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(56) Documents Cited:
EP 1230911 A **WO 2007/041548 A**
WO 2005/099657 A **FR 002906722 A**
US 6183758 A **US 20070092461 A**
US 20050266064 A

(58) Field of Search:
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(54) Title of the Invention: **Cosmetic formulation**
Abstract Title: **Topical cosmetic formulation comprising MSM, a vitamin and a carbohydrate**

(57) A topical cosmetic formulation comprising methylsulfonylmethane, a vitamin selected from vitamin A, vitamin E and vitamin B3, a carbohydrate selected froth biolin, sodium hyaluronate, ribose and Fucogel^{RTM}, and a cosmetically-acceptable excipient. Preferred formulations further comprise a proteinaceous compound such as ozone stressed yeast lysate; zinc-glycine complex; or cytokine mimetic milk peptide and optionally a Beauty Active such as Swiss Apple cells; Immortelle Bleue Extract; Galactoarabinan; Arnica; Laminaria; or Butterbur. Further embodiments include methods of enhancing the appearance of skin by oral administration of methylsulfonylmethane concurrently with the use of such a topical formulation.

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COSMETIC FORMULATION

Field of the Invention

The invention relates to cosmetic formulations and methods for enhancing the appearance of human skin.

Background

Healthy-looking skin has been a goal of many societies, for hundreds of years. Over that time, both men and women have sought beauty treatments to enhance the appearance of their skin. Typical goals of beauty treatments include the reduction of the appearance of lines and wrinkles, and the achievement of an even skin tone and a smooth skin texture.

Many formulations to assist in achieving these goals have been proposed over the years. It is amongst the objects of the present invention to provide a new class of skin-care formulations and methods to assist in these goals.

Summary of the Invention

The inventors have found that by combining a two-fold approach to skin care, improved appearance of the skin may be achieved. The first element of the approach is directed

towards maintaining an optimum nutrition of the skin, through the provision of "Nutritional Actives". Whilst poor nutrition can lead to disease states affecting the skin, the nutritional approaches described herein are not directed at preventing, curing or treating disease states, but solely with providing skin cells with the a balance of nutrients designed to enable them to perform well in the production and maintenance of healthy-looking skin; i.e. the invention relates to cosmetic formulations and methods rather than medical methods or formulations.

Having provided the nutrients required by skin cells, the second element of the approach is directed to the provision of "Beauty Actives" - a class of components that act to enhance the appearance of the skin. The combination of these two approaches within the same formulation, or treatment regime, acts synergistically to improve the overall appearance of the skin.

Accordingly, the invention provides a topical cosmetic formulation comprising: methylsulfonylmethane; a vitamin, selected from the group comprising: Vitamin A; Vitamin E; and Vitamin B3; and a carbohydrate selected from the group comprising: Biolin; Sodium hyaluronate; Ribose; and Fucogel; and a cosmetically-acceptable excipient.

Methylsulfonylmethane (MSM), a Nutritional Active, is an organosulfur compound of formula $(CH_3)_2SO_2$ (CAS Number 67-71-0, IUPAC name dimethylsulfone). MSM is a highly bioavailable form of sulfur, easily taken into cells, and that intervenes at all levels of cell activity, supporting the dermal matrix. The inventor has found that MSM has benefits for the appearance of the skin when applied topically, and also when taken orally, and especially so when taken in oral and topical combination. This aspect of a combined oral and topical approach will be discussed further below. Preferred topical formulations would contain at least 0.1% (w/w) methylsulfonylmethane, preferably more than 1%(w/w), more preferably more than 2%(w/w) and most preferably approximately 4%(w/w).

Biolin is a mixture of gluco-oligosaccharide and inulin. The gluco-oligosaccharide (an alpha glucan oligosaccharide) may be obtained by enzymatic synthesis from sugars, using a glycosyltransferase. A method of its manufacture is described in US Patent 5,518,733 and references therein. The gluco-oligosaccharide is also available commercially from the manufacturer BioEurope Solabia, France. Inulin, a naturally-occurring plant polysaccharide (CAS 9005-80-5), may be extracted from the root of chicory (*Cichorium intybus*), and is available commercially. Biolin contains at least 60% Inulin and 5-20% of alpha glucan oligosaccharide. Biolin (one of the Nutritional Actives) acts as a cosmetic prebiotic, favouring the growth of beneficial skin flora (such as *Staphylococcus capitis, Corynebacterium xerosis, Micrococcus kristinae, M. lylae, M. sedentarius, Lactobacillus pentosus, L. gasseri, L. salivarius and L. acidophilus*) whilst disadvantaging the growth of more harmful organisms (such as *Candida albicans, Staphylococcus aureus, S. epidermis, Corynebacterium minutissium, Propionibacterium acnes, P. granulosum, Salmonella typhimurium, Escherichia coli and Malassezia furfur).*

Fucogel, another Nutritional Active, is a 1% aqueous solution of a biosaccharide gum (CAS number 194237-89-3) having an average molecular weight of *ca.* 10^6Da and having the form of a repeating sequence of 1-3 linked L-fucose, D-galactose and galacturonic acid sugars. Carbon 4 of the galacuronic acid may be partly acetylated. Fucogel may be produced from fermentation of raw materials such as plant sorbitol and plant peptone. Its structure is described in Guetta, O. *et al*, Biomacromolecules, 2003, 4 (5), pp 1362–1371., and it is available commercially from Solabia, France.

Fucogel and Hyaluronic acid both have the property of increasing moisture retention by the skin. Ribose is a key precursor in the cellular production of the energy-transport molecule ATP (adenosine triphosphate), and has been shown in commercial trials to have a positive effect on the reduction of wrinkles in skin when applied topically.

In preferred embodiments, the composition further comprises a proteinaceous compound selected from the group comprising: ozone stressed yeast lysate; zinc-glycine complex; and cytokine mimetic milk peptide. These components act to stimulate skin cell respiration, promote wound healing and act as anti-oxidants to protect cellular DNA,

RNA and skin lipids after sun exposure. Preferred topical formulations would contain a total peptide concentration of at least 0.05% (w/w), preferably more than 0.1%(w/w), more preferably more than 0.25%(w/w) and most preferably approximately 0.5%(w/w).

Ozone stressed lysate is described in US Patent Application 11/248522 and in International Patent Application WO2006/044482 and is also available commercially from Arch Personal Care Products, USA.

Zinc glycine complex comprises $Zn(Gly)_2$ and is also an inducer of metallothionein. Its action is described in Matsaki, H. *et al,* J. Dermatological Science, 45(1), 73-75, 2007, *"A Zinc (II)-Glycine complex is an effective inducer of metallothionein and removes oxidative stress"*. Zinc glycine complex is available commercially from Nikkol Group, Japan. As well as providing a proteinaceous component, the use of a zinc-lysine complex also provides a source of the mineral zinc.

Cytokine mimetic milk peptides are available is available commercially as "Milk Peptide Complex" from CLR - Chemisches Laboratorium Dr Kurt Richter GmbH. Alternatively, whey protein may be substituted. The milk peptides act as a collagen booster by stimulating the synthesis of Collagen Type I.

In further preferred embodiments, the composition further comprises a lipid selected from the group comprising phytosterols and essential fatty acids. The addition of lipids assists the reconstitution of the lipid matrix of the epidermis, and in particular, phytosterols boost skin lipid content and assist with moisture retention. These actions lead to increased softness and elasticity in the skin, and serve to replenish dry and dehydrated skin.

Essential fatty acids (i.e. those fatty acids incapable of being synthesized by the human body) are known in themselves, and are sometimes referred to by the term "Vitamin F". For these cosmetic formulations, the essential fatty acids are best provided by components such as Rosehip seed oil and Kukui oil (from the nut *Aleurites moluccana*). Both Rosehip seed oil and Kukui oil are, e.g. rich in both linoleic and linolenic acids. Preferred topical

formulations would contain at least 0.2% (w/w) of essential fatty acid-containing oils, preferably more than 0.5%(w/w), more preferably more than 1%(w/w) and most preferably approximately 2%(w/w).

Phytosterols are steroid alcohols of plant origin. For these cosmetic formulations, they are preferably provided by components such as Shea butter, sweet almond oil, rice germ oil and sesame seed oil. All of these oils have a relatively high phytosterol content. Preferred topical formulations would contain at least 1% (w/w) of phytosterol-containing oils, preferably more than 2%(w/w), more preferably more than 5%(w/w) and most preferably approximately 10%(w/w).

In especially preferred embodiments, the composition further comprises a beauty active selected from the group comprising: Swiss Apple cells; Immortelle Bleue Extract; Galactoarabinan; Arnica extract; Laminaria; and Butterbur. These actives all have the properties of protecting skin cells against oxidative stress and DNA damage from e.g. UV or free radical attack.

Methods for preparing Swiss Apple cell extracts are described in US Patent Application US2008/0299092, and are also available commercially from Mibelle under the trade mark PhytoCellTec Malus domestica.

Immortelle Bleue extract is an extract from the leaf, stems or flowers of the plant Statice, *Limonium narbonense* and is available from Codif Recherche & Nature, France.
Arnica extract is an aqueous extract from the flowers of the plant *Arnica Montana.* Whilst the precise active ingredients of the extract are not fully understood, it is believed that some of the useful constituents include sesquiterpene lactones, flavonoids and polysaccharides. Arnica extract is widely available, e.g. from Arch Personal Care Products (USA) under the trade mark NAB Arnica Extract.

A suitable galactoarabinan is available under the registered trade mark LaraCare A200, available from Larex Inc, White Bear Lake, USA.

Butterbur Extract is an extract from plants of the genus *Petasites* and are described in Thomet, O.A.R. *et al*, "*Role of petasin in the potential anti-inflammatory activity of a plant extract of Petasites hybridus*", Biochemical Pharmacology, 61(8), 15 April 2001, 1041-1047. A suitable extract is also available commercially from Arch Personal Care Products (USA) under the trade mark NAB Butterbur Extract.

Also included within the scope of the invention is a topical cosmetic formulation substantially as described herein.

Also included within the scope of the invention is a method for cosmetic enhancement of human skin comprising the administration of an oral dose of methylsulfonylmethane and concurrent topical application of a cosmetic formulation described above.

Also included within the scope of the invention is a method for cosmetic enhancement of human skin substantially as described herein.

Also included within the scope of the invention is a cosmetic treatment kit for performing the method of either claim 5 or 6 comprising an oral formulation of methylsulfonylmethane and a topical cosmetic formulation as described or claimed herein.

The inventor has found that co-administration of an oral dose of methylsulfonylmethane in combination with the topical preparations described herein produce a surprisingly increase effect on enhancing the appearance of the skin.

Description of Preferred Embodiments

The inventors have found that the following compositions to be particularly effective:

Example 1: Day Cream

Component	**Preferred Concentration (w/v)**	**Minimum Concentration (w/v)**	**Maximum Concentration (w/v)**
Methylsulfonylmethane	4%	0.1%	8%
Milk Peptides	0.5%	0.05%	5%
O_3-Stressed Yeast lysate	0.3%	0.1%	3%
Sodium hyaluronate	0.1%	0.02%	1%
Prebiotic Oligosaccharide (Biolin)	0.5%	0.05%	5%
Lipid supplement (phytosterols such as Shea butter, Jojoba oil, Sesame Oil and Rice Germ Oil)	Total of 8%	Total of 2%	Total of 15%
Essential Fatty Acids (as Rosehip seed oil, Kukui seed oil)	Total of 2%	Total of 0.2%	Total of 8%
Immortelle Bleue Extract	0.5%	0.01%	5%
Swiss Apple Cell Culture	0.3%	0.05%	3%

These components are formulated with appropriate cosmetically acceptable excipients such as water, glycerine, other oils and gums, and may further include fragrance and pH regulators as required.

Example 2: Eye Gel

Component	**Preferred Concentration (w/v)**	**Minimum Concentration (w/v)**	**Maximum Concentration (w/v)**
Methylsulfonylmethane	4%	0.1%	8%
Zinc-Glycine Complex	0.5%	0.05%	2%
Milk Peptides	0.5%	0.05%	5%
O_3-Stressed Yeast lysate	0.3%	0.1%	3%
Vitamin E (as tocopherol)	0.1%	0.01%	0.5%
Vitamin B3 (as niacinamide)	1%	0.1%	5%
Sodium hyaluronate (Proturon)	0.8%	0.1%	5%
Biosaccharide gum (Fucogel)	3%	0.5%	8%
Immortelle Bleue Extract	0.5%	0.01%	5%
Swiss Apple Cell Culture	0.3%	0.05%	3%
Galactoarabinan	0.3%	0.5%	3%
Arnica and Laminaria Extract	Total of 3%	Total of 0.5%	Total of 10%

These components are formulated with appropriate cosmetically acceptable excipients such as water, glycerine, other oils and gums, and may further include fragrance and pH regulators as required.

Example 3: Serum

Component	**Preferred Concentration (w/v)**	**Minimum Concentration (w/v)**	**Maximum Concentration (w/v)**
Methylsulfonylmethane	4%	0.1%	8%
Zinc-Glycine Complex	0.5%	0.05%	2%
Milk Peptides	0.5%	0.05%	5%
O_3-Stressed Yeast lysate	2%	0.1%	5%
Vitamin E (as tocopherol)	0.1%	0.01%	0.5%
Ribose	0.5%	0.1%	2.5%
Biolin	0.5%	0.05%	3%
Sodium hyaluronate (Proturon)	0.8%	0.1%	5%
Biosaccharide gum (Fucogel)	1%	0.1%	8%
Immortelle Bleue Extract	2%	0.2%	10%
Butterbur extract	1%	0.1%	8%
Swiss Apple Cell Culture	0.3%	0.05%	3%
Galactoarabinan	0.3%	0.5%	3%

These components are formulated with appropriate cosmetically acceptable excipients such as water, glycerine, other oils and gums, and may further include fragrance and pH regulators as required.

Example 4: Night Cream

Component	**Preferred Concentration (w/v)**	**Minimum Concentration (w/v)**	**Maximum Concentration (w/v)**
Methylsulfonylmethane	4%	0.1%	8%
Milk Peptides	0.5%	0.05%	5%
Vitamin A (as Rosehip seed oil)	1%	0.1%	5%
Vitamin B3 (as niacinamide)	1%	0.1%	5%
Vitamin E (as tocopherol)	0.1%	0.01%	0.5%
Sodium hyaluronate (Proturon)	0.1%	0.05%	1%
Lipid supplement (phytosterols such as Shea butter, Jojoba oil, Sesame Oil and Rice Germ Oil)	Total of 10%	Total of 2%	Total of 20%
Essential Fatty Acids (as Rosehip seed oil, Kukui seed oil)	Total of 2%	Total of 0.2%	Total of 8%
Swiss Apple Cell Culture	0.3%	0.05%	3%

Again, these components are formulated with appropriate cosmetically acceptable excipients such as water, glycerine, other oils and gums, and may further include fragrance and pH regulators as required.

Example 5: Combination oral and topical treatment

A preferred combination oral and topical treatment for the improvement of skin appearance is one oral dose per day of 1000mg Methylsulfonylmethane (e.g. as a tablet) and daily topical administration of a cosmetic formulation as described herein. Oral doses of between 250mg and 2000mg of Methylsulfonylmethane may also be employed. Typically, such an oral dose would be taken daily for a period of at least 45 days and used with a combination of formulations described herein, such as a day cream and a night cream.

CLAIMS

1. A topical cosmetic formulation comprising:

methylsulfonylmethane;

a vitamin, selected from the group comprising:

Vitamin A;

Vitamin E; and

Vitamin B3; and

a carbohydrate selected from the group comprising:

Biolin;

Sodium hyaluronate;

Ribose; and

Fucogel; and

a cosmetically-acceptable excipient.

2. A formulation according to claim 1 further comprising a proteinaceous compound selected from the group comprising:

ozone stressed yeast lysate;

zinc-glycine complex; and

cytokine mimetic milk peptide.

3. A formulation according to either Claim 1 or Claim 2 further comprising a lipid selected from the group comprising:

phytosterols; and

essential fatty acids.

4. A formulation according to any preceding claim further comprising a beauty active selected from the group comprising:

Swiss Apple cells;

Immortelle Bleue Extract;

Galactoarabinan;

Arnica;

Laminaria; and

Butterbur.

5. A topical cosmetic formulation substantially as described herein.

6. A method for cosmetic enhancement of human skin comprising the administration of an oral dose of methylsulfonylmethane and concurrent topical application of a cosmetic formulation according to any of claims 1 to 5.

7. A method for cosmetic enhancement of human skin substantially as described herein.

8. A cosmetic treatment kit for performing the method of either claim 6 or 7 comprising an oral formulation of methylsulfonylmethane and a topical cosmetic formulation according to any of claims 1 to 5.

Application No: GB0912239.1 **Examiner:** Dr Rowena Dinham

Claims searched: 1-8 **Date of search:** 27 October 2009

Patents Act 1977: Search Report under Section 17

Documents considered to be relevant:

Category	Relevant to claims	Identity of document and passage or figure of particular relevance
X	1-5 & 7	US 2005/0266064 A (McCARTHY) See especially para [0050] and Example compositions 1, 2, 3 and 19
Y	1-5 & 7	US 2007/0092461 A (GUPTA) See especially para [0050], para [0057], para [0070], para [0106] and Example 15
Y	1-5 & 7	EP 1230911 A (VAN GENY NAT PROD) See especially para [0011]-[0013] and Example 1
Y	1-5 & 7	US 6183758 A (SCOTT) See especially Example
Y	1-5 & 7	WO 2007/041548 A (PROCTER & GAMBLE) See especially page 2 line 9-30 and Claim 1
Y	1-5 & 7	FR 2906722 A (SEPHAR) See especially Examples
A	6 & 8	WO 2005/099657 A (THIENNA INC) See especially page 2 line 25- page 3 and Table 2

Categories:

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.

Field of Search:

Search of GB, EP, WO & US patent documents classified in the following areas of the UKC^{X} :

Worldwide search of patent documents classified in the following areas of the IPC

A61K; A61Q

The following online and other databases have been used in the preparation of this search report

WPI, EPODOC, MEDLINE, BIOSIS, CAPLUS, EMBASE, SCISEARCH, TXTE, TXTT, INTERNET

International Classification:

Subclass	Subgroup	Valid From
A61K	0008/46	01/01/2006
A61K	0008/60	01/01/2006
A61K	0008/67	01/01/2006
A61K	0008/73	01/01/2006
A61Q	0019/00	01/01/2006