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CA 2257810 C 2008/08/12

(11)(21) **2 257 810**

(12) **BREVET CANADIEN  
CANADIAN PATENT**

(13) **C**

(86) Date de dépôt PCT/PCT Filing Date: 1997/06/05  
(87) Date publication PCT/PCT Publication Date: 1997/12/18  
(45) Date de délivrance/Issue Date: 2008/08/12  
(85) Entrée phase nationale/National Entry: 1998/12/08  
(86) N° demande PCT/PCT Application No.: EP 1997/002984  
(87) N° publication PCT/PCT Publication No.: 1997/047171  
(30) Priorité/Priority: 1996/06/10 (GB9612067.0)

(51) Cl.Int./Int.Cl. *A61K 8/365* (2006.01),  
*A61K 31/00* (2006.01), *A61K 31/19* (2006.01),  
*A61K 31/60* (2006.01), *A61K 47/36* (2006.01),  
*A61K 9/08* (2006.01), *A61P 17/10* (2006.01),  
*A61Q 19/10* (2006.01), *C11D 3/20* (2006.01),  
*C11D 3/48* (2006.01)

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(54) Titre : COMPOSITION DE NETTOYAGE DE LA PEAU COMPRENANT UN ACIDE  $\alpha$ -HYDROXY OU UN AUTRE  
ACIDE ET UNE BASE DE DETERGENT  
(54) Title: SKIN WASH COMPOSITION COMPRISING AN  $\alpha$ -HYDROXY ACID OR OTHER ACID AND A DETERGENT  
BASE

(57) Abrégé/Abstract:

A skin wash composition intended for topical application to water-wetted skin comprising an  $\alpha$ -hydroxy acid active ingredient formulated in a mild and non-irritant detergent base consisting of a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant.



**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b>  <b>A61K 7/48, 7/50</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 97/47171</b>  <b>(43) International Publication Date:</b> 18 December 1997 (18.12.97)
<b>(21) International Application Number:</b> PCT/EP97/02984  <b>(22) International Filing Date:</b> 5 June 1997 (05.06.97)  <b>(30) Priority Data:</b> 9612067.0                      10 June 1996 (10.06.96)                      GB  <b>(71) Applicant (for all designated States except US):</b> SMITHKLINE BEECHAM PLC [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> CHARLTON, Lynda, Rosemary [GB/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB). MCGILLYCUDDY, Juliet, Teresa [IE/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB). OWEN, Sharon [GB/GB]; SmithKline Beecham Consumer Healthcare, St. George's Avenue, Weybridge, Surrey KT13 0DE (GB).  <b>(74) Agent:</b> WHITE, Susan, Mary; SmithKline Beecham plc, Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).		<b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> SKIN WASH COMPOSITION  <b>(57) Abstract</b>  A skin wash composition intended for topical application to water-wetted skin comprising an $\alpha$ -hydroxy acid active ingredient formulated in a mild and non-irritant detergent base consisting of a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant.		

## SKIN WASH COMPOSITION COMPRISING AN $\alpha$ -HYDROXY ACID OR OTHER ACID AND A DETERGENT BASE

The present invention relates to compositions for topical application to the skin surface, in particular to skin wash compositions which are applied to water-wetted skin and subsequently rinsed off with water. Specifically, the present invention relates to skin wash compositions comprising an  $\alpha$ -hydroxy acid and other acids as defined herein as an active ingredient formulated in a mild and non-irritant detergent base.

Compounds generally known in the field of cosmetic and therapeutic skin treatments as  $\alpha$ -hydroxy acids and other acids as defined herein include compounds such as salicylic acid, lactic acid and glycolic acid. These compounds constitute the active ingredients of a number of commercially available products which are applied to the skin in order to confer a beneficial effect with respect to appearance and skin condition, in particular smoothness and suppleness. Salicylic acid for example has been shown to have keratolytic and comedolytic activity as well as anti-bacterial efficacy and has been used in the treatment and prevention of mild to moderate acne for more than 100 years. Lactic acid has a beneficial effect on skin hydration and is a constituent of a number of skin tonic and moisturising products.

$\alpha$ -Hydroxy acids and other acids as defined herein, whilst conferring a beneficial effect on the skin, may cause local irritation when applied to sensitive areas of the skin, in particular the face. Moreover, local irritation may be exacerbated by the carrier system in which the active ingredient is formulated. For example, skin wash compositions and in particular face wash compositions which are generally formulated with a soap-free detergent base selected for effective cleansing and foaming, may confer an irritant effect due to the use of ionic surfactants commonly employed in such detergent systems.

A further problem associated with formulating compositions containing  $\alpha$ -hydroxy acids and other acids as defined herein arises because of the desirability to formulate the composition at an acid pH at which the most efficacious free-acid form of the acid will predominate. For skin wash compositions, this problem is exacerbated by the

difficulty of obtaining a detergent base system at sufficiently low pH. A skin wash composition described as having a gentle yet effective cleanser for acne treatment and containing 2.0% w/w salicylic acid in a detergent base comprising a mixture of anionic and amphoteric surfactants is commercially available. Analysis of this product, shows that it has a pH of 5. It follows, having regard to the pKa of salicylic acid which is attributed the value 2.97, that the free-acid form of the hydroxy acid does not predominate in this product and that its efficacy is accordingly not fully optimised.

10 An embodiment of the present invention may provide a skin wash composition containing an  $\alpha$ -hydroxy acid or other acid as defined herein and a detergent base which has good cleansing and foaming characteristics, is mild and non-irritant and wherein the pH of the composition approaches the pKa of the acid such that the efficacy of the acid is enhanced. This object is achieved according to the present invention which is based  
15 on the unexpected finding that a detergent base comprising a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant not only has the desired cleansing and foaming characteristics and is mild and non-irritant when applied to the skin but also enables compositions to be formulated at low pH.

20 According to the present invention there is provided a skin wash composition comprising from 0.1 to 10 %w/w of an  $\alpha$ -hydroxy acid or other acid as defined herein and a detergent base consisting of a mixture of a non-ionic alkylpolyglucoside surfactant and an amphoteric surfactant wherein the pH of the composition is in the range 3.0 to 4.5.

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According to an aspect of the present invention, there is provided a skin wash composition comprising from 0.1 to 10 % w/w of an  $\alpha$ -hydroxy acid, salicylic, maleic or pyruvic acid and a detergent base consisting of a mixture of from 2.0 to 15% w/w of a non-ionic alkylpolyglucoside surfactant and from 2.0 to 8.0% w/w of an amphoteric  
30 surfactant wherein the pH of said composition is in the range 3.0 to 4.5.

According to another aspect of the present invention, there is provided an aqueous skin wash composition comprising from 0.1 to 10% w/w of an  $\alpha$ -hydroxy, salicylic, maleic or pyruvic acid and an amount of a detergent base not exceeding 30% w/w and which detergent base consists of a mixture of an amount of a non-ionic alkylpolyglucoside surfactant not exceeding 20% w/w and an amount of an amphoteric surfactant not exceeding 10% w/w wherein the pH of the composition is in the range 3.0 to 4.5.

According to another aspect of the present invention, there is provided a use of the composition as defined herein for the manufacture of a medicament for use in the treatment and/or prophylaxis of acne.

According to another aspect of the present invention, there is provided a use of a composition as defined herein for use in the treatment and/or prophylaxis of acne.

According to another aspect of the present invention, there is provided a non-therapeutic method of improving the appearance and/or condition of human skin comprising the administration of a composition as defined herein.

According to another aspect of the present invention, there is provided a commercial package comprising the composition as defined herein together with instructions for its use for the treatment and/or prophylaxis of acne.

Suitable acids for incorporation into skin wash compositions of the invention include salicylic acid, lactic acid, citric acid, glycolic acid, malic acid, maleic acid, pyruvic acid and hydroxy-octanoic acid. Preferred acids are salicylic acid, lactic acid and glycolic acid, especially salicylic acid and lactic acid. Salicylic acid will suitably be present in compositions of the invention at a concentration in the range 0.2 to 5.0% w/w, more suitably in the range 1.0 to 3.0% w/w. A preferred concentration for

salicylic acid is 2.0 %w/w. Lactic acid will suitably be present in compositions of the invention at a concentration in the range 0.1 to 5.0 %w/w, more suitably in the range 0.5 to 2.5 %w/w. A preferred concentration for lactic acid is 1 %w/w. Glycolic acid will suitably be present at a concentration in the range 2.0 to 10.0 %w/w.

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As used herein, the term alkylpolyglucoside surfactant means a non-ionic surfactant derived from common natural organic monomer units as found in starch, fats and sugars, and most suitably derived from D-glucose monomer units.

Alkylpolyglucosides derived from D-glucose are acetal compounds in which the alkyl  
10 residue has a carbon chain length of from 8 to 16 carbon atoms and the degree of glucosidation (or polymerisation), ie. the average number of glucose units per alkyl radical, is between 1.1 and 6. A range of suitable alkylpolyglucosides are commercially available either individually or as mixtures or blends. Compositions according to this invention will generally contain mixtures or blends of different  
15 alkylpolyglucosides. Preferred alkylpolyglucosides for use in the present invention include decyl glucoside and lauryl glucoside and mixtures thereof.

Alkylpolyglucoside surfactants generally comprise up to 20 %w/w of the skin wash composition, suitably from 2.0 to 15.0 %w/w and preferably from 4.0 to 10.0 %w/w of the composition. It will be appreciated that the amount of alkylpolyglucoside will  
20 be determined to some extent by the nature and amount of amphoteric surfactant present in the composition.

In principle, any amphoteric surfactant which is acceptable for topical application to the skin may contribute, with the alkylpolyglucoside surfactant, to the detergent base  
25 but, in view of their inherent mildness and good foaming performance, the preferred amphoteric surfactant will belong to the class of compounds known as betaines.

Structurally, betaine compounds contain a carboxylate functional group and a quaternary nitrogen function separated by a methylene moiety. They include n-alkyl betaines such as cetyl betaine and behenyl betaine, and n-alkylamido betaines such as  
30 cocoamidopropyl betaine. The amphoteric surfactant component of the detergent base for compositions of the present invention may be a single compound or a mixture of

blend of two or more different substances. A preferred amphoteric surfactant is cocoamidopropyl betaine. Amphoteric surfactants will generally comprise up to 10 %w/w of the skin wash composition, suitably from 2.0 to 8.0 %w/w and preferably from 2.5 to 6.0% w/w of the skin wash composition. The amount of amphoteric  
5 surfactant will to some extent be determined by the alkylpolyglucoside surfactant component of the detergent base.

Typically, the detergent base consisting of the mixture of non-ionic alkylpolyglucoside surfactant and amphoteric surfactant will constitute up to 30  
10 %w/w of the skin wash composition. Suitably the detergent base will constitute from 5.0 to 20.0 %w/w and more suitably from 8.0 to 18.0 %w/w of the skin wash composition.

Control of pH to within defined limits is an essential feature of the present invention.  
15 A pH within the desired range 3.0 to 4.5 is conferred partly by the inherent properties of the acid and specific surfactants and quantities thereof making up the detergent base and partly, where required, by use of a suitable neutralising agent for the acid. Any topically acceptable neutralising agent which is compatible with the other components of the composition can be used. It has been found that the neutralising  
20 agent tromethamine is particularly suitable for skin wash compositions containing  $\alpha$ -hydroxy acids or other acids as defined herein. Other suitable neutralising agents include sodium hydroxide and triethanolamine. The amount of neutralising agent will be determined by the acid/base properties of the other ingredients which make up the composition and the pH selected for the composition.

25 The skin wash compositions of the invention may also contain additional topically acceptable skin conditioning and soothing agents, for example in the form of anti-inflammatory agents and vitamins or vitamin derivatives, typically at low concentrations, for example in the range 0.01 to 2.0 %w/w of the total composition.  
30 Examples of topically acceptable anti-inflammatory agents include allantoin and

bisabolol. A preferred vitamin derivative is vitamin E acetate which has anti-inflammatory properties.

Additionally, compositions of the present invention will suitably contain

5 pharmaceutically and cosmetically acceptable additives or excipients conventional in the field of topical medicines and cosmetics, including for example thickeners, moisturisers, re-fatting agents, preservatives, conditioners, chelating agents, colouring agents, fragrances, UV filters and/or emulsifiers. The additives or excipients used in any given composition will be compatible both with each other and with the essential

10 ingredients of the composition such that there is no interaction 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.

Suitable thickeners include polymeric high molecular weight, non-ionic surfactants

15 consisting of a long chain ( $C_{12}$  to  $C_{18}$ ) polyethylene glycol fatty acid or fatty acid residue. Examples include PEG 200 hydrogenated glyceryl palmitate, PEG 55 propylene glycol oleate, PEG 150 distearate and PEG 200 glyceryl tallowate. Suitable low molecular weight thickeners include cocamide DEA, laureth-3 and glyceryl monolaurate. A thickener comprising a polyurethane resin, propylene glycol and

20 water sold under the trade name Acrysol 44 also performs well in detergent base skin wash compositions. A thickener will suitably comprise up to 10.0 %w/w of the composition, more suitably from 2.0 to 5.0 %w/w. Preferred moisturisers include glycerin, propylene glycol, sorbitol and polyethylene glycol. A moisturiser may comprise up to 15%w/w of the composition, more generally from 2.0 to 6.0 %w/w of

25 the composition. Suitable re-fatting agents generally comprising 0.5 to 5.0 %w/w of the composition, preferably 0.75 to 2.0 %w/w include polyethylene glycol 7 and glyceryl cocoate. Suitable preservatives generally comprising 0.01 to 1.00 %w/w of the composition and suitably 0.10 to 0.30 %w/w, include phenoxyethanol and methyl dibromo glutaronitrile and mixtures thereof. Suitable conditioners, generally

30 comprising 0.1 to 5.0 %w/w of the composition and suitably 1.0 to 3.5%w/w include hydroxycetyl hydroxyethyl dimonium chloride and polyquaternium 39. Suitable



chelating agents, generally comprising up to 1.0 %w/w of the composition and suitably 0.1 to 0.3 %w/w include ethylene diamine tetra-acetic acid (EDTA), hydroethylene diamine triacetic acid (HEEDTA), diethylene triamine penta-acetic acid (DPTA) and cyclohexane diamine tetra-acetic acid (CTDA).

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The balance of the composition is typically water and/or other non-alcohol solvent so as to make up 100 %w/w of the composition. The preferred solvent is water which will generally constitute more than 50 %w/w of the skin wash composition. Other suitable non-alcohol solvents which may be included to aid solution of the  $\alpha$ -hydroxy acid include glycols such as propylene glycol and macrogols.

The skin wash compositions of the invention may be prepared by methods well known in the art and readily available to the skilled formulator. Generally the acid and the surfactants making up the detergent base, together with any additives, are dissolved in solvent, the pH of the resulting mixture is checked and adjusted if appropriate and the viscosity of the composition is set to the desired level by addition of thickening agents. The present invention extends to a process for preparing a skin wash composition as hereinbefore defined comprising the admixture of the  $\alpha$ -hydroxy acid or other acid as defined herein with the detergent base in an aqueous solvent system and adjusting the pH as required such that the pH of the composition is in the range 3.0 to 4.5.

The present invention additionally encompasses the use of a skin wash composition as hereinbefore defined wherein the acid is salicylic acid for the manufacture of a medicament for the treatment and/or prophylaxis of acne. The use of compositions of the present invention as hereinbefore defined as a cosmetic treatment for improving the appearance and condition of human skin also forms part of the invention.

The following examples further describe and demonstrate compositions falling within the scope of the invention. For the avoidance of doubt, the examples are solely for the purpose of illustration and are not limiting with respect to the scope of the invention.

**Example 1 - Skin Wash Composition containing Lactic Acid**

A composition comprising the following ingredients was prepared. The resulting

5 composition had a pH of approximately 3.5.

Ingredient		%w/w
10	$\alpha$ -hydroxy acid : lactic acid	1.0
	detergent base : decyl glucoside	3.5
	lauryl glucoside	3.6
	cocoamidopropyl betaine	5.0
	thickener : PEG 120 methyl glucose dioleate	3.2
	preservative : phenoxyethanol	0.25
	solvent : water	to 100 %
15		

**Example 2 - Skin Wash Composition containing Salicylic Acid**

A composition comprising the following ingredients was prepared. The resulting  
composition was a clear product having a pH of 4.5.

20

Ingredient		%w/w
25	acid : salicylic acid	2.0
	detergent base : lauryl glucoside	2.4
	decyl glucoside	2.0
	cocamidopropyl betaine	2.8
	neutralising agent : Tromethamine	1.5
	thickener : PEG 120 methyl glucose dioleate	4.0
	solvent : de-ionised water	to 100 %

30

**Example 3 - Skin Wash Composition containing Salicylic Acid**

The composition of Example 2 containing the additional excipients indicated below was prepared. The resulting clear product had a pH of 4.5.

5

conditioner	:	hydroxycetyl hydroxyethyl dimonium chloride
chelating agent	:	EDTA
preservative	:	phenoxyethanol
anti-inflammatory agent	:	allantoin & vitamin E acetate

**CLAIMS:**

1. A skin wash composition comprising from 0.1 to 10 % w/w of an  $\alpha$ -hydroxy acid, salicylic, maleic or pyruvic acid and a detergent base consisting of a mixture of from 2.0 to 15% w/w of a non-ionic alkylpolyglucoside surfactant and from 2.0 to 8.0% w/w of an amphoteric surfactant wherein the pH of said composition is in the range 3.0 to 4.5.
2. A composition according to claim 1, wherein the acid is citric acid, malic acid, maleic acid, pyruvic acid, hydroxy-octanoic acid, salicylic acid, lactic acid or glycolic acid.
3. A composition according to claim 2, wherein the acid is salicylic acid.
4. A composition according to claim 3 comprising from 0.2 to 5.0% w/w salicylic acid.
5. A composition according to claim 4 comprising 1.0 to 3.0% w/w salicylic acid.
6. A composition according to claim 2, wherein the  $\alpha$ -hydroxy acid is lactic acid which comprises from 0.1 to 5.0% w/w of the composition.
7. A composition according to claim 6 comprising from 0.5 to 2.5% w/w lactic acid.
8. A composition according to claim 2, wherein the  $\alpha$ -hydroxy acid is glycolic acid which comprises from 2.0 to 10.0% w/w of the composition.
9. A composition according to any one of claims 1 to 8, wherein the alkylpolyglucoside surfactant is decyl glucoside, lauryl glucoside or a mixture thereof.
10. A composition according to any one of claims 1 to 9, wherein the amphoteric surfactant comprises at least one betaine.

11. A composition according to claim 10, wherein the betaine is cocoamidopropyl betaine.
12. A composition according to any one of claims 1 to 11, further comprising a neutralizing agent.
13. A composition according to claim 12, wherein the said neutralizing agent is tromethamine, sodium hydroxide or triethanolamine.
14. A method for the preparation of a composition as defined in any one of claims 1 to 13, which method comprises admixing the  $\alpha$ -hydroxy acid, salicylic, maleic or pyruvic acid with the detergent base in an aqueous solvent system and adjusting the pH as required.
15. A composition as defined in any one of claims 3 to 5 and 9 to 13 for use in the treatment or prophylaxis of acne.
16. Use of a composition as defined in any one of claims 3 to 5 and 9 to 13 for the manufacture of a medicament for use in the treatment or prophylaxis of acne.
17. Use of a composition as defined in any one of claims 3 to 5 and 9 to 13 for the treatment or prophylaxis of acne.
18. An aqueous skin wash composition comprising from 0.1 to 10% w/w of an  $\alpha$ -hydroxy, salicylic, maleic or pyruvic acid and an amount of a detergent base not exceeding 30% w/w and which detergent base consists of a mixture of an amount of a non-ionic alkylpolyglucoside surfactant not exceeding 20% w/w and an amount of an amphoteric surfactant not exceeding 10% w/w wherein the pH of the composition is in the range 3.0 to 4.5.
19. A composition according to claim 18, wherein the acid is citric acid, malic acid, maleic acid, pyruvic acid, hydroxy-octanoic acid, salicylic acid, lactic acid or glycolic acid.

20. A composition according to claim 19, wherein the acid is salicylic acid.
21. A composition according to claim 20 comprising from 0.2 to 5.0% w/w salicylic acid.
22. A composition according to claim 21 comprising 1.0 to 3.0% w/w salicylic acid.
23. A composition according to claim 18 or 19, wherein the  $\alpha$ -hydroxy acid is lactic acid which comprises from 0.1 to 5.0% w/w of the composition.
24. A composition according to claim 23 comprising from 0.5 to 2.5% w/w lactic acid.
25. A composition according to claim 18 or 19, wherein the  $\alpha$ -hydroxy acid is glycolic acid which comprises from 2.0 to 10.0% w/w of the composition.
26. A composition according to any one of claims 18 to 25, wherein the alkylpolyglucoside surfactant is decyl glucoside, lauryl glucoside or a mixture thereof.
27. A composition according to any one of claims 18 to 26, wherein the alkylpolyglucoside surfactant comprises from 2.0 to 15% w/w of the composition.
28. A composition according to any one of claims 18 to 27, wherein the amphoteric surfactant comprises at least one betaine.
29. A composition according to claim 28, wherein the betaine is cocoamidopropyl betaine.
30. A composition according to any one of claims 18 to 29, wherein the amphoteric surfactant comprises from 2.0 to 8.0% w/w of the composition.
31. A composition according to any one of claims 18 to 30 further comprising a neutralizing agent.

32. A composition according to claim 31, wherein the neutralizing agent is tromethamine, sodium hydroxide or triethanolamine.
33. A method for the preparation of a composition as claimed in any one of claims 18 to 32, which method comprises admixing the  $\alpha$ -hydroxy acid or a salicylic, maleic or pyruvic acid with the detergent base in an aqueous solvent system and adjusting the pH.
34. A composition as defined in any one of claims 18 to 32 for use in the treatment or prophylaxis of acne.
35. Use of a composition as defined in any one of claims 18 to 32 for the manufacture of a medicament for use in the treatment or prophylaxis of acne.
36. Use of a composition as defined in any one of claims 18 to 32 for the treatment or prophylaxis of acne.
37. A commercial package comprising the composition as defined in any one of claims 1 to 13, 17 and 18 to 32 together with instructions for its use for the treatment or prophylaxis of acne.