoms of dandruff such as scalp skin itching and flaking.

There is no suggestion in WO04/00085 that flavonoid
5 compounds (of which over 5,000 have been chemically isolated
and reported) would possess such activity. Furthermore it
has been observed that the selected flavonoid compounds of
the invention are significantly more hydrophilic (with a
ClogP < 4.5) than those compounds which have generally been
10 documented in the literature as exhibiting CBR activation.

Summary of the invention

According to the invention there is provided a hair and/or
scalp care composition comprising a flavonoid compound of
general formula (I): (I)



20 in which:

R₁, R₃ and R₄ are each, independently, -H, -F, -Cl, -Br, -I, -OH, lower alkyl (e.g. C₁₋₆ alkyl) or lower alkoxy (e.g. C₁₋₆ alkoxy); and

R₂ is -H or an alkenyl group.

5

In another aspect, the invention provides a method of treating and/or preventing inflammatory skin conditions such as the scalp skin itching and flaking associated with dandruff, which method comprises topically applying a composition according to the invention to the hair and/or skin, preferably to the hair and/or scalp.

According to another aspect the present invention provides use of pinostrobin (5-hydroxy-7-methoxyflavanone) in the manufacture of a composition for activating cannabinoid receptors in the skin.

Detailed Description of the Invention and Preferred Embodiments

20

R₁ in general formula (I) is preferably -H or -OH.

R₂ in general formula (I) is preferably -H or a CH₂CH=C(CH₃)₂ (prenyl) group.

25

R₃ and R₄ in general formula (I) are preferably independently selected from -OH and -OCH₃.

Specific examples of suitable flavonoid compounds of general formula (I) are:

30

a compound which has the structural formula (II) (termed

- 4A -

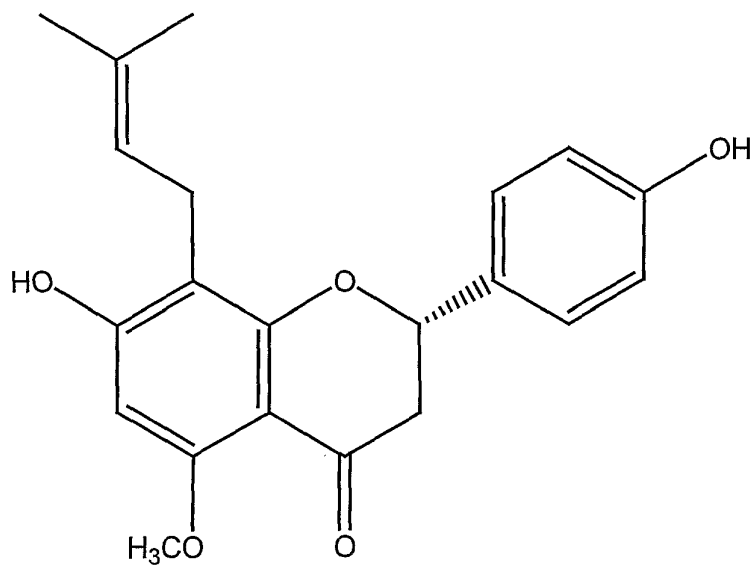
isoxanthohumol
prenylflavanone) :

or

4',7-dihydroxy-5-methoxy-8-

- 5 -

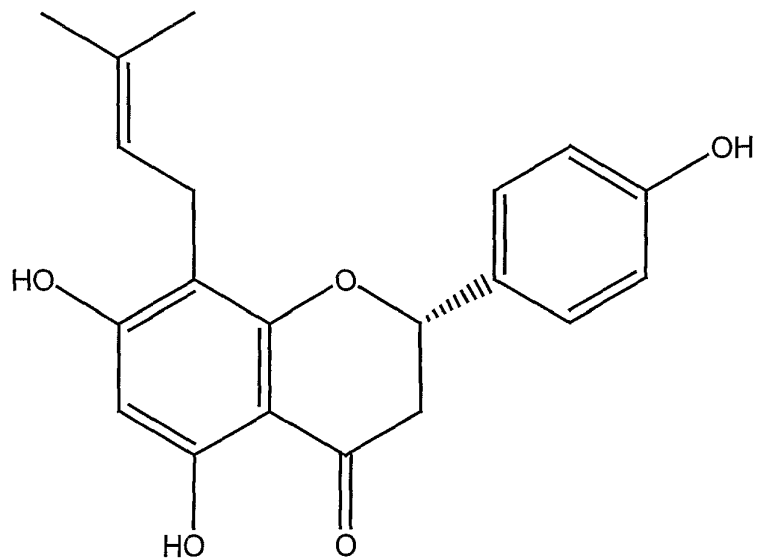
(II)



5 a compound which has the structural formula (III) (termed 8-prenylnaringenin or 4',5,7-trihydroxy-8-prenylflavanone):

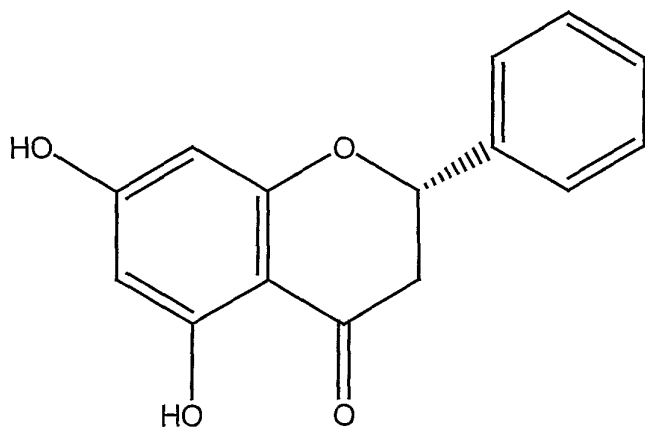
- 6 -

(III)



- 5 a compound which has the structural formula (IV) (termed pinocembrine or 5,7-dihydroxyflavanone):

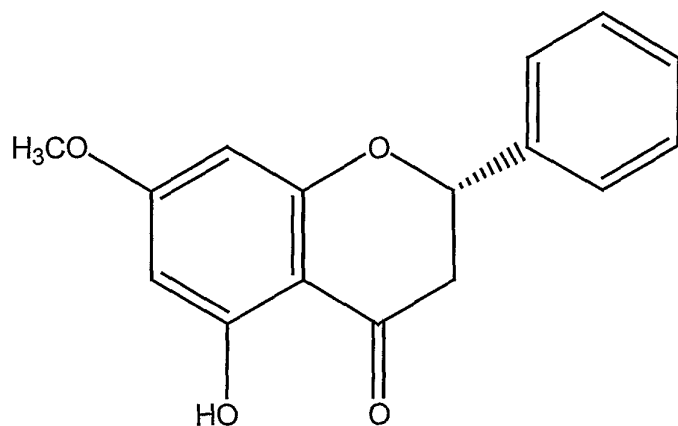
(IV)



10

- a compound which has the structural formula (V) (termed pinostrobin or 5-hydroxy-7-methoxyflavanone):

(V)

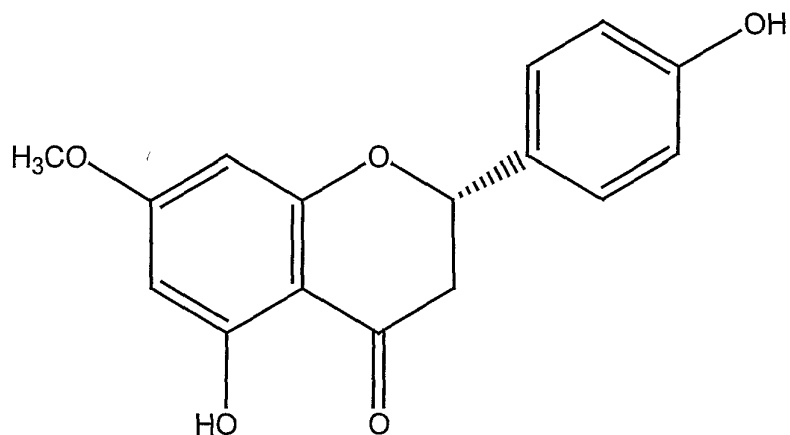


5

a compound which has the structural formula (VI) (termed sakuranetin or 5,4'-dihydroxy-7-methoxyflavanone):

10

(VI)



Preferred is a compound which has the structural formula (V) (pinostrobin). The inventors have found that this compound can activate both of the two similar, but distinct, types of

- 8 -

membrane receptor which have been termed Cannabinoid Receptor 1 (CB1R) and Cannabinoid Receptor 2 (CB2R) (Matsuda et al, Nature 346, 561-564 (1990), Munro et al, Nature, 365, 61-65 (1993)). CB1R is by far the predominant form in the central nervous system, whereas both CB1R and CB2R are located in the peripheral tissues, including the skin. Herein a reference to a CBR activator includes either or both CB1R and CB2R activators.

10 The above flavonoid compounds of general formula (I) are natural products and may be obtained from suppliers such as Apin Chemicals Limited (Oxon., UK)., Sigma-Aldrich and Interbioscreens.

15 Mixtures of two or more flavonoid compounds of general formula (I) may also be used in compositions of the invention.

The amount of flavonoid compound(s) of general formula (I) in the compositions of the invention is preferably selected in the range of from 0.05 to 20%, more preferably from 0.1 to 10%, most preferably from 0.25 to 5wt% by weight based on total weight.

25 Antidandruff Agent

Preferably, compositions according to the invention comprise from 0.01% to 30% by weight, more preferably 0.1% to 10%, most preferably 0.5 to 2% by weight of an antidandruff agent. By "antidandruff agent" is meant a different compound from the flavonoid compound of general formula (I). Antidandruff agents are compounds that are active against

- 9 -

dandruff and are typically antimicrobial agents, preferably antifungal agents.

Suitable antidandruff agents include compounds selected from
5 zinc pyrithione, climbazole, ketoconazole, octopirox and mixtures thereof.

The preferred antifungal agent is zinc pyrithione (ZnPTO) which, on account of its relative insolubility in aqueous
10 systems, is generally used in hair treatment compositions as a particulate dispersion. The zinc pyrithione may be used in any particle form including, for example, crystalline forms such as platelets and needles and amorphous, regularly or irregularly shaped particles. If zinc pyrithione is
15 present in the composition, a suspending agent is preferably used to prevent or inhibit the settling of the particles out of the composition. The average particle diameter of the zinc pyrithione particles (i.e, their maximum dimension) is typically from about 0.2 to about 50 μm , preferably from
20 about 0.4 to about 10 μm , more preferably from 0.4 to 1 μm .

Antifungal agents typically display a minimum inhibitory concentration of about 50 mg/ml or less against *Malassezia*.

25 If the antifungal agent is soluble in aqueous systems, it may be present in solution in a composition used in the invention.

- 10 -

Product Forms

Compositions of the present invention are typically for topical application to the hair and/or scalp and may be formulated as transparent or opaque emulsions, lotions, creams, pastes or gels.

Hair and/or scalp care compositions of the invention may be rinse off products or leave on products. Rinse off products are intended to be substantially rinsed off the hair and/or the scalp of the user with water after use. Leave on products are intended not to be rinsed off the hair and/or the scalp of the user immediately after use (ie, within at least the first 2 hours, preferably at least four hours, after application of the composition). Leave on products include, for example, lotions, creams and hair oils that are intended for topical application to the hair and/or the scalp. Rinse off compositions include shampoos and hair conditioners, as well as hair and/or scalp treatment products which are intended to be left on the hair and/or scalp for up to 2 hours (eg, 5 minutes to 2 hours) before being rinsed off.

Preferred product forms are shampoos, conditioners, hair oils and lotions.

Shampoo Compositions

Shampoo compositions according to the invention will typically comprise one or more anionic cleansing surfactants which are cosmetically acceptable and suitable for topical application to the hair.

- 11 -

5 Anionic Cleansing Surfactant

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

20 Typical anionic cleansing surfactants for use in shampoo compositions of the invention include sodium oleyl succinate, ammonium lauryl sulphosuccinate, ammonium lauryl sulphate, sodium dodecylbenzene sulphonate, triethanolamine dodecylbenzene sulphonate, sodium cocoyl isethionate, sodium
25 lauryl isethionate and sodium N-lauryl sarcosinate. The most preferred anionic surfactants are sodium lauryl sulphate, sodium lauryl ether sulphate(n)EO, (where n ranges from 1 to 3), ammonium lauryl sulphate and ammonium lauryl ether sulphate(n)EO, (where n ranges from 1 to 3).

30

Mixtures of any of the foregoing anionic cleansing surfactants may also be suitable.

- 12 -

The total amount of anionic cleansing surfactant in shampoo compositions of the invention is generally from 5 to 30, preferably from 6 to 20, more preferably from 8 to 16 percent by weight of the composition.

5

Co-surfactant

Shampoo compositions according to the invention can optionally include co-surfactants, to help impart aesthetic,
10 physical or cleansing properties to the composition.

A preferred example is an amphoteric or zwitterionic surfactant, which can be included in an amount ranging from 0 to about 8, preferably from 1 to 4 wt%.

15

Examples of amphoteric and zwitterionic surfactants include alkyl amine oxides, alkyl betaines, alkyl amidopropyl betaines, alkyl sulphobetaines (sultaines), alkyl glycinate, alkyl carboxyglycinates, alkyl amphopropionates,
20 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 include lauryl amine oxide, cocodimethyl
25 sulphopropyl betaine and preferably lauryl betaine, cocamidopropyl betaine and sodium cocamphopropionate.

Another preferred example is a nonionic surfactant, which can be included in an amount ranging from 0 to 8, preferably from
30 2 to 5 percent by weight of the composition.

- 13 -

For example, representative 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
5 alkylene oxides, usually ethylene oxide and generally having from 6 to 30 ethylene oxide groups.

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

Further nonionic surfactants which can be included in shampoo compositions of the invention are the alkyl polyglycosides (APGs). Typically, the APG is one which comprises an alkyl
15 group connected (optionally via a bridging group) to a block of one or more glycosyl groups. Preferred APGs are defined by the following formula:



20

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
25 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 may be selected from the group comprising

- 14 -

glucose, xylose, lactose, fructose, mannose and derivatives thereof. Preferably G is glucose.

The degree of polymerisation, n, may have a value of from
5 about 1 to about 10 or more. Preferably, the value of n lies in the range of from about 1.1 to about 2. Most preferably the value of n lies in the range of from about 1.3 to about 1.5.

10 Suitable alkyl polyglycosides for use in the invention are commercially available and include for example those materials identified as: Oramix NS10 ex Seppic; Plantaren 1200 and Plantaren 2000 ex Henkel.

15 Other sugar-derived nonionic surfactants which can be included in shampoo compositions of the invention include the C₁₀-C₁₈ N-alkyl (C₁-C₆) polyhydroxy fatty acid amides, 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
20 fatty acid amides, such as C₁₀-C₁₈ N-(3-methoxypropyl) glucamide.

A preferred blend of cleansing surfactants is a combination of ammonium lauryl ether sulphate, ammonium lauryl sulphate,
25 PEG 5 cocamide and cocamide MEA (CTFA designations).

The shampoo composition can also optionally include one or more cationic co-surfactants included in an amount ranging from 0.01 to 10, more preferably from 0.05 to 5, most
30 preferably from 0.05 to 2 percent by weight of the

- 15 -

composition. Useful cationic surfactants are described hereinbelow in relation to conditioner compositions.

The total amount of surfactant (including any co-surfactant,
5 and/or any emulsifier) in shampoo compositions of the invention is generally from 5 to 50, preferably from 5 to 30, more preferably from 10 to 25 percent by weight of the composition.

10 Cationic Polymer

A cationic polymer is a preferred ingredient in shampoo compositions according to the invention, for enhancing conditioning performance of the shampoo.

15

The cationic polymer may be a homopolymer or be formed from two or more types of monomers. The molecular weight of the polymer will generally be between 5 000 and 10 000 000, typically at least 10 000 and preferably in the range 100 000
20 to about 2 000 000. The polymers will have cationic nitrogen containing groups such as quaternary ammonium or protonated amino groups, or a mixture thereof.

The cationic nitrogen-containing group will generally be
25 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, 3rd edition. The ratio of the cationic
30 to non-cationic monomer units is selected to give a polymer having a cationic charge density in the required range.

- 16 -

Suitable cationic conditioning 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 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.

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

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

Suitable cationic conditioning polymers include, for example:

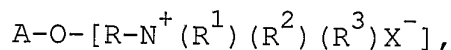
- copolymers of 1-vinyl-2-pyrrolidine and 1-vinyl-3-methyl-imidazolium salt (e.g. chloride salt), referred to in the industry by the Cosmetic, Toiletry, and Fragrance Association, (CTFA) as Polyquaternium-16.

- 17 -

This material is commercially available from BASF Wyandotte Corp. (Parsippany, NJ, USA) under the LUVIQUAT tradename (e.g. LUVIQUAT FC 370);

- 5 - copolymers of 1-vinyl-2-pyrrolidine and dimethylaminoethyl methacrylate, referred to in the industry (CTFA) as Polyquaternium-11. This material is available commercially from Gaf Corporation (Wayne, NJ, USA) under the GAFQUAT tradename (e.g., GAFQUAT 755N);
- 10
- cationic diallyl quaternary ammonium-containing polymers including, for example, dimethyldiallylammonium chloride homopolymer and copolymers of acrylamide and dimethyldiallylammonium chloride, referred to in the
- 15 industry (CTFA) as Polyquaternium 6 and Polyquaternium 7, respectively;
- mineral acid salts of amino-alkyl esters of homo-and copolymers of unsaturated carboxylic acids having from 3
- 20 to 5 carbon atoms, (as described in U.S. Patent 4,009,256);
- cationic polyacrylamides(as described in W095/22311).
- 25 Other cationic conditioning polymers that can be used include cationic polysaccharide polymers, such as cationic cellulose derivatives, cationic starch derivatives, and cationic guar gum derivatives. Suitably, such cationic polysaccharide polymers have a charge density in the range
- 30 from 0.1 to 4 meq/g.
- Cationic polysaccharide polymers suitable for use in compositions of the invention include those of the formula:

- 18 -



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. R^1 , R^2 and R^3 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 R^1 , R^2 and R^3) is preferably about 20 or less, and X is an anionic counterion.

Cationic cellulose is available from Amerchol Corp. (Edison, NJ, USA) in their Polymer JR (trade mark) and LR (trade mark) series of polymers, as salts of hydroxyethyl cellulose reacted with trimethyl ammonium substituted epoxide, referred to in the industry (CTFA) as Polyquaternium 10. 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 Amerchol Corp. (Edison, NJ, USA) under the tradename Polymer LM-200.

Other suitable cationic polysaccharide polymers include quaternary nitrogen-containing cellulose ethers (e.g. as

- 19 -

described in U.S. Patent 3,962,418), and copolymers of etherified cellulose and starch (e.g. as described in U.S. Patent 3,958,581).

- 5 A particularly suitable type of cationic polysaccharide polymer that can be used is a cationic guar gum derivative, such as guar hydroxypropyltrimonium chloride (commercially available from Rhone-Poulenc in their JAGUAR trademark series).

10

Examples are JAGUAR C13S, which has a low degree of substitution of the cationic groups and high viscosity. JAGUAR C15, having a moderate degree of substitution and a low viscosity, JAGUAR C17 (high degree of substitution, high
15 viscosity), JAGUAR C16, which is a hydroxypropylated cationic guar derivative containing a low level of substituent groups as well as cationic quaternary ammonium groups, and JAGUAR 162 which is a high transparency, medium viscosity guar having a low degree of substitution.

20

Preferably the cationic conditioning polymer is selected from cationic cellulose and cationic guar derivatives.

Particularly preferred cationic polymers are JAGUAR C13S, JAGUAR C15, JAGUAR C17 and JAGUAR C16 and JAGUAR C162.

25

The cationic conditioning polymer will generally be present in compositions 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 percent by weight of the composition.

30

When cationic conditioning polymer is present in a shampoo composition according to the invention, it is preferred if the copolymer is present as emulsion particles with a mean

- 20 -

diameter ($D_{3,2}$ as measured by light scattering using a Malvern particle sizer) of 2 micrometres or less.

5

Hair Conditioner Compositions

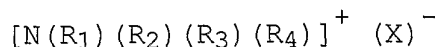
- 10 Compositions in accordance with the invention may also be formulated as conditioners for the treatment of hair (typically after shampooing) and subsequent rinsing.

Hair conditioner compositions according to the invention will
15 suitably comprise a cationic conditioning surfactant that is cosmetically acceptable and suitable for topical application to the hair.

Cationic Conditioning Surfactant

20

Examples of suitable cationic conditioning surfactants are those corresponding to the general formula:



25

in which R_1 , R_2 , R_3 , and R_4 are independently selected from (a) an aliphatic group of from 1 to 22 carbon atoms, or (b) an aromatic, alkoxy, polyoxyalkylene, alkylamido, hydroxyalkyl, aryl or alkylaryl group having up to 22 carbon
30 atoms; and X is a salt-forming anion such as those selected from halogen, (e.g. chloride, bromide), acetate, citrate,

- 21 -

lactate, glycolate, phosphate nitrate, sulphate, and alkylsulphate radicals.

The aliphatic groups can contain, in addition to carbon and hydrogen atoms, ether linkages, and other groups such as amino groups. The longer chain aliphatic groups, e.g., those of about 12 carbons, or higher, can be saturated or unsaturated.

Preferred cationic conditionings surfactants are monoalkyl quaternary ammonium compounds in which the alkyl chain length is C16 to C22.

Other preferred cationic conditioning surfactants are so-called dialkyl quaternary ammonium compounds in which R1 and R2 independently have an alkyl chain lengths from C16 to C22 and R3 and R4 have 2 or less carbon atoms.

Examples of suitable cationic surfactants 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, cocotrimethylammonium chloride, PEG-2 oleylammonium chloride and salts of these where the chloride is replaced by halogen, (e.g. , bromide), acetate, citrate, lactate,

- 22 -

glycolate, phosphate nitrate, sulphate, or alkylsulphate. 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
5 may also be suitable. A particularly useful cationic conditioning surfactant is cetyltrimethylammonium chloride, available commercially, for example as GENAMIN CTAC, ex Hoechst Celanese.

- 10 Salts of primary, secondary, and tertiary fatty amines are also suitable cationic conditioning surfactants. The alkyl groups of such amines preferably have from about 12 to about 22 carbon atoms, and can be substituted or unsubstituted.
- 15 Particularly useful are amido substituted tertiary fatty amines. Such amines, useful herein, include stearamidopropyldiethylamine, stearamidoethyldiethylamine, stearamidoethyldimethylamine, palmitamidopropyldimethylamine, palmitamidopropyldiethylamine, palmitamidoethyldiethylamine,
20 palmitamidoethyldimethylamine, behenamidopropyldimethylamine, behenamidopropyldiethylamine, behenamidoethyldiethylamine, behenamidoethyldimethylamine, arachidamidopropyldimethylamine, arachidamidopropyldiethylamine,
25 arachidamidoethyldiethylamine, arachidamidoethyldimethylamine, diethylaminoethylstearamide. Also useful are dimethylstearamine, dimethylsoyamine, soyamine, myristylamine, tridecylamine, ethylstearylamine, N-tallowpropane diamine, ethoxylated (with 5 moles of ethylene
30 oxide) stearylamine, dihydroxyethylstearylamine, and arachidyl behenylamine. These amines are typically used in combination with an acid to provide the cationic species.

- 23 -

The preferred acid useful herein includes L- glutamic acid, lactic acid, hydrochloric acid, malic acid, succinic acid, acetic acid, fumaric acid, tartaric acid, citric acid, L- glutamic hydrochloride, and mixtures thereof; more preferably

5 L-glutamic acid, lactic acid, citric acid. Cationic amine surfactants included among those useful in the present invention are disclosed in U.S. Patent 4,275,055 to Nachtigal, et al., issued June 23, 1981.

10 The molar ratio of protonatable amines to H^+ from the acid is preferably from about 1:0.3 to 1:1.2, and more preferably from about 1:0.5 to about 1:1.1.

In the conditioners of the invention, the level of cationic

15 conditioning surfactant is suitably from 0.01 to 10, preferably from 0.05 to 5, more preferably from 0.1 to 2 percent by weight of the total composition.

Fatty Materials

20

Hair conditioner compositions according to the invention preferably additionally comprise fatty materials.

By "fatty material" is meant a fatty alcohol, an alkoxyated

25 fatty alcohol, a fatty acid or a mixture thereof.

Preferably, the alkyl chain of the fatty material is fully saturated.

- 24 -

Representative fatty materials comprise from 8 to 22 carbon atoms, more preferably 16 to 22. Preferred fatty materials include cetyl alcohol, stearyl alcohol and mixtures thereof.

5 Alkoxylated, (e.g. ethoxylated or propoxylated) fatty alcohols having from about 12 to about 18 carbon atoms in the alkyl chain can be used in place of, or in addition to, the fatty alcohols themselves. Suitable examples include ethylene glycol cetyl ether, polyoxyethylene (2) stearyl
10 ether, polyoxyethylene (4) cetyl ether, and mixtures thereof.

The level of fatty material in conditioners of the invention is suitably from 0.01 to 15, preferably from 0.1 to 10, and
15 more preferably from 0.1 to 5 percent by weight of the composition. The weight ratio of cationic surfactant to fatty material is suitably from 10:1 to 1:10, preferably from 4:1 to 1:8, optimally from 1:1 to 1:7, for example 1:3.

20 Hair conditioner compositions of the invention can also contain a cationic polymer. Suitable cationic polymers are described hereinabove in relation to shampoo compositions.

Hair Oils and Lotions

25

Hair oils are also suitable product forms according to the invention. Hair oils predominantly comprise water-insoluble oily conditioning materials. Lotions are aqueous emulsions comprising water-insoluble oily conditioning materials.

30 Suitable surfactants can also be included in lotions to improve their stability to phase separation.

Other Optional Ingredients

- 25 -

Compositions of this invention may contain any other ingredient normally used in hair treatment formulations.

5 Suspending Agents

Hair treatment compositions according to the invention such as shampoos suitably comprise from 0.1 to 5 wt% of 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 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. Polyacrylic acid is available commercially 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 940, Carbopol 941 and Carbopol 980. An example of a suitable copolymer of a carboxylic acid containing a monomer and acrylic acid esters is Carbopol 1342. All Carbopol (trade mark) materials are available from Goodrich.

Suitable cross-linked polymers of acrylic acid and acrylate esters are Pemulen TR1 or Pemulen TR2. A suitable

- 26 -

heteropolysaccharide gum is xanthan gum, for example that available as Kelzan mu.

Further Conditioning Agents

5

Hair treatment compositions according to the invention such as shampoos and conditioners suitably contain further conditioning agents such as silicone conditioning agents and non-silicone oily conditioning agents.

10

Suitable silicone conditioning agents include polydiorganosiloxanes, in particular polydimethylsiloxanes which have the CTFA designation dimethicone. Also suitable for use in compositions of the invention (particularly shampoos and conditioners) are polydimethyl siloxanes having hydroxyl end groups, which have the CTFA designation dimethiconol. Also 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. These materials can impart body, volume and stylability to hair, as well as good wet and dry conditioning. Also suitable are functionalised silicones, particularly amino-functionalised silicones.

15

20

25

Suitable non-silicone oily conditioning agents are selected from hydrocarbon oils, fatty esters and mixtures thereof.

30

The further conditioning agent is suitably present in shampoo or conditioner compositions at a level of from 0.05 to 10, preferably from 0.2 to 5, more preferably from about 0.5 to 3 percent by total weight of further conditioning agent based on total weight of the composition.

- 27 -

Hair treatment compositions of the invention may contain other optional ingredients for enhancing performance and/or consumer acceptability, such as fragrance, dyes and pigments, pH adjusting agents, pearlescers or opacifiers, viscosity modifiers, preservatives, and natural hair nutrients such as botanicals, fruit extracts, sugar derivatives and amino acids.

The invention is further illustrated with reference to the following, non-limiting examples, in which all percentages are by weight based on total weight unless otherwise specified.

EXAMPLES

Examples 1 to 5

Flavonoid compounds of general formula (I) above were evaluated for their ability to activate Cannabinoid Receptor 1 (CB₁R) and Cannabinoid Receptor 2 (CB₂R).

CB₁R experiments were performed using membranes from HEK293 cells over-expressing human recombinant CB₁, as described by the manufacturer (Perkin-Elmer) and using [3H]CP-55,490 as the radioligand.

CB₂R experiments were performed using membranes from HEK293 cells over-expressing human recombinant CB₂, as described by the manufacturer (Perkin-Elmer), and using [3H]CP-55,495 as the radioligand.

- 28 -

Data of active compounds are expressed in K_i (mM) and are means $\pm$ SEM of n=3 determinations.

5 The values that are stated for each of the compounds is an EC50 value. This is defined as the molar concentration of an agonist, which produces 50% of the maximum possible response for that agonist. The values documented are in micromolar units.

10 The absence of a value in the table indicates that greater than 25 micromolar concentration was required for 50% binding of the ligand to the receptor.

Also, the ClogP values of the compounds were calculated
15 using SYBYL v6.8 (Tripos Inc., Missouri).

- 29 -

The results are shown in the following Table:

Example	Flavonoid	CB1R Activity	CB2R Activity	ClogP
1	isoxanthohumol (4',7-dihydroxy-5-methoxy-8-prenylflavanone)	7.50	-	4.46
2	8-prenylnaringenin (4',5,7-trihydroxy-8-prenylflavanone)	4.60	-	4.40
3	pinocembrine (5,7-dihydroxyflavanone)	-	15.50	3.11
4	pinostrobin (5-hydroxy-7-methoxyflavanone)	0.80	9.10	3.63
5	sakuranetin (5,4'-dihydroxy-7-methoxyflavanone)	3.80	-	2.97

- 30 -

Example 6

The following is an example of a shampoo composition according to the invention:

5

Ingredient	Example 6
Chemical Name	a.i. weight %
SLES 2EO	14
Cocoamidopropylbetaine	2
Guar hydroxypropyltrimonium chloride	0.1
Dimethiconol	1
Crosslinked polyacrylic acid	0.4
Zinc pyrithione	0.5
Pinostrobin	0.6
Mica + titanium dioxide	0.2
Sodium benzoate	0.5
Water	to 100

- 30A -

The reference in this specification to any prior publication
(or information derived from it), or to any matter which is
known, is not, and should not be taken as an acknowledgment
or admission or any form of suggestion that that prior
5 publication (or information derived from it) or known matter
forms part of the common general knowledge in the field of
endeavour to which this specification relates.

Throughout this specification and the claims which follow,
10 unless the context requires otherwise, the word "comprise",
and variations such as "comprises" or "comprising", will be
understood to imply the inclusion of a stated integer or
step or group of integers or steps but not the exclusion of
any other integer or step or group of integers or steps.

The claims defining the invention are as follows:

1. Use of pinostrobin (5-hydroxy-7-methoxyflavanone) in the manufacture of a composition for activating cannabinoid receptors in the skin.
5
2. Use according to claim 1 in which the pinostrobin is present in a composition further comprising from 0.01 to 30% by weight of an antidandruff agent.
10
3. Use according to claim 2 characterised in that the antidandruff agent comprises a compound selected from zinc pyrithione, climbazole, ketoconazole, octopirox and mixtures thereof.
15
4. Use according to any one of the preceding claims in which the pinostrobin is present in a shampoo composition comprising an anionic cleansing surfactant in an amount of from 5 to 30wt%.
20
5. Use according to any one of claims 1 to 4 in which the pinostrobin is present in a conditioner composition comprising a cationic conditioning surfactant in an amount of from 0.01 to 10wt%.
25
6. Use according to any one of claims 1 to 5 in which the pinostrobin is present in a hair oil or lotion.
7. Use according to any one of the preceding claims characterised in that the amount of pinostrobin is from
30 0.05 to 20% by weight and preferably from 0.1 to 10% by

weight.

8. Use of pinostrobin (5-hydroxy-7-methoxyflavanone)
substantially as hereinbefore described with reference
5 to the examples.