

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
4 August 2005 (04.08.2005)

PCT

(10) International Publication Number  
**WO 2005/070378 A1**

- (51) International Patent Classification<sup>7</sup>: **A61K 7/20**
- (21) International Application Number:  
PCT/GB2005/000135
- (22) International Filing Date: 17 January 2005 (17.01.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0401113.6 19 January 2004 (19.01.2004) GB
- (71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **GORDON, Jennifer, Jane** [GB/GB]; GlaxoSmithKline Consumer Healthcare, St George's Avenue, Weybridge Surrey KT13 0DE (GB). **VELADA, Jose, Luis** [ES/GB]; GlaxoSmithKline Consumer Healthcare, St George's Avenue, Weybridge Surrey KT13 0DE (GB).
- (74) Agent: **REEVES, Julie, Frances**; GlaxoSmithKline, Corporate Intellectual Property, 980 Great West Road, Brentford Middlesex TW8 9GS (GB).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



**WO 2005/070378 A1**

(54) Title: TOOTH WHITENING COMPOSITION

(57) Abstract: The present invention provides an anhydrous liquid tooth whitening composition comprising a peroxide-containing compound and an orally acceptable carrier wherein the carrier includes a humectant, a bioadhesive agent, and a film-forming agent consisting essentially of a water-insoluble film-forming agent and a solvent for the film-forming agent.

## TOOTH WHITENING COMPOSITION

The present invention relates to a tooth whitening composition for bleaching tooth  
5 enamel. Specifically the present invention relates to an anhydrous tooth whitening  
composition comprising a peroxide.

White teeth have long been considered cosmetically desirable. Unfortunately, teeth  
almost invariably become discoloured in the absence of intervention. The tooth  
10 structure which is generally responsible for presenting a stained appearance is the  
enamel layer. Several factors contribute to enamel discoloration, but the three main  
factors are believed to be: (i) formation of plaque and tartar matrices on the tooth  
surface which then entraps stains; (ii) ingestion of certain drugs during gestational  
tooth formation; and (iii) discoloration due to oral cavity traumatization following  
15 which blood break-down products seep into the mineralized area of the teeth during  
enamel formation. This invention is primarily concerned with the first factor of  
tooth discoloration, that is, the natural stain which accumulates on teeth.

Over-the-counter teeth whitening preparations have been developed to address the  
20 cosmetic preference of many to restore luster to tooth enamel discolored by surface  
entrapped materials. While all dentifrices and mouthwashes contain some cleaning  
and polishing agents, some enamel deposits become intractable to being fully  
removed by these agents under normal use conditions. For example, smokers often  
develop discolored enamel because the tars and particulate in exhaled cigarette  
25 smoke collect on the teeth. Further, a number of comestibles, such as tea, or some  
medicinal agents, can stain or discolor tooth enamel.

There are various approaches to enamel whitening currently in general use. One  
approach is a physical abrading of the stain to effect stain removal. Harsher  
30 abrasives, also known as polishing agents, than those used in typical non-whitening  
toothpaste preparations, are employed in this approach. Most, if not all of these  
preparations are toothpastes, gels or powder dentifrices. The mechanical process

may be supplemented or even replaced by a chemical process which may involve an oxidative or enzymatic step to effect stain removal.

The chemical process generally utilizes a tooth whitening or bleaching formulation  
5 applied to a stained tooth surface for a specified period, after which the formulation is removed. Oxidizing agents represent one of the most widely distributed and utilized active agents in commercially available tooth whitening or bleaching products. Peroxide-containing agents such as carbamide peroxide, hydrogen peroxide and calcium peroxide are the most commonly used oxidizing agents, and  
10 are typically formulated into a liquid, solution, gel or paste. However it is known that products containing such agents may lose their whitening efficacy with time. In addition aqueous peroxide formulations may have only a brief period of efficacy when applied to teeth in the oral cavity because of rapid decomposition of peroxide on exposure to the enzyme, catalase, present in high concentrations in saliva.

15 Moreover low viscosities of aqueous peroxide solutions do not allow the peroxide whitening agent to remain in contact with teeth for the necessary time period to effect substantive whitening because of constant flushing effects of salivary secretions. WO 03/099246 (Colgate-Palmolive) aims to address these problems with the provision of an aqueous tooth whitening liquid composition comprising an  
20 orally acceptable vehicle comprising water and monohydric alcohol having dispersed therein a film forming combination of a poly(ethylene oxide) and a carbomer. However there remains a need for alternatives that do not suffer drawbacks encountered with known formulations. Moreover it would be desirable to provide simple formulations that do not require extensive stabilization, that are easy to  
25 manufacture and are sufficiently substantive and robust to enable once-a-day application. In addition it would be highly desirable to provide a composition that is capable of producing an instant whitening effect on the teeth whilst the bleaching process is taking place.

30 It is an object of the present invention to provide a composition that meets these requirements. This object is met according to the invention by the provision of an

anhydrous liquid tooth whitening composition comprising a peroxide-containing compound and an orally acceptable carrier wherein the carrier includes a humectant, a bioadhesive agent, and a film-forming agent consisting essentially of a water-insoluble film-forming agent and a solvent for the film-forming agent.

5

The composition of the invention is essentially anhydrous. Water or an aqueous medium is not used as a carrier or vehicle in the composition. Whilst free water is not added to the composition, it will be understood that small amounts of water, i.e. less than 5%w/w, preferably less than 3%w/w, may be present as a result of being  
10 introduced with other materials e.g. by using a "stock" hydrogen peroxide aqueous solution such as a 30%w/w hydrogen peroxide solution.

The composition of the invention is suitably in the form of a varnish that may conveniently be painted onto the teeth. Following its application, the composition  
15 dries *in situ* to form an adherent film which sticks firmly to the teeth. The film is sufficiently strong and adherent to remain on the teeth for a period of time e.g. up to a few hours or even longer e.g. up to twelve hours or more. Suitably the composition is applied at night time, allowing peroxide activity to take place during  
20 sleep periods. During use, the peroxide is released slowly from the film, in an amount and at such a rate as required to effect stain removal. The film may be removed from the user's teeth by any convenient means e.g. brushing and/or by rinsing with a mouthwash.

The term "painted onto the teeth" above is intended to encompass all manner of  
25 applying the whitening composition to teeth and includes sponging, coating, daubing, spraying, wiping and rubbing. Preferably the composition is applied to the teeth with a soft applicator brush. Suitably the composition is housed in a container such as a bottle, and the composition is applied with a soft applicator brush. The  
30 bottle and brush may be provided in kit form e.g. as may be used with a conventional nail varnish kit. Alternatively the composition may be housed in a dispensing device such as a pen with an applicator brush attached thereto e.g. generally of the type used with the Brite Smile To Go™ Whitening pen.

Peroxide-containing compounds used as whitening agents in the present invention include the following compounds and mixtures thereof: hydrogen peroxide e.g. as 30%w/w aqueous solution, carbamide peroxide, calcium peroxide, percarbonates and hydrogen peroxide polymer complexes for example hydrogen peroxide  
5 complexes with solid linear or crosslinked poly(-vinyl-pyrrolidone) (PVP) homopolymers and its copolymers, such as Peroxydone™ K30, Peroxydone™ K90, Peroxydone™ XL10; and hydrogen peroxide complexes with copolymers of vinyl-pyrrolidone and vinyl acetate, such as Plasdone® S-630. These various Peroxydone™ and Plasdone® polymers are available from International Specialty  
10 Products (ISP), 1361 Alps Road, Wayne, New Jersey 07470, US. Insoluble crosslinked polymeric matrices that retain hydrogen peroxide for a certain period of time may also be used. An example of this is Poly-Pore® 337HP which is an allyl methacrylate crosspolymer and is available from AMCOL Health & Beauty Solutions, Inc., 301 Laser Lane, Lafayette, LA 70507, US.

15

Mixtures of different peroxide sources, as hereinabove described, may be used to provide variable peroxide release. For example both immediate and slow release peroxide may be achieved by using a combination of aqueous hydrogen peroxide and carbamide peroxide and/or hydrogen peroxide complexes with solid vinyl-  
20 pyrrolidone (VP) polymers. Carbamide peroxide, and mixtures of carbamide peroxide with hydrogen peroxide (30% aqueous solution) and optionally with a hydrogen peroxide complex with vinyl-pyrrolidone e.g. Peroxydone™ hydrogen peroxide polymer complexes e.g. Peroxydone™ K90, are preferred.

25 Suitably the total amount of peroxide present in the liquid whitening composition of the invention is in the range of 1 to 30% w/w, preferably in the range 2 to 20% w/w, even more preferably in the range 3 to 10% w/w.

A humectant is a key component of a composition of the invention. It has been  
30 found that the absence of a humectant results in the formation of brittle and fragile films that cannot be adequately spread onto teeth. Suitable humectants include the

following and mixtures thereof: glycerin, sorbitol, propylene glycol, sugars such as glucose or sucrose, and low molecular weight polyethylene glycols (PEGs) i.e. in the range 200-600 e.g. PEG 200, 300, 400, and 600, available from Dow Chemicals USA, PO Box 1206, Midland MI48642. Preferred humectants include  
5 glycerin and PEGs.

Suitably the humectant is present in an amount ranging from 0.5 to 30%w/w, preferably in the range 1 to 15%w/w.

A bioadhesive agent is included in a composition of the invention. The bioadhesive  
10 agent enhances substantivity of the composition to teeth. Suitably the bioadhesive agent of the invention exhibits mucoadhesive behaviour i.e. it has an affinity for biological surfaces such as teeth. Examples of suitable bioadhesive agents include carbomers, copolymers of methyl vinyl ether and maleic anhydride, natural gums, vinyl-pyrrolidone polymers and copolymers and mixtures thereof.

15

Carbomers are synthetic high molecular weight polymers of acrylic acid that are crosslinked with either allylsucrose or allylethers of pentaerythritol. Carbomers sold under the trade name "Carbopol ®", available from Noveon Inc, 9911 Brecksville Road, Cleveland, Ohio 44141-3247, are preferred and include  
20 Carbopol® 934 or 974, 940, 941, 980 and Ultrez 10™. Other suitable carbomers include partially neutralized carbomers e.g. PNC400, available from 3V Sigma, PO Box 219, Via Torquato Tasso, 58,24100, Bergamo, Italy and carbomer copolymers such as crosslinked copolymers of acrylic acid with alkylacrylate where the alkyl chain is C10-30 e.g. Pemulen TR1 and Pemulen TR2, available from Noveon Inc.  
25 as above.

Copolymers of methyl vinyl ether and maleic anhydride are available commercially in a range of molecular weights under the trade name "Gantrez®" (ISP), specifically Gantrez® AN. Other Gantrez® copolymers that may be used include  
30 the free acid form of the Gantrez® AN available as Gantrez® S, a mixed sodium

and calcium salt of Gantrez® S available as Gantrez® MS, and half ester derivatives of Gantrez® S available as Gantrez® ES.

5 Natural gums such as gum karaya, xanthan gum, guar gum, arabic gum tragacanth are also suitable bioadhesive agents. Xanthan gum is especially preferred and has been found to impart surprisingly good substantivity properties to compositions of the invention.

10 Suitable vinyl-pyrrolidone polymers include poly(-vinyl-pyrrolidone) (PVP) and cross-linked PVP. A suitable copolymer as hereinbefore described includes Plasdone® S-630. PVP is a preferred polymer, in particular a high molecular weight PVP e.g. in the range 1,300,000 e.g. Plasdone® K-90.

15 Preferably the bioadhesive agent is selected from xanthan gum, a carbomer and PVP and mixtures thereof. Even more preferably the bioadhesive agent is a mixture of a carbomer such as a Carbopol and a high molecular weight PVP e.g. Plasdone® K-90.

20 Suitably the bioadhesive agent is present in an amount ranging from 0.5 to 30% w/w, preferably from 1 to 20%w/w.

On application to teeth, the film-forming component of the composition forms a protective film or barrier which retains the other components, i.e. excipients and the peroxide-containing compound, of the composition in a matrix-type environment.  
25 The only component which is not retained is the solvent for the film-forming agent which evaporates from the site of application. Suitably the film-forming component of the composition consists essentially of a water-insoluble film-forming agent such as a water-insoluble microcrystalline cellulose, e.g. ethyl cellulose, a poly(urethane) or a poly(acrylamide). Ethyl cellulose is a preferred film-forming  
30

agent. Suitably the film-forming component is present in an amount ranging from 5 to 30% preferably 10 to 25%w/w.

A solvent is required for the film-forming agent. The solvent is a carrier for the  
5 film-forming agent. During use the solvent rapidly evaporates to leave a highly substantive film on the teeth. The deposited film is comprised of a peroxide, a humectant, a bioadhesive agent and a water-insoluble film-forming agent. Examples of suitable solvents include monohydric alcohols such as ethanol or isopropyl alcohol. Suitably the solvent is present in an amount ranging from 30 to 80%,  
10 preferably 40 to 70%w/w.

Additionally, compositions of the present invention will suitably contain acceptable additives or excipients conventional in the field of oral care products including for example chelating agents such as ethylenediaminetetraacetic acid and/or citric acid,  
15 colouring agents, flavouring agents, a fluoride source such as sodium fluoride or sodium monofluorophosphate, an antisensitivity agent such as strontium or potassium salts e.g. strontium chloride, and sweetening agents. The additives or excipients used in any given composition will be compatible both with each other and with the essential ingredients of the composition such that there is no interaction  
20 which would impair the performance of the active ingredients. All additives or excipients must of course be non-toxic and of sufficient purity to render them suitable for human use.

The liquid whitening compositions of the present invention are prepared by adding  
25 and mixing the ingredients of the composition in a suitable vessel such as a stainless steel tank provided with a mixer. In the preparation of the composition the ingredients are suitably added to the mixer in the following order: peroxide, chelating agents (if used), humectant, solvent for the film-forming agent to form a solution. The film-forming agent is then added, followed by addition of the  
30 bioadhesive agent. The whitening composition prepared is then suitably packaged and stored as required.



Advantageously the composition of the invention is suitably prepared in the form of a "single component" system i.e. all components of the whitening composition, i.e. excipients and the peroxide-containing compound, are self-contained in a desired pre-mixed proportion. Accordingly there is no requirement for the components of the composition to be physically separated from each other prior to use in order to avoid any undesirable interactions, as may occur with some peroxide-containing formulations. In a second aspect of the invention there is provided a kit of parts comprising an anhydrous liquid tooth whitening composition as hereinbefore described, a container for housing the composition and an applicator for applying the composition to teeth to be whitened.

Compositions according to the present invention may be applied topically to the teeth as appropriate in the form of lotions, gels, mousses, sprays or aerosols.

- In an alternative aspect there is provided a method of whitening teeth comprising:
- a. preparing a tooth whitening composition as hereinbefore described;
  - b. painting the composition onto teeth to be whitened, suitably at night-time
  - c. maintaining the composition in contact with the teeth for a plurality of hours per day e.g. up to twelve hours per day,
  - d. repeating steps b and c for multiple days e.g. up to fourteen days, to thereby whiten the teeth.

The present invention is illustrated by the following examples but is not limited thereby.

#### Example 1

A whitening composition was prepared having the following ingredients:

Ingredient	%w/w
Glycerin	3.00
Ethanol	67.00

Carbamide peroxide	3.00
Hydrogen peroxide (30%)	3.00
Peroxydone K-90	10.00
Ethyl cellulose	14.00
Total	100.00

## Example 2

A whitening composition was prepared having the following ingredients:

<b>Ingredient</b>	<b>%w/w</b>
Glycerin	4.00
Ethanol	66.00
Carbamide peroxide	3.00
Hydrogen peroxide	3.00
Peroxydone K-90	11.00
Xanthan gum	2.00
Ethyl cellulose	11.00
Total	100.00

## 5 Example 3

A whitening composition was prepared having the following ingredients:

<b>Ingredient</b>	<b>%w/w</b>
Carbamide peroxide	17.00
Ethanol	45.00
Ethyl cellulose	15.00
Carbopol 974P NF	1.00
Glycerin	22.00
Total	100.00

## Example 4

10 A whitening composition was prepared having the following ingredients:

<b>Ingredient</b>	<b>%w/w</b>
Carbamide peroxide	5.60
Hydrogen peroxide (30%)	6.90
Ethanol	62.10
Ethyl cellulose	11.30
Plasdone K-90	9.00
Xanthan gum	2.20
Glycerin	2.80
Citric Acid	0.05
EDTA	0.05

Total	100.00
-------	--------

## Example 5

An instant whitening composition was prepared having the following ingredients:

Ingredient	%w/w
Ethanol	65.00
Ethyl cellulose	5.00
Peroxydone K-90	22.90
Mica	2.00
Glycerin	4.00
Titanium dioxide	1.00
Citric Acid	0.05
EDTA	0.05
Total	100.00

5

## Example 6

A whitening aerosol spray composition was prepared having the following ingredients:

Ingredient	%w/w
Ethanol	45.00
Hydrogen peroxide (30%)	10.00
Ethyl cellulose	5.00
Peroxydone XL10	10.00
Glycerin	5.00
DME	25.00
Total	100.00

10 Example 7

A whitening aerosol spray composition was prepared having the following ingredients:

Ingredient	%w/w
Ethanol	45.00
Hydrogen peroxide (30%)	15.00
Ethyl cellulose	8.00
Peroxydone XL10	2.00
Glycerin	5.00
DME	25.00
Total	100.00

Determination of Bleaching Effects using Bovine Enamel Night Time Whitening Model

5

Introduction

The bleaching effects of compositions disclosed in Examples 1-3 above were determined and compared to the bleaching effects observed with a commercially available preparation (a whitening product available as "Crest Night Effects").

10

Method

Bovine teeth were used and L\* (from the CIE 1976 L\*a\*b\* colour space scale) was measured at the start of the experiment using a spectrophotometer. Formulations were applied to the teeth and these were placed into a container such that a liquid substantivity challenge was applied to the treated teeth. At the end of the treatment time the teeth were rinsed and dried and L\* was remeasured using a spectrophotometer. This method was repeated for a number of days to mimic in-vivo nighttime use of the product. At the end of the experiment the overall change in L\* i.e.  $\Delta L$  was calculated.

20

Results

Sample	$\Delta L$ after 12hrs treatment
Example 1	4.49
Example 2	5.55
Example 3	3.31
Crest Night Effects	4.02
Deionised water	-1.83

### Conclusions

The results indicate that change in 'L' after 12 hours treatment was comparable to  
5 that observed with a commercially available nighttime product. The results are  
illustrated graphically in Figure 1 on page 1/1.

A further randomized, single centre, parallel and examiner-blind study was  
10 undertaken.

### Introduction

Healthy subjects with a Vita Shade Guide value of A2 or grater on two of the 4  
maxillary incisors were enrolled. The maxillary anterior teeth were treated for 14  
15 days at home by applying the treatment for 30 seconds once daily after brushing at  
night. The treatment groups were:

- (1) Example 4 Formulation
- (2) Commercial paint-on product containing 10% hydrogen peroxide
- 20 (3) Brushing twice daily alone

### Method

All subjects were requested to refrain from eating , drinking and smoking for 30  
minutes after the gels were applied. All subjects brushed with the same  
25 dentifrice twice daily using the same make of toothbrush for one minute using a  
timer. To follow the change in intrinsic tooth colour, shade assessments were  
performed at baseline and after 7 and 14 days of treatment. An analysis of  
covariance (ANCOVA) model using the baseline mean subject-wise Vita Shade  
score as covariate including treatment group, age group and smoking status was  
30 used.

Results

	<b>Example 4</b>	<b>Commercial Product</b>	<b>Brushing twice daily alone</b>
No. subjects	32	32	32
Baseline Mean	7.98	8.12	8.81
7 days	1.09	1.33	-0.05
14 days	2.21	2.14	0.00

Conclusion

5

The results show that a significant change in shade was observed after 14 days treatment with the Example 4 formulation.

10

15

20

25

Claims

- 5 1. An anhydrous liquid tooth whitening composition comprising a peroxide-containing compound and an orally acceptable carrier wherein the carrier includes a humectant, a bioadhesive agent, and a film-forming component consisting essentially of a water-insoluble film-forming agent and a solvent for the film-forming agent.
- 10 2. An anhydrous liquid tooth whitening composition according to claim 1 wherein the peroxide is selected from carbamide peroxide, and mixtures of carbamide peroxide with hydrogen peroxide and/or a hydrogen peroxide complex with vinyl pyrrolidone.
- 15 3. An anhydrous liquid tooth whitening composition according to claim 1 or claim 2 wherein the humectant is glycerin.
- 20 4. An anhydrous liquid tooth whitening composition according to any one of claims 1 to 3 wherein the bioadhesive agent is selected from xanthan gum, a carbomer and PVP and its copolymers and mixtures thereof.
- 25 5. An anhydrous liquid tooth whitening composition according to any one of claims 1 to 4 wherein the film forming agent is ethyl cellulose.
- 30 6. An anhydrous liquid tooth whitening composition according to any one of claims 1 to 5 wherein the solvent is ethanol.
7. A kit of parts comprising an anhydrous liquid tooth whitening composition according to any one of claims 1 to 6, a container for housing the composition and an applicator for applying the composition to teeth to be whitened.

8. A method of whitening teeth comprising:
- a. preparing a tooth whitening composition according to any one of claims 1 to 6;
  - 5 b. painting the composition onto teeth to be whitened;
  - c. maintaining the composition in contact with the teeth for a plurality of hours per day; and then
  - d. repeating steps b and c for multiple days to thereby whiten the teeth.

10

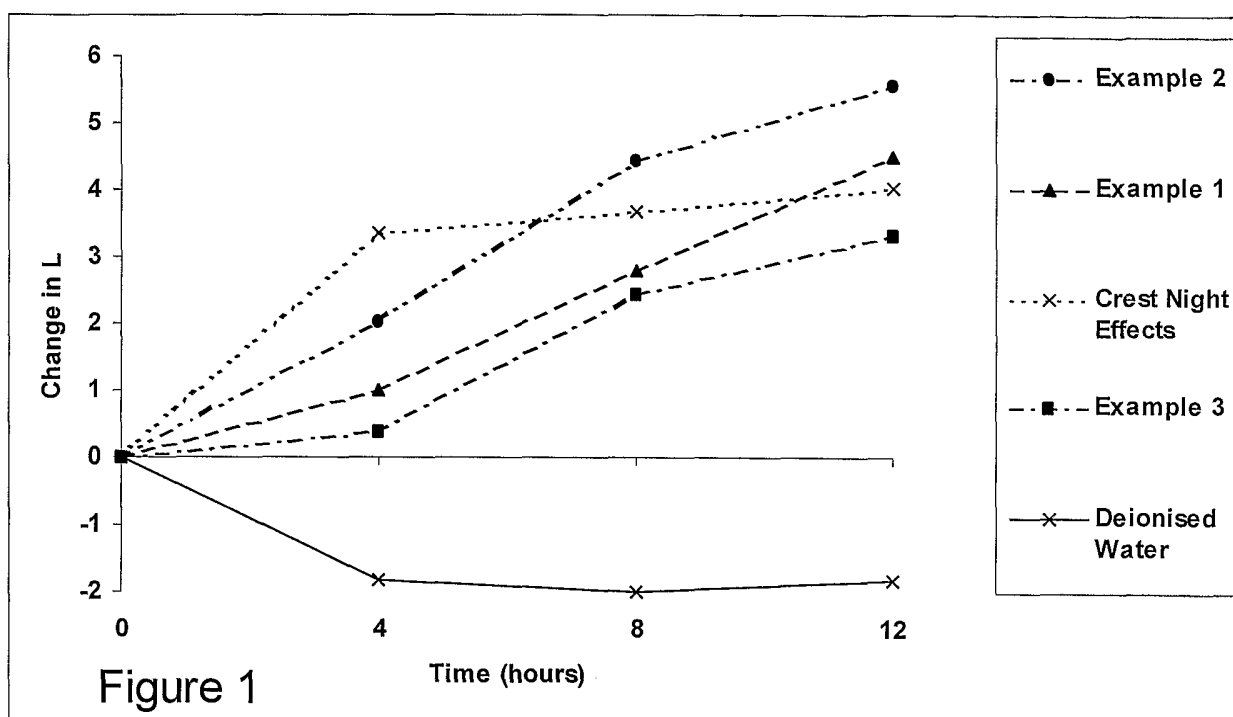
15

20

25

30





# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB2005/000135

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K7/20

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)  
IPC 7 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 practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ, BIOSIS

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2003/152528 A1 (SINGH PARMINDER ET AL) 14 August 2003 (2003-08-14) page 2, paragraph 22 - page 3, paragraph 41; examples 4,5 page 5, paragraph 59 - page 6, paragraph 71; claims 1-14,53-61 page 12, paragraph 133	1-8
Y	US 5 631 000 A (PELLICO ET AL) 20 May 1997 (1997-05-20) column 1, line 57 - column 4, line 37; claims; examples	1-8

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "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)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "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
- "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

12 April 2005

Date of mailing of the international search report

19/04/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Loloiu, C

INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB2005/000135

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/01940 A (THE PROCTER & GAMBLE COMPANY; YUE, JIANG; CRISANTI, MARK, MATTHEW; MAJ) 11 January 2001 (2001-01-11) page 3, line 5 - line 13; tables 3ex.1-6,6,ex.1-2 page 4, line 5 - line 16 page 10, line 6 - line 16; claim 1	1-8
A	US 2001/021374 A1 (MONTGOMERY R. ERIC) 13 September 2001 (2001-09-13) page 4, paragraph 39	1-8
A	US 6 306 370 B1 (JENSEN STEVEN D ET AL) 23 October 2001 (2001-10-23) column 3, line 24 - column 5, line 47 column 7, line 7 - column 9, line 50; examples 5,7	1-8
P,X	WO 2004/041102 A (ISP INVESTMENTS INC) 21 May 2004 (2004-05-21) page 3; examples 1,2	1-7
E	WO 2005/018591 A (COLGATE-PALMOLIVE COMPANY; FEI, LIN; CHOPRA, SUMAN, K; MANDADI, PRAKAS) 3 March 2005 (2005-03-03) page 2, line 16 - page 3, line 2; examples A,D,E page 3, line 17 - page 6, line 7	1-3,6

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
PCT/GB2005/000135

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
US 2003152528	A1	14-08-2003	US 2003170308 A1	11-09-2003
			US 2003235549 A1	25-12-2003
			US 2004105834 A1	03-06-2004
			US 2004258723 A1	23-12-2004
			WO 2004071323 A2	26-08-2004
			CA 2445086 A1	07-11-2002
			EP 1390085 A1	25-02-2004
			JP 2004536898 T	09-12-2004
			WO 02087645 A1	07-11-2002
US 5631000	A	20-05-1997	US 5718886 A	17-02-1998
WO 0101940	A	11-01-2001	AT 238766 T	15-05-2003
			AT 285220 T	15-01-2005
			AU 769263 B2	22-01-2004
			AU 5602700 A	22-01-2001
			AU 5907300 A	22-01-2001
			AU 768471 B2	11-12-2003
			AU 5907400 A	22-01-2001
			AU 5907500 A	22-01-2001
			BR 0012122 A	07-05-2002
			BR 0012145 A	30-04-2002
			CA 2373868 A1	11-01-2001
			CA 2373983 A1	11-01-2001
			CA 2375093 A1	11-01-2001
			CN 1360493 A	24-07-2002
			CN 1360494 A	24-07-2002
			CZ 20014704 A3	12-06-2002
			CZ 20014709 A3	11-09-2002
			DE 60002471 D1	05-06-2003
			DE 60002471 T2	19-02-2004
			DE 60016927 D1	27-01-2005
			EP 1196136 A1	17-04-2002
			EP 1200064 A1	02-05-2002
			EP 1196137 A1	17-04-2002
			ES 2199168 T3	16-02-2004
			HK 1047035 A1	05-03-2004
			HU 0201620 A2	28-09-2002
			HU 0201865 A2	28-11-2002
			JP 2003525210 T	26-08-2003
			JP 2003531814 T	28-10-2003
			MA 25681 A1	01-04-2003
			MX PA02000269 A	21-06-2002
			NO 20020004 A	28-02-2002
NO 20020005 A	28-02-2002			
PL 353998 A1	15-12-2003			
PL 357159 A1	12-07-2004			
RU 2223746 C2	20-02-2004			
RU 2222315 C2	27-01-2004			
SK 19412001 A3	06-08-2002			
SK 19422001 A3	06-08-2002			
WO 0101940 A1	11-01-2001			
WO 0101941 A1	11-01-2001			
WO 0101958 A1	11-01-2001			
WO 0101942 A1	11-01-2001			
US 6589512 B1	08-07-2003			
US 6692727 B1	17-02-2004			
US 6649147 B1	18-11-2003			

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No PCT/GB2005/000135
---

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0101940 A		ZA 200110448 A	24-07-2002
US 2001021374 A1	13-09-2001	US 6221341 B1 US 2004101497 A1	24-04-2001 27-05-2004
US 6306370 B1	23-10-2001	US 5855870 A US 5851512 A AU 1612100 A WO 0028953 A1 US 6086855 A US 6183251 B1 US 6036943 A US 5985249 A	05-01-1999 22-12-1998 05-06-2000 25-05-2000 11-07-2000 06-02-2001 14-03-2000 16-11-1999
WO 2004041102 A	21-05-2004	US 2004086468 A1 AU 2003287056 A1 WO 2004041102 A2	06-05-2004 07-06-2004 21-05-2004
WO 2005018591 A	03-03-2005	US 2005036956 A1 WO 2005018591 A1	17-02-2005 03-03-2005