Use of an extract of decaffeinated coffee beans in the preparation of a composition intended to stimulate the sebaceous function of the skin by oral administration

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Abstract: The present invention relates to the use of an extract of decaffeinated coffee beans in the preparation of a composition formulated for oral administration and intended to stimulate the sebaceous function of the skin, and in particular to correct the disorders associated with a dry skin. The invention relates in particular to cosmetic, nutritional or pharmaceutical compositions intended for administration by the oral route for the stimulation of the sebaceous function of the skin. The invention also relates to cosmetic procedures for the treatment of dry skins.
USE OF AN EXTRACT OF DECAFFEINATED COFFEE BEANS IN THE PREPARATION OF A COMPOSITION INTENDED TO STIMULATE THE SEBACEOUS FUNCTION OF THE SKIN BY ORAL ADMINISTRATION

The present invention relates to the use of an extract of decaffeinated coffee beans in the preparation of a composition formulated for oral administration and intended to stimulate the sebaceous function of the skin, and in particular to correct the disorders associated with a dry skin. The invention relates in particular to cosmetic, nutritional or pharmaceutical compositions intended for administration by the oral route for the stimulation of the sebaceous function of the skin. The invention also relates to cosmetic procedures for the treatment of dry skins.

An oligoseborrheic dry skin is characterised by an inadequate secretion and excretion of sebum. Conventionally, a concentration of sebum lower than $100 \mu g/cm^2$ measured on the forehead is considered as characteristic of such a dry skin.

A dry skin is often associated with a desquamation deficiency, a dull complexion, an atonic skin texture. Micro-inflammatory symptoms, dermatitis in particular, appear more frequently in cases of dry skin.

Sensations of discomfort such as spasmodic twitches are usually felt in the face by subjects with a dry skin.

All of these disorders progress with age, since chronological ageing is conventionally accompanied by loss of function of the sebaceous adnexa.

On the other hand, it is conventionally admitted that normally greasy skins exhibit an improved picture on ageing compared with dry skins. This effect might be due to the fact that vitamin E is excreted by the sebaceous route (Thiele et al., *J. Invest. Dermatol.* 1999; 113; 1006-10).
The sebum is the natural product of the sebaceous gland which constitutes an adnex of the pilosebaceous unit. Together with the sweat, produced by the eccrine or apocrine glands, it constitutes a natural hydrating agent of the epidermis.

The sebaceous secretion is under the control of different afferences of nervous origin. Cartlidge et al. (Br. J. Dermatol – 1972; 86(1), 61-63) have defined the modulatory role of the cholinergic system (para-lymphatic) system on seborrhea. It is known, moreover, that the dopaminergic system, when it is destabilised, as is the case in the Parkinson syndrome, leads to hyper-seborrhea which can be corrected by L-DOPA (JC Villares et al., Acta Neurol Scand, 80(1), 5Z-63). It is also known that the cholinergic system, through the intermediary of the muscarinic receptor subtype, antagonises the release of dopamine (Pharmacologie, M. Schorderet et al., p 71, Ed. Frison-Roche, ISBN 2-05-100910-4).

An activation of the dopaminergic system and/or an inhibition of the cholinergic system (via the muscarinic receptors) might thus lead to a diminution of lipogenesis and/or excretion of sebum.

On the other hand, a limitation of the dopaminergic stimulation and/or an activation of the cholinergic system (via the muscarinic receptors) might lead to an increased secretion and/or production of sebum. A cholinomimetic activity of the muscarinic type has been found in alcoholic fractions of decaffeinated or undecaffeinated coffee beans (SY Tse, J. Pharm Sci., 1991, 80(7), 665-669 and SY Tse, J. Pharm Sci., 1992, 81(7),449-452).

The invention results from the demonstration of the fact that the oral administration of a composition containing an extract of decaffeinated coffee beans may have a beneficial effect on the stimulation of the sebaceous function of the skin.
Coffee trees are small trees with smooth-margined, perennial, coriaceous, glossy leaves (10-15 x 4-6 cm). The white, fragrant flowers are grouped in whorls at the axil of the leaves. The fruit is a green drupe, which becomes red at maturity and usually contains two planar-convex berries which are made contiguous through their planar face. Although only two species supply the essential needs of the coffee market (C. arabica and C. canephora), many species of coffee trees exist in the wild state in the tropical forests of East Africa.

The berry is oval (10-15 x 6-8 mm), convex on the dorsal face, flattened on the ventral face which is traversed by a longitudinal groove, the hilum. Hard and greenish, it is odourless. The microscopic examination of the green coffee powder reveals fusiform fibres derived from the tegument and cells of albumen: polyhedral, their wall is nacreous and irregularly thickened in a bead-like structure; they contain oily droplets.

The coffee “bean” is obtained by the moist route (fermentation, washing) or the dry route (drying, followed by mechanical decortication) starting from the coffee “cherry”, i.e. from the drupes. The reduction to pulp removes the red epicarp and the fleshy mesocarp; it leads to the coffee “husk”. It is after husking (removal of the lignified endocarp) that the coffee “berry” (or bean) is obtained.

More than 50% of the dry matter of the green coffee berry is represented by carbohydrates, essentially polysaccharides. The proteins represent 10 to 12% of this mass, the lipids 10 to 18%. The unsaponifiable fraction of the crude lipids is considerable (more than 10%): in addition to sterols, hydrocarbons, tocopherols, diterpenic alcohols (cafestol, kahweol and kauranic derivatives) are observed to be present in the free state and, in particular, in the state of fatty acid esters. The coffee berry contains about 5% of phenolic acids: quinic acid, caffeic acid, chlorogenic acid. The
caffeine content is variable: from 0.6 to 2% and more than 3% for certain 
*canephora* (robusta variety).

On torrefaction the texture and the composition of the berry change considerably. The water content is reduced, the berry swells, the 
5 polysaccharides are very degraded (forming in particular soluble products), pigments form (polycondensed furans) and the extremely complex flavour develops (several hundred compounds: alcohols, phenols, aldehydes, furanic and pyrrolic derivatives, hydrocarbons, thiophenes, etc.).

As far as the applicant is aware, it has never been suggested that an 
10 extract of decaffeinated coffee beans be used in the preparation of a composition formulated for oral administration and intended for the stimulation of the sebaceous function of the skin, in particular for the treatment of dry skins.

Hence the object of the invention is the use of an extract of decaffeinated coffee beans in the preparation of a composition intended to stimulate the sebaceous function of the skin, said composition being formulated for oral administration.

In the text which follows "coffee beans" must be understood to mean the bean obtained by the moist route (fermentation, washing) or by the dry route (drying followed by mechanical husking) starting from the coffee "cherry", after husking as described above.

"Extract" must be understood to mean all of the compounds obtained starting from an alcoholic or aqueous-alcoholic extraction of a crude product, in this instance decaffeinated coffee beans, roasted or unroasted.

25 The production of sebum by the skin can be determined by the measurement of the amount of sebum according to the standard so-called
sebumetric procedure described, for example, in the L'Oréal patent FR 2368708 or FR 2404845.

By "stimulation of the sebaceous function of the skin" is meant a significant stimulation of the amount of sebum in the skin.

The species of coffee trees selected for the preparation of the extracts of coffee beans used in the compositions are advantageously selected from the *Coffea* species.

In a particular embodiment, the extract is derived from coffee beans selected from the species *Coffea arabica*, *Coffea robusta*, *Coffea canephora* or *Coffea iberica*. The extract may be obtained starting from roasted coffee beans. It can also be obtained from unroasted coffee beans.

For use according to the invention, the extract of coffee beans is decaffeinated.

In particular, a coffee bean extract can be obtained by an aqueous-alcoholic or alcoholic extraction of coffee beans, and preferably by an extraction with the aid of methanol, ethanol or propanol. Preferably, it does not contain the fractions of coffee beans extractable by non-polar solvents.

Methods for the preparation of decaffeinated coffee extracts are described in particular by S.Y.H. Tse (see above) and in the Examples presented hereafter.

The invention also relates to cosmetic, nutritional or pharmaceutical compositions suitable for oral administration containing the extract of decaffeinated coffee beans, intended to stimulate the sebaceous function of the skin. In particular, the compositions according to the invention are intended for the treatment and/or the prevention of dry skins or skin ageing. The proportion of decaffeinated coffee bean extract in the composition will of course be determined as a function of the desired effect on the
stimulation of the sebaceous function of the skin and the mode of administration of the composition.

The composition intended for administration by the oral route may be made available in any galenical form suitable for this mode of administration, for example in the form of scored or unscored tablets, granules, capsules, gelatine capsules, solutions, suspensions or solutions containing an appropriate excipient.

The composition may be any food or pharmaceutical product, or a cosmetic product for oral application. Examples for food or pharmaceutical carriers are milk, yogurt, curd, cheese, fermented milks, milk based fermented products, ice-creams, fermented cereal based products, milk based powders, infant formulae or pet food, or tablets, liquid bacterial suspensions, dried oral supplement, wet oral supplement, dry tube-feeding or wet tube-feeding.

Preferably, a composition according to the invention is a nutritional supplement, presented in the form of a solid composition of the tablet, granule, capsule, gelatine capsule type and containing an extract of decaffeinated coffee beans as defined above and at least one adjuvant suitable for oral administration.

In this respect the adjuvants for oral compositions, in particular for dietary supplements, are known to the specialist. Mention may be made, among others and for purely illustrative purposes, of lubricants such as magnesium stearate, products for instantaneous solubilisation, gelling agents, thickeners, moisturisers, fatty and/or aqueous compounds, preservatives, texturizing, flavouring and/or coating agents, anti-oxidants and colouring materials usually used in foods.

The composition according to the present invention may contain, in addition, lipids, polyphenols, taurine, probiotic microorganisms, vitamins
and/or oligo-elements. If probiotics are used, they may be included in a live form, semi-active or in a desactivated form, e.g., as a lyophilized powder. Also culture supernatants of the micro-organisms may be included in the composition. They may be selected from the group consisting of Lactic acid bacteria, in particular Lactobacilli and/or Bifidobacteria and are more preferably selected among the group consisting of *Lactobacillus johnsonii*, *Lactobacillus reuteri*, *Lactobacillus rhamnosus*, *Lactobacillus paracasei*, *Lactobacillus casei*, *Bifidobacterium bifidum*, *Bifidobacterium breve*, *Bifidobacterium animalis*, *Bifidobacterium infantis*, *Bifidobacterium dolescentis* and *Bifidobacterium pseudocatenulatum*. According to a most preferred embodiment the strains used are *Lactobacillus johnsonii* (La1) deposited on June 30, 1992, under Budapest Treaty with the Institute Pasteur and receiving the deposit no. CNCM I-1225 or *Lactobacillus paracasei* (ST11) deposited on January 12, 1999, with the Institute Pasteur according to the Budapest Treaty and receiving the deposit no. CNCM I-2116. The following compounds may for example be used alone or in combination: zinc and its salts including zinc sulfate and zinc glucanate, the vitamins B5, B6, B8, C, E or PP, β-carotene and the carotenoids, extracts of garlic in particular in the form of allyl sulfide or oil garlic, selenium, curcumin, the curcuminoids, niacin, lithospermic acid and adenosine. It is understood that the specialist will select such active compounds and, where possible, combine them in such a manner as to improve the effects expected of the composition which is the object of the invention by preventing the desired activity of interest from being inhibited or attenuated.

The composition intended for oral administration contains an extract of decaffeinated coffee beans in a quantity ranging from 0.1% to 80% by weight of the composition and preferably from 1% to 50% by weight of the composition.

Chlorogenic acid which is a phenolic compound naturally present in some coffee bean extracts, is not involved in the treatment of dry skins.
Chlorogenic acid is thus not an active agent of the compositions for the treatment and/or the prevention of dry skins according to the invention.

Accordingly, in a specific embodiment, chlorogenic acid is present in the composition containing decaffeinated coffee beans in a quantity inferior or equal to 0.1% by weight of the composition.

The invention also relates to a cosmetic procedure for the prevention and/or the treatment of dry skins, or to a procedure for the prevention and/or the cosmetic treatment of skin ageing, which consists of administering by the oral route a composition containing an extract of coffee beans, such as described above.

The daily doses of decaffeinated coffee bean extract administered by the oral route for the treatment of dry skins may preferably be comprised between 0.01 and 5000 mg/day. Preferentially, the coffee bean extract is present in the composition according to the invention in a quantity permitting its administration at a dose comprised between 0.5 and 1000 mg/day.

Definitions of the specific embodiments of the invention as claimed herein follow.

According to a first embodiment of the invention, there is provided a composition when used for stimulating a sebaceous function of skin, said composition containing an extract of decaffeinated coffee beans and being formulated for oral administration.

According to a second embodiment of the invention, there is provided a method for treating and/or preventing dry skin or for treating and/or preventing skin ageing of a subject, said method comprising the step of administering orally to the subject a composition containing an extract of decaffeinated coffee beans that stimulates a sebaceous function of the skin.

According to a third embodiment of the invention, there is provided a method for stimulating a sebaceous function of skin of a subject, said method
comprising the step of administering orally to the subject a composition containing an extract of decaffeinated coffee beans.

According to a fourth embodiment of the invention, there is provided use of a decaffeinated coffee bean extract in the preparation of an orally administrable composition for stimulating a sebaceous function of skin by oral administration.

The characteristics of the invention mentioned above as well as others will become more clearly apparent in the light of the Examples presented hereafter.

EXAMPLES

Example 1: Preparation of a roasted extract of Coffea robusta

0.5 kg of roasted coffee beans is reduced to a powder by grinding with the Turrax apparatus at 24000 rev/min for 1 minute at 4°C (ice bath).

The powder obtained is mixed with 5 litres of 0.05M phosphate buffer at pH 8.5. The entire mixture is stirred for 30 minutes at 4°C, then centrifuged at
10000 G at 4°C. The supernatant is filtered through a 0.22 µm filter (sterilizing filtration).

The extract is then fractionated by ultrafiltration through a Sartorius type membrane in order to remove from it oxidation phenomena.

The extract is then lyophilized. 29.5 grams of active extract called "lyophilized extract" are thus obtained.

Caffeine is then removed by supercritical chromatography (CO₂ is used as carrier gas). 25.5 grams of active extract called "decaffeinated lyophilized extract" are thus obtained.

Example 2: Examples of formulations illustrating the invention and in particular the compositions according to the invention.

These compositions were obtained by the simple mixing of the different constituents.

Composition 1: Soft capsules

Excipients:

Soya oil........................................................................40 mg
Wheat germ oil ........................................................85 mg
Soya lecithins ............................................................25 mg

Vitamins:

Natural tocopherols ..................................................3 mg
Vitamin C palmitate ..................................................150 mg

Constituents:

Decaffeinated lyophilized extract of Coffea robusta ......15 mg
Borage oil ....................................................................200 mg
Blackcurrant pip oil ..................................................150 mg
Composition 2: Soft capsules

Excipients:
- Soya oil .................................................. 40 mg
- Wheat germ oil ........................................ 85 mg
- Soya lecithins ........................................... 25 mg

Vitamins:
- Natural tocopherols .................................. 3 mg

Constituents:
- Decaffeinated lyophilized extract of Coffea robusta .... 150 mg
- Borage oil ............................................... 200 mg
- Evening primrose oil .................................. 200 mg

Composition 3: Soft capsules

Excipients:
- Soya oil .................................................. 40 mg
- Wheat germ oil ........................................ 85 mg
- Soya lecithins ........................................... 25 mg

Vitamins:
- Natural tocopherols .................................. 3 mg

Constituents:
- Decaffeinated lyophilized extract of Coffea robusta .... 50 mg
- Borage oil ............................................... 200 mg
- Evening primrose oil .................................. 200 mg
- Lyophilized Lactobacillus ............................. 200 mg

Composition 4: Soft capsules

Excipients:
- Soya oil .................................................. 40 mg
- Wheat germ oil ........................................ 5 mg
Soya lecithins ........................................... 25 mg

Vitamins:

Natural tocopherols ..................................... 3 mg

Constituents:

5  Decaffeinated lyophilized extract of *Coffea robusta* ..... 150 mg
   Borage oil .............................................. 200 mg
   Evening primrose oil ................................. 200 mg
   Vitamin C ............................................... 50 mg
   Calcium glucanate .................................... 200 mg

10  Magnesium stearate .................................. 400 mg
   Lyophilized *Lactobacillus* sp. ...................... 300 mg

"Comprising" and like words

The term "comprise" and variants of the term such as "comprises" or "comprising" are used herein to denote the inclusion of a stated integer or stated integers but not to exclude any other integer or any other integers, unless in the context or usage an exclusive interpretation of the term is required.
The claims defining the invention are as follows:

1. A composition when used for stimulating a sebaceous function of skin, said composition containing an extract of decaffeinated coffee beans and being formulated for oral administration.

2. The composition according to Claim 1, wherein the extract is derived from coffee beans selected from the species *Coffea arabica*, *Coffea robusta*, *Coffea canephora* or *Coffea iberica*.

3. The composition according to Claim 1 or Claim 2, wherein said extract is derived from roasted coffee beans.

4. The composition according to any one of Claims 1 to 3, wherein said extract is obtained by an aqueous-alcoholic or alcoholic extraction.

5. The composition according to any one of Claims 1 to 4, wherein said composition is in solid form and comprises at least one adjuvant suitable for oral administration.

6. The composition according to any one of Claims 1 to 5, wherein said extract represents from 0.1% to 80% of the total weight of the composition.

7. The composition according to any one of Claims 1 to 6, wherein said extract represents from 1% to 50% of the total weight of the composition.

8. The composition according to any one of the preceding Claims, wherein chlorogenic acid comprises less than or equal to 0.1% by weight of the composition.

9. A method for treating and/or preventing dry skin or for treating and/or preventing skin ageing of a subject, said method comprising the step of administering orally to the subject a composition containing an extract of decaffeinated coffee beans that stimulates a sebaceous function of the skin.

10. The method according to Claim 9, wherein the dry skin of the subject is characterised by any one of the following:
a concentration of sebum lower than 100 μg/cm² in a forehead area of the subject;
inadequate secretion and excretion of sebum;
desquamation deficiency;
dull complexion;
an atonic skin texture; and
dermatitis.

11 A method for stimulating a sebaceous function of skin of a subject, said method comprising the step of administering orally to the subject a composition containing an extract of decaffeinated coffee beans.

12 The method according to any one of Claims 9 to 11, wherein the extract is derived from coffee beans selected from the species Coffea arabica, Coffea robusta, Coffea canephora or Coffea iberica.

13 The method according to any one of Claims 9 to 12, wherein said extract is derived from roasted coffee beans.

14 The method according to any one of Claims 9 to 12, wherein said extract is obtained by an aqueous-alcoholic or alcoholic extraction.

15 The method according to any one of Claims 9 to 14, wherein said composition is in solid form and comprises at least one adjuvant suitable for oral administration.

16 The method according to any one of Claims 9 to 15, wherein said extract represents from 0.1% to 80% of the total weight of the composition.

17 The method according to any one of Claims 9 to 16, wherein said extract represents from 1% to 50% of the total weight of the composition.

18 The method according to any one of Claims 9 to 17, wherein chlorogenic acid comprises less than or equal to 0.1% by weight of the composition.
19 The method according to any one of Claims 9 to 18 further comprising a preliminary step of identifying a subject having skin requiring such treatment or prevention.

20 Use of a decaffeinated coffee bean extract in the preparation of an orally administrable composition for stimulating a sebaceous function of skin by oral administration.

21 The composition as defined in Claim 1 and substantially as hereinbefore described in the accompanying Examples.

22 The method as defined in Claim 9 or Claim 11, said composition being substantially as hereinbefore described in the accompanying Examples.

Date: 26 March 2008