



- (51) **International Patent Classification:**
A61K 31/215 (2006.01) A61P 27/02 (2006.01)
A61K 36/185 (2006.01)
- (21) **International Application Number:** PCT/IB20 14/06 1842
- (22) **International Filing Date:** 30 May 2014 (30.05.2014)
- (25) **Filing Language:** Italian
- (26) **Publication Language:** English
- (30) **Priority Data:** FI2013A000128 30 May 2013 (30.05.2013) IT
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- (81) **Designated States** (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,

[Continued on nextpage]

(54) **Title:** A SOLUTION FOR EYELID MARGIN HYGIENE AND A DEVICE FOR ITS APPLICATION

(57) **Abstract:** A solution for eyelid margin hygiene, and a kit comprising said solution with applicators for applying it to the eyelid margins are described.

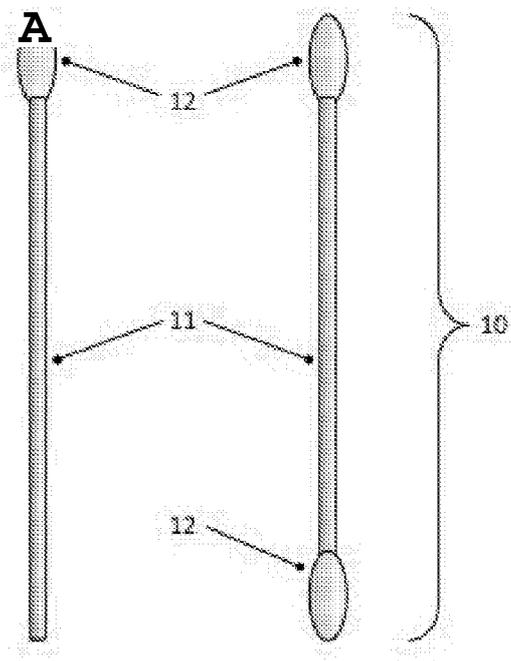


Fig 1



OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW,
 SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ,
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
 ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available):

ARIPO (BW, GH,
 GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,
 UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,
 TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU,
 LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK,
 SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
 GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(H))
- of inventorship (Rule 4.17(iv))

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

A SOLUTION FOR EYELID MARGIN HYGIENE AND A DEVICE FOR ITS APPLICATION

Field of the invention

The present invention relates to products for eyelid hygiene and particularly for eyelid margin hygiene.

State of the art

The generic term eyelid hygiene is commonly used to mean all those norms, activities and practices designed to cleanse and/or disinfect the skin of the eyelid, the eyelashes, and the eyelid margins. The most common indications for which ophthalmologists recommend performing eyelid hygiene procedures are eyelid dermatitis, anterior blepharitis, posterior blepharitis, Meibomian gland dysfunction (MGD), recurrent styes and chalazia, and post-operative eyelid cleansing.

When eyelid hygiene has the purpose of cleansing the orifices of the Meibomian glands, as in the case of posterior blepharitis, MGD, internal styes and chalazia, it is fundamentally important for this to be done as precisely and effectively as possible at eyelid margin level. In patients with these conditions and dysfunctions, the orifices of the Meibomian glands are obstructed due to an accumulation of epithelial cells (hyperkeratinization) and the presence of thickened Meibomian sebum.

The products and devices for eyelid hygiene currently available on the market mainly consist of medicated cotton gauze or nonwoven fabric pads packaged singly under sterile conditions. Some products are available in the form of a liquid, gel or foam and sold for use as eyelid cleansers with or without the aid of cotton gauze pads.

As an alternative to the above-mentioned products and devices, the ophthalmologist will often recommend that patients dip the tip of a cotton wool bud in various fluid substances (warm water, baby shampoo, chamomile, antibiotic eye drops, artificial tears) and use it to cleanse the eyelid margins in an effort to keep the glandular orifices clean (see, for instance, Sue Stevens "How to clean eyelids" Community Eye Health Journal Vol. 24, No. 75, 31 October 2011).

Both the premedicated cotton pads and the cleansing products are very useful and easy to use when patients need to cleanse the eyelid skin and eyelashes. Patients

complain of having severe difficulty, however, when the same products are prescribed for hygiene of the eyelid margin. The dimensions of the cotton pads, their consistency and manageability do not enable a sufficiently precise and effective cleansing of the eyelid margins.

In addition, the above-mentioned alternative practices often expose patients to the classic risks of DIY: the cotton wool buds are never sterile and may be a source of eyelid and eye contamination; the substances used are not always indicated for ophthalmological use; patients rarely have a thorough understanding of the correct procedure to perform and this can expose them to pointless or even hazardous manoeuvres.

The patent application US 2011/0124725 describes a treatment for dry eye involving eye drops or ointments for instilling in the eye, or the treatment of Meibomian gland obstruction/dysfunction. According to said patent application, jojoba oil is used as a carrier of local anaesthetics to prepare patients for the performance of an invasive surgical procedure (intraductal probing) of the Meibomian glands. The text makes no reference to eyelid hygiene or the treatment of (posterior or anterior) blepharitis, chalazion or stye, which form the therapeutic objects of the present patent application, nor to the possible use of jojoba oil in combination with cotton wool buds as a non-invasive self-medication product based on the principles of cleansing both mechanically and by affinity.

The consequence of all the above is that eyelid hygiene performed using the products currently available on the market is not effective for the treatment of disorders such as MGD, posterior blepharitis, seborrhoeic blepharitis, recurrent styes and chalazia. Hence the evident interest in products and devices suitable for cleansing the eyelid margins that are easy to use and designed for said purpose.

Brief description of the figures

Figure 1 shows a detail of the device according to the invention.

Summary of the invention

A solution for eyelid margin hygiene, and a kit comprising said solution with applicators for applying it to the eyelid margins are described.

Detailed description of the invention

The present invention enables the above-described problems to be overcome by means of a solution for eyelid margin hygiene and a kit comprising said solution and an applicator for applying it to the eyelid margins.

The solution according to the invention consists of jojoba oil, extracted preferably by cold pressing from *Simmondsia chinensis* seeds, possibly in combination with: natural or synthetic antibacterial, anti-inflammatory and/or antioxidant agents, thinners, and preserving agents.

The antibacterial agent for use according to the invention may be chosen, for instance, from among: terpinen-4-ol, thymol, *Mimosa tenuiflora* liposoluble extract, piroctone olamine, azythromycin, tetracycline, and their derivatives.

When included, these products are normally in quantities in the range of 0.01 to 0.05%, and preferably 0.03% (w/V calculated on the total volume of the solution).

An example of anti-inflammatory agent for use according to the invention is α -bisabolol; when added, it is normally in quantities in the range of 0.01 to 1%, and preferably 0.5% (w/V calculated on the total volume of the solution).

The antioxidant for use according to the invention may be chosen, for instance, from among: vitamin E (0.1 to 0.5%), butylhydroxyanisole (BHA) and butylhydroxytoluene (BHT) (0.01 to 0.05%).

Suitable thinners for use according to the invention include vegetable oils (e.g. castor oil), mineral oils (e.g. vaseline oil), or synthetic oils (e.g. dicaprylyl carbonate); the thinners are naturally added in the quantities needed to achieve the required final density.

Finally, the preserving agents are those commonly used in solutions for ophthalmological use, such as combinations of parabens, in the quantities commonly used for this purpose.

According to the invention, however, it is preferable to avoid the use of preserving agents, which are not considered essential, partly because the solution is preferably marketed in sterile single doses, as explained in more detail below.

A solution according to the invention may thus consist of 100% jojoba oil, extracted from *Simmondsia chinensis* seeds by cold pressing, or it may, for instance, comprise the following formulation: jojoba oil 99.97% and terpinen-4-ol 0.03%.

The jojoba oil used according to the present invention is the product as available commercially, and the compositions containing any of the various additives or other components are prepared according to the known methods normally used in the pharmaceutical sector for the preparation of products of this type.

As shown in Figure 1, the applicator 10 according to the invention normally consists of a stick 11 that serves as a grip, with at least one of its two ends carrying a bud 12 made of a material suitable for being impregnated with the solution when the product is to be used.

The stick 11 is made of any rigid material suitable for the purpose, such as plastic, wood, metal, etc. (preferably rigid plastic), while the material comprising the one or more bud(s) 12 is cotton, a nonwoven fabric, natural or synthetic bristles, etc.

The buds 12 preferably have a tapered shape, with the end forming a rounded tip that makes it easier to follow the perimeter of the eyelid margin.

The applicators are preferably contained singly or in pairs inside sterile wrappings suitable for the purpose, such as plastic, paper, plastic-coated paper or cellophane sachets, or other material suited to the purpose.

The solution may be contained in a multiple-dose drip-counter container (and in this case it is preferable for the solution to contain appropriate preserving agents, as explained above), or in single-dose phials (ophtioles) made of polyethylene, normally containing a volume in the range of 0.35 to 1 ml, and preferably 0.5 ml, prepackaged and containing a volume of solution corresponding, for instance, to 0.15 - 0.5 ml, and preferably 0.25 ml, and in this case it will be unnecessary to add any preserving agents.

At the time of using the product, having removed the applicator from its sterile container, the user can medicate one of the buds with the solution contained in the single dose or with the required number of drops drawn from the multi-dose drop-counter container, and then apply the solution by rubbing the medicated tip of the applicator along the margins of the eyelids held suitably detached from the eye bulb.

The shape, manageability and stiffness of the applicator enable a straightforward and accurate mechanical cleansing of the orifices of the Meibomian glands, removing cell residues, thickened secretions, bacteria and their toxic metabolites.

from the eyelid margins. The high wax ester content in jojoba oil enables a cleansing by affinity of the impaired Meibomian sebum and restores the lipid component of the lacrimal film.

A study was conducted on 9 patients with MGD and chronic blepharitis already receiving treatment for dry eye with eye drops and other products. The patients were treated for 4 weeks with the solution according to the invention and using the above-described applicators.

After the treatment, 89% of the patients reported an improvement or stabilisation of their dry eye symptoms and an improvement in the ocular and palpebral clinical signs. During the course of the study, 55% of the patients reduced or suspended their use of eye drops and other products for dry eye syndrome.

CLAIMS

1. A solution for use in treatments for hygiene of the eyelid margin consisting of jojoba oil, possibly in combination with natural or synthetic antibacterial, anti-inflammatory and/or antioxidant agents, thinners and preserving agents.
2. A solution according to claim 1 wherein said jojoba oil is extracted by cold pressing from *Simmondsia chinensis* seeds.
 - i. A solution according to claims 1 and 2 wherein said antibacterial agents are chosen from among: terpinen-4-ol, thymol, *Mimosa tenuiflora* liposoluble extract, piroctone olamine, usnic acid, azythromycin, tetracycline and their derivatives, or mixtures thereof, contained in quantities in the range of 0.01 to 0.05%, and preferably 0.03% (w/V calculated on the total volume of the solution).
4. A solution according to claims 1 to 3 wherein said anti-inflammatory agent is α -bisabolol in quantities in the range of 0.01 to 1%, and preferably 0.5% (w/V calculated on the total volume of the solution).
5. A solution according to claims 1 to 4 wherein said antioxidants are chosen from among vitamin E in the range of 0.1 to 0.5%, butylhydroxyanisole (BHA) and butylhydroxytoluene (BHT) between 0.01 and 0.05%.
3. A kit comprising a solution according to claims 1 to 6 and an applicator for applying said solution to the eyelid margins.
 - J. A kit according to claim 6 wherein the solution, preferably containing appropriate preserving agents, is contained inside a multi-dose drop-counter container, or in single-dose phials, or ophtioles.
3. A kit according to claims 6 and 7 wherein said applicator (10) consists of a stick (11) that serves as a grip, with at least one of the two ends carrying a bud (12) of material suitable for being impregnated with the solution when the product is to be used.
9. A kit according to claim 8 wherein said stick (11) is made of a rigid material suited to the purpose, while the bud(s) (12) consist of cotton, a nonwoven fabric, natural or synthetic bristles or the like.
10. A kit according to claim 9 wherein said buds (12) have a tapered shape with a rounded tip.

11. A kit according to claims 1 to 10 wherein the applicators are contained singly or in pairs inside sterile wrappings suited to the purpose.
12. The use of a solution according to claims 1 to 5 for eyelid margin hygiene.

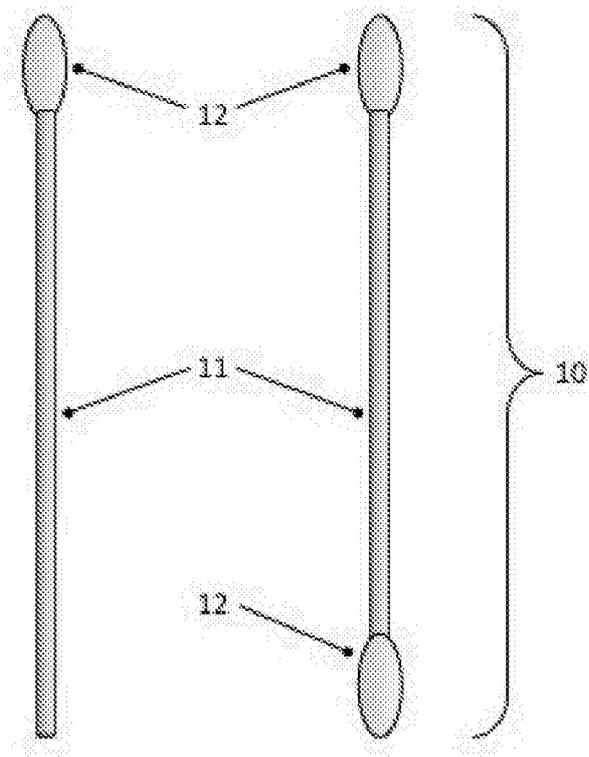


Fig. 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2014/061842

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/215 A61K36/185 A61P27/02
 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)
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 , BIOSIS, INSPEC, BEI LSTEIN Data, CHEM ABS Data, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/124725 AI (MASKIN STEVEN [US]) 26 May 2011 (2011-05-26)	1, 2, 12
Y	the whole document paragraphs [0015] , [0036] ; claims -----	1-12
Y	SUE STEVENS: "How to clean eyelids" , COMMUNITY EYE HEALTH JOURNAL, vol . 24, no. 75, 31 October 2011 (2011-10-31) , page 20, XP055092840, the whole document -----	1-12
X,P	EP 2 633 852 AI (BIODUE S P A [IT]) 4 September 2013 (2013-09-04) the whole document -----	1

Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :
 "A" document defining the general state of the art which is not considered to be of particular relevance
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 "P" document published prior to the international filing date but later than the priority date claimed
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 "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
 "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
 "&" document member of the same patent family

Date of the actual completion of the international search 10 October 2014	Date of mailing of the international search report 20/10/2014
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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 Orlando, Michele
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2014/061842

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011124725 A1	26-05-2011	US 2011124725 A1	26-05-2011
		US 2013131171 A1	23-05-2013

EP 2633852 A1	04-09-2013	NONE	
