APPLICATION FOR PATENT

INVENTOR

ADDRESS

INVENTION

ABSTRACT

CLAIMS

DESCRIPTION

INVENTOR

DATE

SIGNATURE

AUSTRALIAN PATENT ABRIDGMENT

AUSTRALIA

(11) AU-B-89734/82

TM FORM OF SHAMPOO
CONVENTION APPLICATION FOR A PATENT

89734/82

L'OREAL
of 14, rue Royale, 75008 Paris, France

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LODGED 25 OCT 1982

by L. J. Dyson
Reg'd Patent Attorney

TO: THE COMMISSIONER OF PATENTS.

CONSTITUTION, IN THE FORM OF A SHAMPOO, BASED ON ANTHRACINE OR A DERIVATIVE THEREOF, AND ITS USE IN THE TREATMENT OF SKIN DISEASES

which is described in the accompanying complete specification. This application is a convention application and is based on the application numbered 81.19952 and 82.05864 for a patent or similar protection made in France on 23rd October 1981 and 5th April 1982.

The address for service is Messrs. Edwd. Waters & Sons, Patent Attorneys, 50 Queen Street, Melbourne, Victoria, Australia.

L'OREAL

Dated this 25th day of October 1982

L. J. Dyson
Reg'd Patent Attorney

Form 10
DECLARATION IN SUPPORT OF A CONVENTION APPLICATION FOR A PATENT OR PATENT OF ADDITION

In support of the Convention Application made by

L'OREAL

(hereinafter referred to as the applicant) for a Patent for an invention entitled:

COMPOSITION, IN THE FORM OF A SHAMPOO, BASED ON ANTHRalin OR A DERIVATIVE THEREOF, AND ITS USE IN THE TREATMENT OF SKIN DISEASES

I. (9) ANDRE VIOUT,

of 14, rue Royale, 75008 Paris, France.

do solemnly and sincerely declare as follows:

1. I am authorised by the applicant for the patent to make this declaration on its behalf.

2. The basic application as defined by Section 141 of the Act was made in FRANCE on the 23rd day of October, 1981, by


4. The basic application referred to in paragraph 2 of this Declaration was the first application made in a Convention country in respect of the invention the subject of the application.

DECLARED at Paris, France, this 11th day of October, 1982.

To: The Commissioner of Patents.

André VIOUT
Directeur du Département Brevets
1. A composition, in the form of a shampoo suitable for application to the scalp which contains, in aqueous solution or aqueous dispersion, anthralin or a derivative thereof, at least one fatty acid alkyl ester, the fatty acid having from 5 to 18 carbon atoms and the alkyl radical having from 2 to 18 carbon atoms, and at least one anionic or non-ionic surface-active agent, the said composition being stable to oxidation for about one week when stored at a temperature of about +4°C.
Complete Specification

Composition, in the form of a shampoo, based on anthralin or a derivative thereof, and its use in the treatment of skin diseases

The following statement is a full description of this invention, including the best method of performing it known to us:

R₁–CHOH–CH₂–O–(CH₂–CHOH–CH₂)₉–H
DESCRIPTION

"COMPOSITION, IN THE FORM OF A SHAMPOO, BASED ON ANTHRALIN OR A DERIVATIVE THEREOF, AND ITS USE IN THE TREATMENT OF SKIN DISEASES"

The present invention relates to a composition, in the form of a shampoo, based on anthralin or one of its derivatives, and to its use for the treatment of scalp diseases, in particular psoriasis.

Psoriasis is a particularly frequent form of dermatosis which manifests itself as lesions found not only on the elbows, on the back of the forearms, on the knees, on the legs and in the sacro-lumbar regions, but also on the scalp.

Amongst the various substances which have already been recommended for the treatment of psoriasis, special mention must be made of anthralin or dithranol (1,8,9-trihydroxyanthracene), which has proved particularly active, but the use of which is not without certain disadvantages insofar as this compound is readily degraded by oxidation to give dark-coloured polymeric products capable of staining the skin and clothes.

Furthermore, the known compositions, which are generally based on vaseline as the carrier, are unsuitable for treatment of the scalp insofar as they are difficult to remove.
Compositions in the forms of a shampoo have never been recommended hitherto on account of the very high instability of anthralin and its derivatives in aqueous solutions. In fact, the compositions change colour after only a few hours, which denotes decomposition of the anthralin; this decomposition also results from the presence of the surface-active agent, which is capable of having a degrading effect.

After much research in this field, it has been found possible, according to the present invention, to develop shampoos having a good stability to oxidation and capable of being stored, without degradation, for about one week at a temperature of about +4°C, which makes it possible, after mixing of the anhydrous part and the aqueous part of the compositions according to the invention, which can be in the form of a two-part pack, to carry out several successive treatments with the same shampoo without having to mix the two parts again each time the shampoo is used.

This good stability of the shampoos according to the invention is essentially due to the presence of certain fatty acid alkyl esters in the composition and also in preferred embodiments to certain surface-active agents in particular of the anionic or non-ionic type.

The present invention provides a composition,
in the form of a shampoo, based on anthralin or one of its derivatives, for the treatment of the scalp, this composition containing, in aqueous solution or aqueous dispersion, anthralin or one of its derivatives, a fatty acid alkyl ester, the fatty acid having from 5 to 18 carbon atoms and the alkyl radical, which is branched or unbranched, having from 2 to 18 carbon atoms, and at least one anionic or non-ionic surface-active agent, the said composition being stable to oxidation for about one week when stored at a temperature of about +4°C.

Amongst the fatty acid alkyl esters corresponding to the above definition, there may be mentioned: isodecyl neopentanoate, cetyl octanoate, stearyl octanoate, isopropyl laurate, ethyl myristate, isopropyl myristate, isopropyl palmitate, 2-ethylhexyl palmitate, butyl stearate, isopropyl stearate, 2-ethylhexyl stearate, isocetyl stearate and mixtures thereof.

Amongst the anthralin derivatives which can also be stabilised by fatty acid alkyl esters, there may be mentioned the compounds described in French Patent Applications Nos. 80/22,454 and 80/22,455.

The anionic or non-ionic surface-active agents which can be used in the compositions according to the invention are suitably those whose solutions, after two months at 45°C, have the same foaming power and a
The anthralin derivatives used according to the invention have the formula

\[
\begin{align*}
\text{OH} & \quad \text{HD} & \quad \text{OH} \\
\end{align*}
\]

in which \( R_1 \) and \( R_2 \) together form one of the radicals:

(i) \[
\begin{align*}
\text{N-R}_3
\end{align*}
\]

(ii) \[
\begin{align*}
\text{CO}_2\text{R}_4 & & \text{CO}_2\text{R}'_4 \\
\end{align*}
\]

(iii) \[
\begin{align*}
\text{CO}_2\text{R}_5 & & \text{CO}_2\text{R}'_5 \\
\end{align*}
\]

in which \( R_3, R_4 \) and \( R'_4 \), which may be identical or different, represent a hydrogen atom, a straight or branched alkyl radical of 1 to 8 carbon atoms, a monohydroxy-alkyl radical, having 2 to 8 carbon atoms, optionally interrupted by one or more atoms of oxygen, a cycloalkyl radical of 4 to 6 carbon atoms, or a phenyl or benzyl radical and \( R_5 \) and \( R'_5 \), which may be identical or different, represent a hydrogen atom, a linear or branched alkyl radical of 1 to 8 carbon atoms with the proviso that both \( R_5 \) and \( R'_5 \) are not methyl, a monohydroxy-alkyl radical of 2 to 8 carbon atoms, optionally
substituted by one or more oxygen atoms, a cycloalkyl radical of 4 to 6 carbon atoms, or a phenyl or benzyl radical or may have the formula

![Chemical structure image]

in which \( R_1 \) is one of:

(a) 

(b) 

(c) 

(d)
and

(e)

\[-\text{CH-CH-R}_6\]
\[\text{R}_7\]
\[\text{R}_7'\]

in which
R₂ represents a hydrogen atom, a linear or branched alkyl radical of 1 to 8 carbon atoms, a linear or branched mono- or poly-hydroxyalkyl radical of 1 to 3 carbon atoms, a carbamyl radical or a phenyl radical, R₃, R₄ and R₅ which may be identical or different, represent a hydrogen atom, an alkyl radical of 1 to 8 carbon atoms, a mono- or poly-hydroxyalkyl radical of 3 to 8 carbon atoms, optionally substituted by an oxygen atom, or a cycloalkyl radical of 3 to 6 carbon atoms, or R₃ and R₄ together represent a divalent radical of the formula \(-(\text{CH}_2)_n-\) where n is 4 or 5, \(-(\text{CH}_2)_2-\text{O-CH}_2\)-, or \(-(\text{CH}_2)_2-N-(\text{CH}_2)_2-\)

wherein R₈ represents a hydrogen atom, a methyl radical or a 2-hydroxyethyl radical, R₆ represents -\text{CO}_2\text{R}_5, -\text{CN}-, -\text{CHO}, -\text{CONH}_2 or -\text{CONH-CH}_2-\text{OH} and R₇ and R₇', which may be identical or different, represent a hydrogen atom or a methyl radical; and their optical isomers.

Examples of these anthralin derivatives are described in French Patent No 2,492,372 and 2,492,373.

The anionic or non-ionic surface-active agents which can be used in the compositions according to the invention are suitably those whose solutions, after two months at 45°C, have the same foaming power and a
pH decrease of not more than two units.

Amongst the anionic surface-active agents which correspond to this definition, there may be mentioned:

- sulphated oxyethyleneated C₈₋C₁₈-alkanols, such as the sodium salt of sulphated lauryl alcohol oxyethyleneated with 2.2 mols of ethylene oxide,

- C₈₋C₁₈-acyl-sarcosines and their salts, such as sodium (coconut alkyl)-sarcosinate, and

- α-C₁₀₋C₂₀-olefine-sulphonates, such as sodium α-C₁₄₋C₁₆-olefine-sulphonates.

The non-ionic surface-active agents which correspond to the above definition and which are preferably used according to the invention are condensation products of monoalcohols, α-diols, alkylphenols or alkanolamides with glycidol. The particularly preferred products are those corresponding to the following formulae:

1) $R_1\text{-CHOH-CH}_2\text{-O-}\overbrace{\text{(CH}_2\text{CHOH-CH}_2\text{-O)-}}^{p}\text{H}$

in which $R_1$ denotes an aliphatic, cycloaliphatic or arylaliphatic radical having from 7 to 21 carbon atoms, and mixtures thereof, it being possible for the aryl-aliphatic chains to contain ether, thioether or hydroxy-methylene groups, and in which $p$ is from 1 to 10 inclusive, these compounds being described more particularly in French Patent 2,091,516;
The non-ionic surface-active agents which give particularly advantageous results in the compositions according to the invention correspond to the following formulae:

1) \[ \text{R}_1\text{-CHOH-CH}_2\text-O\text{(CH}_2\text{-CHOH-CH}_2\text{-O)}\text{p}-\text{H} \]

in which \( \text{R}_1 \) denotes a mixture of alkyl radicals having from 9 to 12 carbon atoms and \( p \) has a statistical value of 3.5;

2) \[ \text{R}_2\text{-O-[C}_2\text{H}_3\text{O-(CH}_2\text{-OH)}\text{q}-\text{H} \]

in which \( \text{R}_2 \) denotes \( 
\text{C}_12\text{H}_25 \) and \( q \) has a statistical value of 4 to 5;
3) \( R_3-\text{CONH-CH}_2-\text{CH}_2-\text{O-CH}_2-\text{CH}_2-\text{O-[CH}_2\text{CHOH-CH}_2\text{-O]}_r \rightarrow \text{H} \)

in which \( R_3 \) denotes a mixture of radicals derived from lauric, myristic, oleic and copra acids and \( r \) has a statistical value of 3 to 4.

According to the invention, the concentration of anthralin or one of its derivatives in the composition is generally from 0.01 to 5%, but preferably from 0.03 to 2%, the concentration of the fatty acid alkyl ester is preferably from 8 and 47.5% and the concentration of the anionic or non-ionic surface-active agent is preferably from 2.5 to 36% by weight, relative to the total weight of the composition.

The shampoo composition can also contain various ingredients insofar as they do not have an adverse influence on the stability: amongst these, there may be mentioned, in particular, certain thickeners, such as silicas and polyethylene powders which are preferably present at a concentration of 0.1 to 20% by weight, in particular of 2 to 15% by weight.

The shampoo composition according to the invention is generally prepared, when it is used for the first time, by mixing an anhydrous part and an aqueous part, which is preferably presented in the form of a two-part pack.

The first part, or anhydrous part, contains the anthralin or one of its derivatives in solution or dispersion, or dispersed, in an anhydrous medium.
dispersion in the fatty acid alkyl ester, the solution or dispersion being stable to oxidation without it being necessary to incorporate a stabiliser or antioxidant therein, and the second part, or aqueous part, contains an aqueous solution of the anionic or non-ionic surfac...

The concentration of anthralin or one of its derivatives in the anhydrous part is preferably 0.1 to 5% and the concentration of the fatty acid alkyl ester is preferably 80 to 95%, this part also being able to contain a thickener.

In the aqueous phase, the concentration of anionic or non-ionic surfac-active agent is preferably 5 to 40%, preferably 7 to 25%, and this phase can also contain a thickener.

When the shampoo is used for the first time, the two parts are mixed in proportions which can vary, according to the desired effectiveness, generally in a ratio of the anhydrous part to the aqueous part of 10:90 to 50:50. The mixture obtained is then applied to the scalp and the hair in an amount of, say, 20 to 30g. It is subsequently left to act for, say, 5 minutes to 1 hour, then emulsified with water and...
rinsed out with copious amounts of water. The treatment is then repeated every day or every other day with the same composition, which has been stored at a temperature of about +4°C.

In general, the two-part pack is such that it makes it possible, after mixing, to carry out a treatment lasting about one week at a rate of 1 to 2 shampoo treatments every two days.

The anhydrous part is preferably packaged in sealed glass ampoules and the aqueous part in bottles. At the time of use, the tips of the ampoules are broken and the solution or dispersion is poured into the bottle. Before each use, it is recommended to shake the mixture thoroughly.

Good results in the treatment of psoriasis are generally obtained after 3 to 5 weeks.

The following Examples further illustrate the present invention.

**EXAMPLE 1**

A shampoo according to the invention is packaged in the form of the following two parts:

1) **Anhydrous part**

   - Anthralin ......................... 0.83 g
   - 50:50 mixture of cetyl octanoate ..
   - 50:50 mixture of stearyl octanoate q.s. ......... 100 g
2) **Aqueous part**

- Sodium salt of sulphated lauryl alcohol oxyethyleneated with 2.2 mols of ethylene oxide 12 g
- Lactic acid q.s. pH 4
- Water q.s. .........................100 g

At the time of use, 25% of the anhydrous part (1) and 75% of the aqueous part (2) are mixed.

The resulting composition has a milky appearance and about 30g thereof are applied to the scalp and hair.

After an application time of 20 minutes, the composition is emulsified with water and rinsed out.

The rest of the composition remains stable for about 7 days when stored at a temperature of about 4°C, and it makes it possible to carry out from two to three further shampoo treatments at one-day intervals.

After two weeks, a regression in the psoriasis is observed and the shampoo treatment can be repeated every day or every other day.

In this example, the anhydrous part can be replaced by one of the following compositions:

(a) - Anthralin ..................... 0.4 g
   - Isopropyl myristate q.s. 100 g

(b) - Anthralin ..................... 0.47 g
   - Ethyl myristate q.s. ..........100 g
EXAMPLES 2 - 6

Following the same procedure as in Example 1, psoriasis of the scalp was treated with the shampoos obtained after mixing the following two-part compositions:

EXAMPLE 2

1) **Anhydrous part**
   - Anthralin 0.2 g
   - Isopropyl myristate q.s. 100 g

2) **Aqueous part**
   - Non-ionic surface-active agent of the formula:
     \[ R_1-CHOH-CH_2-O-(CH_2-CHOH-CH_2-O)_pH \]
     \( R_1 = C_9-C_{12} \)-alkyl and \( p = 3.5 \)
   - Formaldehyde 0.06 g
   - Citric acid q.s. pH = 3
   - Water q.s. 100 g

At the time of use, 25% of the anhydrous part (1) is mixed with 75% of the aqueous part (2).

EXAMPLE 3

1) **Anhydrous part**
   - Anthralin 0.4 g
   - Isopropyl palmitate q.s. 100 g

2) **Aqueous part**
   - Non-ionic surface-active agent of the formula:
R₁-CHOH-CH₂-O(CH₂-CHOH-CH₂-O)ₚ-H
R = C₉-C₁₂-alkyl and p = 3.5  20 g
- Formaldehyde 0.06 g
- Citric acid q.s. pH = 3
- Water q.s. .........................100 g

At the time of use, 25% of the anhydrous part (1) is mixed with 75% of the aqueous part (2).

EXAMPLE 4

1) Anhydrous part
- Anthralin 0.4 g
- Ethyl myristate q.s. 100 g

2) Aqueous part
- (Coconut alkyl)-sarcosinic acid (sold by HAMPSCHIRE under the name "HAMPOSYL-C") 17 g
- Sodium hydroxide q.s. pH = 4.5
- EDTA 0.07 g
- Water q.s. 100 g

At the time of use, 15% of the anhydrous part (1) is mixed with 85% of the aqueous part (2).

In this example, the anhydrous part (1) can be replaced by one of the following compositions:

(a) - Anthralin ......................... 0.40 g
- Isopropyl myristate q.s. ........100 g

(b) - Anthralin ......................... 0.20 g
EXAMPLE 5

1) Anhydrous part
   - Anthralin .......................... 0.2 g
   - Isocetyl stearate q.s. ............100 g

2) Aqueous part
   - Sodium \(\alpha\)-olefine\(\text{C}_{14}-\text{C}_{16}\) - sulphonate
     (sold by AKZO Chemie under the name "ELFAN OS 46") .................. 16.5 g
     (active ingredients)
   - Citric acid q.s. pH = 3.5
   - Water q.s. ...........................100 g

At the time of use, 20% of the anhydrous part (1) is mixed with 80% of the aqueous part (2).

In this example, the anhydrous part (1) can be replaced by one of the following compositions:

(a) - Anthralin .......................... 0.4 g
   - Isopropyl myristate q.s. ..........100 g

(b) - Anthralin .......................... 0.83 g
   - 50:50 mixture of cetyl octanoate
     and stearyl octanoate q.s. .......100 g

(c) - Anthralin .......................... 0.47 g
   - Ethyl myristate q.s. ..............100 g

EXAMPLE 6

1) Anhydrous part
   - Anthralin .......................... 0.47 g
2) **Aqueous part**

- Non-ionic surface-active agent of the formula:

\[
R_1 \text{CHOH-CH}_2\text{-O-} \left( \text{CH}_2\text{-CHOH-CH}_2\text{-O} \right)^p \text{H}
\]

\[R_1 = C_9\text{-}C_{12}\text{-alkyl and } p = 3.5\]

- Acetic acid q.s. pH = 5
- Thickener ......................... 2.3 g
- Water q.s. ......................... 100 g

At the time of use, 25% of the anhydrous part (1) is mixed with 75% of the aqueous part (2).

In this example, the anhydrous part (1) can be replaced by one of the following compositions:

(a) - Anthralin ...................... 2 g

(b) - Anthralin ...................... 1.5 g

- Isocetyl stearate q.s. .......... 100 g

All the shampoos of Examples 2 to 6 showed a good storage stability at a temperature of +4°C for one week, together with an excellent activity in the treatment of psoriasis of the scalp.
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A composition, in the form of a shampoo suitable for application to the scalp which contains, in aqueous solution or aqueous dispersion, anthralin or a derivative thereof, at least one fatty acid alkyl ester, the fatty acid having from 5 to 18 carbon atoms and the alkyl radical having from 2 to 18 carbon atoms, and at least one anionic or non-ionic surface-active agent, the said composition being stable to oxidation for about one week when stored at a temperature of about +4°C.

2. A composition according to Claim 1 in which the fatty acid alkyl ester is isodecyl neopentanoate, cetyl octanoate, stearyl octanoate, isopropyl laurate, ethyl myristate, isopropyl myristate, isopropyl palmitate, 2-ethylhexyl palmitate, isopropyl stearate, butyl stearate, 2-ethylhexyl stearate, isocetyl stearate or a mixture thereof.

3. A composition according to Claim 1 or 2, in which the anionic surface-active agent is a sulphated oxyethyleneated C₈-C₁₈-alkanol, C₈-C₁₈-acyl-sarcosine or a salt thereof, or a sodium α-C₁₀-C₂₀-olefine-sulphonate.
4. A composition according to Claim 1 or 2, in which the non-ionic surface-active agent is

1) \( R_1\text{-CHOH-CH}_2\text{-O-}(\text{CH}_2\text{-CHOH-CH}_2\text{-O})_p\text{-H} \)

in which \( R_1 \) denotes an aliphatic, cycloaliphatic or arylaliphatic radical having from 7 to 21 carbon atoms, said aliphatic chains optionally containing ether, thioether or hydroxymethylene group, and \( p \) is from 1 to 10 inclusive;

2) \( R_2\text{-C}_2\text{H}_3\text{O(CH}_2\text{OH)}_q\text{-H} \)

in which \( R_2 \) denotes an alkyl, alkenyl or alkylaryl radical and \( q \) has an average statistical value of 1 to 10 inclusive;

or 3) \( R_3\text{-CONH-CH}_2\text{-CH}_2\text{-O-CH}_2\text{-CH}_2\text{-O[CH}_2\text{-CHOH-CH}_2\text{-O}}_{1/2}\text{-H} \)

in which \( R_3 \) denotes a linear or branched, saturated or unsaturated aliphatic radical, which can optionally contain one or more hydroxyl groups, which has 8 to 30 carbon atoms and which is of natural or synthetic origin, and \( r \) represents an integral or decimal number from 1 to 5.

5. A composition according to any one of the preceding claims which contains from 0.01 to 5% by weight of anthralin or derivatives thereof, from 8 to 47.5% by weight of fatty acid alkyl ester and from 2.5 to 36% by weight of anionic or non-ionic surface-active agent.
6. A composition according to any one of the preceding claims, which also contains a thickener at a concentration of 0.1 to 20% by weight.

7. A composition according to Claim 1 substantially as described in any one of the Examples.

8. A two-part pack which is capable, after mixing the two parts, of producing a composition as claimed in any one of Claims 1 to 7, the first part being substantially anhydrous and containing the anthralin or derivative thereof in solution or dispersion in the fatty acid alkyl ester, and the second part comprises, in aqueous solution, the anionic or non-ionic surface-active agent at a pH of 4 to 7.

9. A pack according to Claim 8 in which the second part has a pH of 3 to 5.

10. A pack according to Claim 8 or 9 in which the anhydrous part also contains a thickener.

11. A pack according to any one of Claims 8 to 10 in which the aqueous part contains citric acid, lactic acid or acetic acid, in an amount to provide a pH of 2 to 7.

12. A pack according to Claim 8 substantially as hereinbefore described.

DATED this 25th day of October 1982.

L'OREAL

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