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(54) Title: A TOPICAL COMPOSITION FOR HAIR GROWTH

(57) Abstract: The invention relates to a topical composition for hair growth comprising synergistic combination of extracts of plant source. The composition not only retains hair bulb in the anagen state for a longer period of time but also ensures longer length of hair. This is achieved through a composition which comprises a gallic acid ester and an extract of *Glycyrrhiza glabra* or *Sesamum indicum* which is applied on the hair or scalp for the desired benefits.



A TOPICAL COMPOSITION FOR HAIR GROWTH

Technical Field

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The invention relates to a topical composition for hair growth comprising synergistic combination of materials including extracts of plant source.

10 **Background of the Invention**

Hairs are filamentous, keratinized structures consisting of a shaft and a root. The shaft is composed of specialized keratinocytes. The root lies within the hair follicle and comprises the germinative matrix and the keratogenous zone.

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There has been continuous effort to find a safe, reliable method of minimizing hair loss or increasing hair growth and thus reducing baldness to various degrees.

Though hair loss is not a disease, it bothers the persons concerned psychologically and seriously affects the individual's self-esteem. The cause for

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the problem of hair loss is not always the same in all. There are several factors that influence the process by which hair grows and there are many contributory factors that can alter the normal vigorous growth of hair. The hair growth cycle is divided into three phases: an anagen phase, in which the hair is growing actively, with a very substantial level of cell proliferation occurring in the hair follicle; a

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catagen phase, when the follicle slows down its proliferative activity temporarily to permit hair development; and a telogen phase, in which the follicle simply stops growing and regresses, until the hair is shed, and a new anagen phase begins. It is natural to lose some hair on a daily basis as this is a part of the hair renewal process. This cycling process of hair growth continues throughout the life of an

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individual.

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But when this loss becomes excessive it becomes a problem which people try to solve by the use of cosmetic formulations. As appearance and looks are an important aspect in society, hair loss is considered a major problem. Millions of people worldwide suffer from hair loss and are keen to find a solution to treat such hair loss. Different hair growth products and treatments have been developed to solve such a problem but the problem still persists. Compositions comprising extract of plant source are also known.

The present inventors have been working on providing improved hair growth by tackling the problem from two angles – agents that promote health of hair bulb while at the same time increasing the rate of hair bulb growth. They have found that certain synergistic combinations for topical application provide both of these benefits thus ensuring hair that grows long and is healthy.

WO 07/084614A discloses a hair treatment composition for topical application to the skin and/or hair, comprising partially hydrolyzed fucoidan and a pharmaceutical carrier and optionally may also include flavonoids, analgesics, radiation protecting agents, and/or anti-oxidants.

IN248853 discloses a composition for minimizing hair loss comprising 0.001-10% by weight gallic acid or an alkyl ester of gallic acid or a mixture thereof.

The above publications do not disclose the specific combination claimed in the present invention nor provide the enhanced synergistic benefit claimed.

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It is thus an object of the present invention to obviate the drawbacks of the prior art and provide a topical composition with enhanced hair growth properties.

It is another object of the present invention to provide a topical composition with enhanced hair growth properties that are achieved with combination of materials that are available in nature thereby being mild and safe for use on scalp and hair.

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Summary of the Invention

The invention relates to a topical composition for hair growth comprising:

- 5 a. 0.01 to 10% of a gallic acid ester selected from methyl, ethyl or propyl gallate;
- b. 0.01 to 10 % of an extract of *Glycyrrhiza glabra* or *Sesamum indicum*; and
- 10 c. a topically acceptable base.

Detailed Description of the Invention

15 These and other aspects, features and advantages will become apparent to those of ordinary skill in the art from a reading of the following detailed description and the appended claims. For the avoidance of doubt, any feature of one aspect of the present invention may be utilized in any other aspect of the invention. The word “comprising” is intended to mean “including” but not necessarily “consisting of” or

20 “composed of.” In other words, the listed steps or options need not be exhaustive. It is noted that the examples given in the description below are intended to clarify the invention and are not intended to limit the invention to those examples per se. Similarly, all percentages are weight/weight percentages unless otherwise indicated. Except in the operating and comparative examples, or where otherwise

25 explicitly indicated, all numbers in this description and claims indicating amounts of material or conditions of reaction, physical properties of materials and/or use are to be understood as modified by the word “about”. Numerical ranges expressed in the format "from x to y" are understood to include x and y. When for a specific feature multiple preferred ranges are described in the format "from x to

30 y", it is understood that all ranges combining the different endpoints are also contemplated.

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By "A topical composition for hair growth" as used herein, is meant to include a composition for topical application to hair or scalp of mammals, especially humans. By topical is meant that the composition is applied to the external surface of the body. In the present invention this is achieved by applying the
5 composition on the hair or scalp. Compositions for achieving the desired benefits by way of ingestion into the human body are excluded from the scope of the present invention. Such a composition may be generally classified as leave-on or rinse off, and includes any product applied to a human body for also improving the appearance, cleansing, odor control or general aesthetics of scalp and hair. The
10 composition of the present invention can be in the form of a liquid, lotion, cream, foam, scrub, gel, shampoo, conditioner, shower gel or bar. The composition of the present invention is preferably a leave-on composition.

Gallic acid and its esters:

15 For minimizing hair loss alkyl ester is selected from methyl, ethyl or propyl ester or a mixture thereof. It is particularly preferred that the ester is methyl gallate. The source of methyl gallate is preferably an extract from *Acacia nilotica*, *Mangifera indica*, *Anachardium oxydentale*. Alternately it may be chemically synthesized from gallo tannins using reported procedures.

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The source of gallic acid or its esters is synthetic or any gallic acid rich plant source. The source of gallic acid is preferably gall nuts, *Terminalia* species for e.g. *chebula*, *bellerica*, *arjuna* etc, tea, *Embelica officinalis*, *Mucuna pruriens* and other gallic acid rich sources.

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Sesamum indicum is also known as *Sesamum orientale*. The common name is sesame. It is an erect, branched plant that grows to a height of about 60-180 cm. It is an annual plant. It is cultivated throughout the plains of India and also in the hills up to an altitude of about 1200 metres. It is also grown in other countries
30 having climatic conditions like the tropical plains of India mostly as a source of oil seed. It is also used as a spice for seasonings. Sesame is known as Tila, Till, Til,

or Gingelli in different regions of India. There are many varieties of sesame grown in India. The varieties are based on the colour of the seed coat which ranges from white to black. There are many intermediate varieties as well. However, the black and white Sesame are two varieties largely cultivated in India.

- 5 Of these two varieties, the white sesame is more preferred for use in the present invention. The extract of the second active is preferably present in 0.01 to 2% by weight of the composition, conveniently 0.1 to 1.0 % by weight of the composition. The extract of *Sesamum indicum* preferably comprises sesamin, sesamolin, sesamol and sesaminol.

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Glycyrrhiza glabra is perennial herb or under shrub attaining a height up to six feet. It is commonly called as licorice, liquorice or mulethi or sweet wood. It is cultivated in India, Spain, Iran, Russia, China, Italy and Persia. In India it is cultivated in Punjab and Sub Himalayan tracts. The root crown gives out a number

15 of long woody stems which bear compound pinnate leaves. Liquorice is known as Jeshtamadha, Jatimadhu, Atimaduram, Atimadhuranu, or Yashtimadhukam in different parts of India. Root and rhizomes are the parts commonly used. The major bio-active constituent of rhizomes are triterpenoids saponin, glycyrrhizin, glycyrrhizinic acid, glabrin A&B, glycyrrhetol, glabrolide, isoglabrolide, isoflavones,

20 coumarins and triterpene sterols.

The extract of *Glycyrrhiza glabra*, for use in the present invention, preferably comprises higher than 10% of glycyrrhizinic acid.

- 25 The extract of *Glycyrrhiza glabra* or *Sesamum indicum* for use in the composition of the invention preferably an aqueous extract.

The composition of the invention comprises a topically acceptable base. The topically acceptable bases are such as to have a product in preferably a lotion,

30 emulsion, gel, or cream form. The topically acceptable base preferably comprises water. The composition is preferably a gel or a cream.

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The composition according to the invention may also comprise other diluents. The diluents act as a dispersant or carrier for other materials present in the composition, so as to facilitate their distribution when the composition is applied to the skin. Diluents other than water can include liquid or solid emollients, solvents, humectants, thickeners and powders.

The compositions of the present invention can comprise a wide range of other optional components. The CTFA Cosmetic Ingredient Handbook, Second Edition, 1992, which is incorporated by reference herein in its entirety, describes a wide variety of non-limiting cosmetic and pharmaceutical ingredients commonly used in the skin, scalp and hair care industry, which are suitable for use in the compositions of the present invention. Examples include: antioxidants, binders, biological additives, buffering agents, colorants, thickeners, polymers, astringents, fragrance, humectants, opacifying agents, conditioners, exfoliating agents, pH adjusters, preservatives, natural extracts, essential oils, skin sensates, skin soothing agents, and skin healing agents.

The invention will now be illustrated with the help of the following non-limiting examples which are by way of demonstration of the invention only and do not limit the scope of the claims.

The extracts of *Glycyrrhiza glabra* and *Sesamum indicum* in the following examples were obtained from the supplier Phyto Concentrates who have prepared the extract from plant grown in India.

EXAMPLES

In vitro hair bulb culture:

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Anagen hair follicles were isolated from scalp biopsies of volunteers undergoing hair transplant operations. Isolated follicles were maintained in William's E Media (Sigma # W 4128) in the absence or presence of various actives. The movement of hair bulbs from anagen (growth phase) to catagen phase (phase of hair fall) was monitored by daily photography and measurement of the size of the hair bulb.

10

Preparation of actives:

Methyl gallate (MG) was purchased from Sigma and aqueous extracts of all herb samples were purchased from Phyto Concentrates. These were prepared in water as 1% solution and stored at -20°C. Further dilutions of MG and herbs and their combinations were prepared in the media just before addition to the hair follicle culture. The actives were added fresh every time the media was changed (every alternate day) and the growth was followed for a period of 4 days. Morphology of hair bulb and change in length was recorded for every time point (Day 0, Day 2 and Day 4). Each experiment was conducted at least with 6-8 hair follicles per group and the results are averages of 3-5 experiments per active.

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Various herbs were tested of which *Sesamum indicum* (*S.indicum*) and *Glycyrrhiza glabra* (*G.glabra*) in combination with methyl gallate showed both growth and bulb retention in the invitro hair follicle. The methyl gallate was tested at concentrations of 10 and 50 ppm and the herb extracts were tested at at concentrations of 125, 250 and 500 ppm.

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The summary of the data on % hair growth and % bulbs retained in anagen phase is summarised in Table 1.

5 **Table 1**

		G. Glabra		S. Indicum	
		Growth (% of control)	Intact bulbs (%)	Growth (% of control)	Intact bulbs (%)
Control		100	10	100	10
Herb (ppm)	125	146	0	68	6
	250	128	0	99	6
	500	116	0	82	0
Methyl gallate (ppm) + herb (ppm)	10 + 0	46	43	46	43
	50 + 0	42	59	42	59
	10 + 125	88	42	47	50
	10 + 250	121	42	48	54
	10 + 500	64	38	48	50
	50 + 125	49	56	32	69
	50 + 250	84	44	44	75
	50 + 500	54	44	34	83

10 It is essential that there is need to maximize growth of hair as well as maximize retention of hair bulbs in the anagen phase. The data in Table 1 above indicates that while herb extract causes hair growth it does not cause retention of hair bulbs in anagen phase while methyl gallate does both albeit at low levels. The data in the above table especially the highlighted and underlined data indicate that it is possible to improve retention of intact bulbs while maintaining good hair growth by 15 a judicious combination of herb extracts chosen from *G. glabra* and *S.indicum*. Such improvement in both these properties is not observed when extracts of other herbs are used.

20 It is to be appreciated that the concentration of the herb and the gallic acid ester in the above experiments correspond to in-vitro hair bulb conditions. The actual amount of these actives to be included in a composition for hair growth has to be

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- orders of magnitude higher, to account for various factors including loss of active due to possible stability issues in the composition over storage and use, efficiency of spreading of the composition on the hair/ scalp, availability of the active from the bulk of the composition to the desired surface, diffusion of the active from the
- 5 desired surface to the active site where the biochemical reaction occurs among various other known and unknown factors. Thus from experience, the inventors are aware that use of ppm levels of active in an in-vitro assay generally requires percentage levels of incorporation of the actives in a composition.
- 10 The invention thus provides for a composition for hair growth comprising a judicious combination of natural materials.

CLAIMS

1. A topical composition for hair growth comprising:
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- a. 0.01 to 10% of a gallic acid ester selected from methyl, ethyl or propyl gallate;
- b. 0.01 to 10 % of an extract of *Glycyrrhiza glabra* or *Sesamum indicum*;
- 10 and
- c. a topically acceptable base.
2. A composition as claimed in claim 1 wherein said gallic acid ester is methyl gallate.
- 15
3. A composition as claimed in claim 1 or 2 wherein the gallic acid ester is extracted from a plant source selected from *Acacia nilotica*, *mangifera indica* or *anachardium oxydentale*.
- 20
4. A composition as claimed in any one of the preceding claims wherein the extract of *Glycyrrhiza glabra* or *Sesamum indicum* is an aqueous extract.
5. A composition as claimed in claim 4 wherein the extract of *Glycyrrhiza glabra* comprises higher than 10% of glycyrrhizinic acid.
- 25
6. A composition as claimed in claim 4 wherein the extract of *Sesamum indicum* comprises sesamin, sesamol, sesamol and sesaminol.
- 30
7. A composition as claimed in any one of the preceding claims wherein the topically acceptable base comprises water.

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8. A composition as claimed in claim 7 wherein said topically acceptable base is a gel or a cream.
9. A process for growing hair comprising applying to the hair or scalp a
5 composition as claimed in any one of the preceding claims for at least 10 minutes.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/056410

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61Q7/00 A61K8/34 A61K8/97 A61K36/484 A61K36/53
 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, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Week 201034 Thomson Scientific, London, GB; AN 2010-F21050 XP002713622, & CN 101 700 312 A (WANG X) 5 May 2010 (2010-05-05) abstract ----- -/--	1-9

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

<p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p>	<p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>
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Date of the actual completion of the international search 22 April 2014	Date of mailing of the international search report 30/04/2014
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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 Grillenberger, Sonja
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/056410

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	NISHIOKA T ET AL: "Baicalein, an alpha-glucosidase inhibitor from Scutellaria baicalensis", JOURNAL OF NATURAL PRODUCTS, AMERICAN CHEMICAL SOCIETY, US, vol. 61, no. 11, 1 January 1998 (1998-01-01), pages 1413-1415, XP003011527, ISSN: 0163-3864, DOI: 10.1021/NP980163P page 1413, left-hand column	1-9
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Y	DATABASE CAPLUS [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 6 August 2008 (2008-08-06), Hindustan Unilever Ltd., India: "Topical compositions for minimizing hair loss", XP002713623, Database accession no. 2008:930889 abstract	1-9
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/056410

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LIU: "Sesamin is one of the major precursors of mammalian lignans in sesame seed (<i>Sesamum indicum</i>) as observed in vitro and in rats", THE JOURNAL OF NUTRITION, vol. 136, no. 4, 1 January 2006 (2006-01-01), page 906, XP055080424, ISSN: 0022-3166 the whole document</p> <p style="text-align: center;">-----</p>	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/056410

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