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[NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL).</p> <p>(72) Inventors: BOWSER, Paul, Anthony; Dorset House, Latchford Road, Gayton, Wirral, Merseyside L60 3RW (GB). GRIEVERSON, Ailsa, Pauline, Hilary; 60 St Andrews Road, Bebington, Wirral, Merseyside L63 3DJ (GB). HANGAN, Desmond, Bernard; 35 Hookstone Drive, Little Sutton, South Wirral, Merseyside L64 4TE (GB). SCOTT, Ian, Richard; 1 Wilton Drive, Allendale, NJ 07401 (US).</p> </td> <td style="width: 50%; vertical-align: top; padding: 5px;"> <p>(74) Agent: BRYANT, Tracey; Unilever plc, Patent Division, Colworth House, Sharnbrook, Bedford MK44 1LQ (GB).</p> <p>(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, 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), ARIPO patent (KE, MW, SD).</p> <p><b>Published</b></p> <p><i>With international search report.</i></p> <p><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></p> </td> </tr> </table> |                           |                                                                                                                                          | <p>(21) International Application Number: PCT/EP94/02666</p> <p>(22) International Filing Date: 10 August 1994 (10.08.94)</p> <p>(30) Priority Data:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 30%;">9316847.4</td> <td style="width: 30%;">13 August 1993 (13.08.93)</td> <td style="width: 40%;">GB</td> </tr> <tr> <td>9316935.7</td> <td>13 August 1993 (13.08.93)</td> <td>GB</td> </tr> <tr> <td>9316924.1</td> <td>13 August 1993 (13.08.93)</td> <td>GB</td> </tr> </table> <p>(71) Applicant (for AU BB CA GB IE KE LK MN MW NZ SD TT only): UNILEVER PLC [GB/GB]; Unilever House, Blackfriars, London EC4P 4BQ (GB).</p> <p>(71) Applicant (for all designated States except AU BB CA GB IE KE LK MN MW NZ SD TT): UNILEVER N.V. 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| <p>(54) Title: ACYLATED HYDROXYALKANOATES AND THEIR USES</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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                                      |
| <p>(57) Abstract</p> <p>A composition for topical application includes a hydroxyalkanoate derivative having structure (I), where R<sup>1</sup> represents H- or acyl, R<sup>2</sup> represents alkyl of at least 2 carbon atoms, R<sup>3</sup> represents H-, alkyl, substituted or interrupted alkyl or a metallic, ammonium or alkanolammonium counterion. The hydroxyalkanoate derivative penetrates deeply into the skin and undergoes cleavage by enzymes in the skin to liberate the corresponding hydroxyalkanoate which benefits skin condition.</p> <div style="text-align: center; margin: 20px 0;"> <math display="block">  \begin{array}{c}  R^2 \quad O \\    \quad    \\  R^1 [O-CH-C]_m OR^3  \end{array}  \quad (I)  </math> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                           |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |           |                           |    |           |                           |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                           |    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

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ACYLATED HYDROXYALKANOATES AND THEIR USESFIELD OF INVENTION

5 The invention relates to the topical use of hydroxy  
alkanoate derivatives for improving the condition of human  
skin, particularly for moisturising the skin, hair, nails  
and other epithelial tissues, including the mucosae, also  
for reducing skin drying and for delaying the appearance  
10 of or eliminating wrinkles and fine lines on the skin.

The invention also relates to a method for the delivery to  
the epidermis of a hydroxyalkanoate for moisturising the  
skin, hair and nail and to compositions for topical use to  
15 achieve this benefit.

BACKGROUND TO THE INVENTION

Human skin consists essentially of two layers: the inner  
dermis and the outer epidermis, the former functioning  
20 mainly as a mechanical support for the latter.

The epidermis, which can be as little as 0.06 mm thick in  
the case of the eye lid to as much as 0.8 mm on the foot,  
itself comprises four or five layers, namely:

25

(i) the Stratum Malpighii, which is the germinative layer  
of cells at the base of the epidermis that adjoins the  
Dermis.

30 (ii) the Stratum Spinosum, the prickle cell layer which  
represents the first morphologically distinct stage in the  
differentiation of epidermal cells. It consists of  
numerous evenly spaced intercellular bridges -  
tonofilaments - each with a central thickening. The  
35 margins of several of these thickenings accounts for the  
appearance of desmosomes. The tonofilaments form the  
earliest precursor of keratin.

(iii) the Stratum Granulosum, the granular layer immediately above the prickle cell layer, which contains basophilic granules of keratohyalin. Also present in the Stratum Granulosum are the bridges (desmosomes and tonofilaments seen in the prickle cell layers), but their close apposition renders them less visible.

(iv) the Stratum Lucidum, seen especially in the epidermis of the hand and foot, comprises cells which are of even thickness and essentially non-nuclear.

(v) the Stratum Corneum, which lies above the Stratum Lucidum (when present), forms the outermost layer of the epidermis. The Stratum Corneum is composed of dead, flat, fully keratinized cells which lie on top of one another to a depth of from 0.02 to 0.8 mm. The Stratum corneum also possesses lipid materials which effectively form a waterproof barrier to the external surface of the skin.

Beneath the epidermis is the dermis which is composed of collagen, usually accompanied by elastin and reticulin. These materials are fibrous proteins embedded in a mucopolysaccharide ground substance. Several cellular types, together with nervous and vascular networks, are found in the dermis, together with specialised appendages, including sweat glands, hair follicles with associated sebaceous glands.

A soft, supple and flexible skin has a marked cosmetic appeal and these characteristics are attributes of normal functioning epidermis, particularly with respect to the young human subject. The outer layer of the epidermis, i.e. the stratum corneum, can however become dry and flaky following exposure to adverse climatic conditions, or by excessive contact with detergents or solvents which results in a loss of skin moisture. Consequently, the skin can lose its soft, supple and flexible

characteristics.

Emollients such as fats, phospholipids and stearols, have in the past been used to soften dry skin, but this can  
5 leave the skin greasy and unattractive. As an alternative, the topical application to the skin of classical humectants does not alleviate this problem, as these compounds are not particularly skin substantive and are generally rinsed from the skin during washing.

10

It is therefore apparent that there exists a continuing need for an effective methods for treating dry flaky skin to restore its original soft, supple and flexible characteristics, and indeed for maintaining these  
15 attributes of normal functioning epidermis.

In an article by Baiocchi et al in Cosmetics and Perfumery 90, 31-34 (1975), it is stated that sodium stearyl lactylate, when incorporated in a hand cream or lotion,  
20 results in a subjectively smooth and supple but not excessively greasy feeling when such creams or lotions are topically applied to the hands. However, the primary reason for including this lactylate in such formulations is to function as a very efficient emulsifier.

25

In an article by Osipow et al in Drug & Cosmet Ind, May 1969, 64ff, it is disclosed that sodium stearyl lactylate may be used in oil-in-water cosmetic creams as the emulsifier to impart body, lubricity and opalescence to  
30 the cream. It is alleged that its absorption to the skin may enhance its softening action.

In another article by Murphy in Cosmetics and Toiletries 94, 43ff (1979), the sorption of acyl lactylates on the  
35 skin was examined by using pigskin as a model. It is described that sodium isostearyl lactylate appears to reduce dryness and scaling of skin and restores a healthy

texture to dry skin.

Murphy in *Cosmetics and Toiletries* 93, 31 (1978) discusses a systematic approach to skin moisturisation and concludes  
5 that a combination of the pyrrolidone carboxylic acid (PCA) sodium salt, sodium lactate and lactic acid can be used as effective humectants to hold moisture in the skin.

EP 0 530 866 (Unilever) concerns novel sulfoxy alkanoate  
10 surfactants which it is believed are broken down by enzymes naturally present in the skin, or are naturally hydrolysed upon contact with the skin to yield "Benefit Reagents" e.g. Hydroxy acid and/or Fatty Alcohol.

EP 0 442 708 (Unilever) discloses cosmetic compositions  
15 containing 2-hydroxy alkanolic acids. Due to the presence of these acids in compositions, several benefits are imparted to the skin, such as an increase in the elasticity of the skin, particularly of the stratum  
20 corneum. Similarly, EP 0 007 785 (Unilever) discloses cosmetic compositions comprising 2-hydroxy alkanolic acids, which also give various skin benefits when topically applied to the skin.

25 However, the extent to which the moisturisation of skin, or its ability to remain moist without becoming dry, by topical application of so-called "moisturisers" as proposed by other workers in the field of cosmetic science, is not great. A search has therefore been  
30 conducted for other active materials that can be employed in this way for enhancing the moisturisation of skin or, once moisturised, for restricting the extent to which skin moisture loss will occur.

35 It has long been recognised that cream or lotion formulations containing lactic acid, usually as lactate ions in products near neutral pH, when applied topically

to the skin, can improve the flexibility and texture of the skin, and it is believed that lactate contributed to this effect. In studying this approach, we have applied such creams and lotions to the skin and have shown that  
5 although lactate can thereby be deposited on the surface of the stratum corneum which forms the outermost part of the skin, very little actually penetrates through the stratum corneum to the underlying regions of the epidermis, namely to the Stratum Granulosum and other  
10 strata below. This is thought to be due to the hydrophilic (i.e. lipophobic) property of lactate ions which renders them relatively incompatible with the lipids naturally present in the Stratum Corneum, and which thereby present a barrier to the adsorption of  
15 hydrophilic molecules.

While investigating the properties of derivatives of lactic acid that were more lipophilic than lactate itself, (eg. sodium lactate) we discovered that a range of acyl  
20 lactylates were more readily adsorbed on contact with the skin and indeed migrated through the skin to reach the epidermis beneath the Stratum Corneum at a rate and to an extent that was far superior to lactate ions. We also made the discovery using labelled materials and radio  
25 tracer techniques, that these acyl lactylate molecules were cleaved within the epidermis, most likely by the presence of endogenous esterases or other enzymes, to form lactate ions deep in the epidermis, as far as the Stratum Malpighii.

30

We extended our study of acyl lactylates to other molecules in the homologous series, where the head group is not lactylate but an alkyl hydroxy alkanoate of longer chain length, and we were again able to show that  
35 molecular cleavage occurred in the epidermis, following topical application of these molecules, to release in situ the corresponding hydroxy acid. This longer chain length

hydroxy acid was also shown to possess properties which enhanced the moisturisation of skin and/or reduced the extent to which moisture is lost from the skin.

- 5 The invention is accordingly concerned with the generation in situ in the epidermis of hydroxy alkanolic acids and the topical use of their corresponding acyl or alkyl derivatives to achieve this end.

# 10 DEFINITION OF THE INVENTION

Accordingly, one aspect of the invention provides the use of an effective amount of at least 0.001% by weight based on the total composition of a hydroxy alkanate derivative having the structure (1):



20

where

$R^1$  represents  $H-$  or  $C_x H_y O_z N_w -C-\overset{O}{||}$   
 $R^3$  represents  $H-$ ,  $C_x H_y O_z N_w -$  or a metallic, ammonium or alkanolammonium, counterion,  
 25  $p$  is an integer from 2 to 22,  
 $q$  is an integer from 5 to 45,  
 $x$  is an integer of from 1 to 20,  
 $y$  is an integer of from 3 to 41,  
 $z$  is 0, or an integer of from 1 to 10,  
 30  $w$  is 0, or an integer of from 1 to 5, and  
 $m$  is an integer of from 1 to 5

provided that when  $R^1$  is  $H-$ , then  $R^3$  is  $C_x H_y O_z N_w -$ , or when

35

$R^3$  is  $H-$  or a counterion, then  $R^1$  is  $C_x H_y O_z N_w -C-\overset{O}{||}$

- 40 to deliver to the epidermis, as a moisturiser for the skin, the corresponding 2-hydroxyalkanoate having the structure (2):



5

where X represents -H or a counterion;

in a composition intended for topical application to human skin; said compositions otherwise comprising a  
10 cosmetically acceptable vehicle.

The invention also provides a method for delivering to the epidermis a 2-hydroxy alkanoate having the structure (2):

15



20 which comprises the steps of

- i) applying topically to the skin a composition comprising the corresponding hydroxy alkanoate derivative having the structure (1):

25



30 as hereinbefore defined,

- ii) leaving the composition in contact with the skin for at least 10 seconds to permit the hydroxy alkanoate derivative to penetrate through the stratum corneum  
35 to reach the lower strata of the epidermis, and

- iii) cleaving the hydroxy alkanoate derivative in the epidermis by contact with esterases to provide the 2-hydroxy alkanoate.

40

The invention also provides a composition suitable for

topical application to the skin, hair, nails, mucosae and other epithelial tissue, which composition comprises:

- i) a hydroxy alkanoate derivative having the above defined structure (1):



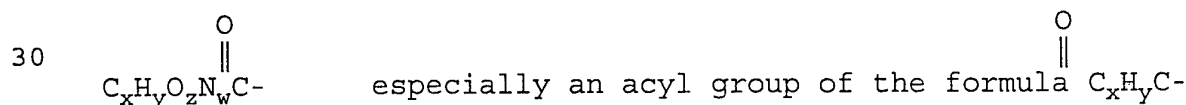
- ii) a cosmetically acceptable vehicle for the hydroxy alkanoate derivative;

the hydroxyalkanoate derivative possessing the ability of penetrating the stratum corneum and hydrolysing by enzymic cleavage within the epidermis to yield the corresponding hydroxyalkanoate having the structure (2):



thereby to moisturise the epithelial tissue.

In the above formulae, it is strongly preferred that  $R^1$  is an acyl group of the above mentioned general formulae



In such a group the value of x is preferably at least 5. A value of at least 9, for instance 9 to 13, is more preferred.

It is preferred that  $C_p H_q$ - represents an alkyl group, especially a straight chain alkyl group. In an alkyl group of formula  $C_p H_q$ - the value of q must of course be  $2p+1$ . Less preferred is that  $C_p H_q$  is alkenyl, such as

straight chain alkenyl.

It is preferred that the vehicle includes water. Certain preferred compositions include water-immiscible oil and/or  
5 water-soluble organic solvent such as ethanol. The amount of oil does not usually exceed 50% by weight of the composition, neither does the amount of water-soluble solvent, although in total these non-water materials may provide more than 50% by weight of the composition.

10

The invention may be applied in the context of a composition which is applied to skin, especially the face, and either left there or at least not removed immediately.

15 Penetration into the skin of hydroxyalkanoate derivative from such compositions can occur even when the hydroxyalkanoate is present at rather low concentration.

Such compositions frequently include some oil or oily  
20 material or organic solvent which is water soluble.

An alternative is to apply the invention in the context of a washing composition containing surfactant, and intended to be rinsed off after use. With such a composition it  
25 will probably be desired to include the hydroxyalkanoate derivative at a higher concentration.

In addition to their benefits in moisturising skin, topical application of the hydroxyalkanoate derivatives  
30 can also improve the skin surface in other respects by eliminating or by preventing the development of, or at least slowing, skin surfaces changes. Examples of such changes include, fine lines, wrinkles, blemishes, blotches, nodules, atrophy, pigmented spots, lesions,  
35 elastoic changes characterised by leathery, coarse, rough, dry and yellowish skin, photo-damages skin, loss of elasticity and other changes associated with ageing. In

summary, the hydroxyalkanoate derivatives can also have marked antiaging benefits to the skin.

The topical application of the hydroxyalkanoate derivatives can also be used for the treatment of spots, pimples and acne, especially for the inhibition of Propionibacterium acnes, which is believed to be a causative organism in the development of acne comedones.

Topical application of the hydroxyalkanoate derivatives can also be used in the treatment of dandruff on the scalp, again in view of the ability of these derivatives to inhibit microorganisms implicated in the development of dandruff.

15

#### DETAILED DISCLOSURE OF THE INVENTION

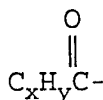
##### The hydroxy alkanoate derivatives

Hydroxy alkanoate derivatives for use in accordance with the invention are chosen from those having the structure (1) as herein defined, and are generally acyl or alkyl derivatives. Acyl derivatives are particularly preferred.

Examples of such acyl derivatives of hydroxy alkanoates include:

i) those where  $R^1$  in structure (1) represents the acyl group:

30



and where  $\text{C}_p\text{H}_q$  represents an alkyl group in the series  $\text{CH}_3\text{CH}_2-$  to  $\text{CH}_3(\text{CH}_2)_{19}-$

35

$m$  is 1 to 5, and

$R^3$  represents -H, or an alkali metal, an alkaline earth metal, ammonium or an alkanolammonium counterion.

Specific examples are the sodium, potassium, calcium, ammonium or triethanolammonium salts or free acids of:

- the n-propionyl derivative of 2-hydroxyoctanoate,  
 5 i.e. 2-(n-propionyloxy)octanoate, and the analogous  
 n-butanoyl,  
 n-hexanoyl,  
 n-octanoyl,  
 n-decanoyl,  
 10 n-dodecanoyl,  
 n-tetradecanoyl,  
 n-hexadecanoyl,  
 n-octadecanoyl,  
 n-linoleoyl,  
 15 n-linolenoyl,  
 $\gamma$ -linolenoyl,  
 n-arachidonoyl,  
 and columbinoyl derivatives of 2-hydroxyoctanoate,  
 2-(n-octanoyloxy)butanoate  
 20 2-(n-decanoyloxy)hexanoate  
 2-(n-dodecanoyloxy)butanoate  
 2-(n-dodecanoyloxy)hexanoate  
 2-(n-dodecanoyloxy)decanoate  
 2-(n-dodecanoyloxy)dodecanoate  
 25 2-(n-dodecanoyloxy)tetradecanoate  
 2-(n-dodecanoyloxy)hexadecanoate and  
 2-(n-dodecanoyloxyoctadecanoate, and the corresponding  
 acyl derivatives of di-, tri-, tetra and pentahydroxy  
 alkanoates.  
 30 ii) those where  $R^1$  in Structure (1) represents the acyl  
 group:



and where  $\text{C}_p\text{H}_q$  represents an alkyl group in the series  
 $\text{CH}_3\text{CH}_2-$  to  $\text{CH}_3(\text{CH}_2)_{19}-$

$C_xH_y-$  represents a branched chain alkyl group  
m is 1 to 5, and

$R^3$  represents -H, an alkali metal, an alkaline  
earth metal, ammonium or an alkanolammonium  
counterion.

5

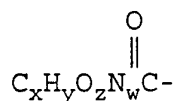
Specific examples are the sodium, potassium, calcium,  
ammonium or triethanolammonium salts or free acids of:

- 10 2-(iso-butanoyloxy)butanoate  
2-(iso-hexanoyloxy)butanoate  
2-(iso-octanoyloxy)butanoate  
2-(iso-octadecanoyloxy)butanoate  
2-(iso-butanoyloxy)octanoate  
15 2-(iso-octanoyloxy)octanoate  
2-(iso-octadecanoyloxy)octanoate  
2-(iso-dodecanoyloxy)octanoate  
2-(ethylglycoloyloxy)butanoate  
2-(ethylglycoloyloxy)octanoate  
20 2-(leucoylloxy)butanoate  
2-(leucoylloxy)octanoate  
2-(mandeloyloxy)butanoate  
2-(mandeloyloxy)octanoate  
2-(ethyl glycoloyloxy)octanoate  
25 2-(12-hydroxy octadecanoyloxy)octanoate  
2-(ethyl glycoloyloxy)butanoate  
2-(12-hydroxy octadecanoyloxy)butanoate, and  
the corresponding acyl derivatives of di-, tri-, tetra and  
pentahydroxyalkanoates.

30

iii) those where  $R^1$  in structure (1) represents the acyl  
group:

35



where  $C_pH_q$  represents an alkyl group in the series  
 $CH_3CH_2-$  to  $CH_3(CH_2)_{19}-$

m is 1 to 5

R<sup>3</sup> represents -H, or an alkali metal, an alkaline earth metal, ammonium or alkanolammonium counterion.

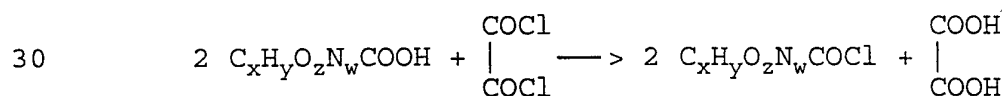
5 Specific examples are the sodium, potassium, calcium, ammonium or triethanolammonium salts or free acids of

- 2-(cocoamidopropanoyloxy)butanoate  
 2-(pyroglutamoyloxy)butanoate  
 10 2-(cholesteroyloxy)butanoate  
 2-(ceramidinoxy)butanoate  
 2-(cocoamidopropanoyloxy)octanoate  
 2-(pyroglutamoyloxy)octanoate  
 2-(cholesteroyloxy)octanoate  
 15 2-(ceramidinoxy)octanoate, and  
 the corresponding acyl derivatives of di-, tri-, tetra- and pentahydroxy alkanoates.

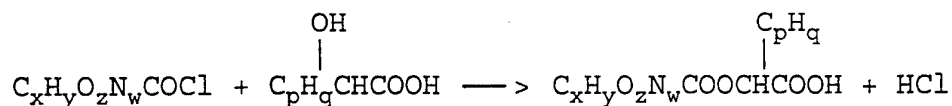
Some compounds of this invention in which R<sup>1</sup> is an acyl group are known compounds for which preparative routes have been published. References includes US-A-4058540, preparations given in EP-A-54435 and Taylor et al, Tetrahedron letters 60 5285 (19).

25 A route for the preparation of such compounds comprises:

- i) forming an acyl chloride by reacting an alkanolic acid with oxalyl chloride, thus:



ii) acylating a 2-hydroxy alkanolic acid with the acyl chloride to form the acyl 2-hydroxy alkanoate thus:



Examples of alkyl esters of hydroxy alkanoates, within structure (1) are:

- those where  $R^1$  in structure (1) represents -H,  
5  $R^3$  represents  $C_xH_y-$ , and  
 $m$  is 1.

Specific examples are:

- 10 methyl 2-hydroxybutanoate  
n-butyl 2-hydroxybutanoate  
n-hexyl 2-hydroxybutanoate  
n-octyl 2-hydroxybutanoate  
n-dodecyl 2-hydroxybutanoate  
15 n-octadecyl 2-hydroxybutanoate  
ethyl 2-hydroxyhexanoate  
ethyl 2-hydroxyoctanoate, and  
n-dodecyl 2-hydroxyoctanoate.

- 20 The 2-hydroxyalkanoic acids are well known compounds.  
Their alkyl esters can be made by conventional  
esterification techniques.

- It is not intended that the above examples form an  
25 exhaustive list of acyl derivatives and alkyl esters of  
hydroxy alkanoates, as there are many more compounds that  
comply with the structure (1), that can be used in  
accordance with the invention.

- 30 The amount of hydroxyalkanoate derivative to be employed  
in accordance with the invention as an effective amount  
will normally be from 0.001 to 50%, preferably at least  
0.1%, e.g. from 0.1 to 30%, and most preferably at least  
0.5%, e.g. from 0.5 to 20% by weight of the composition.

35

As will be explained and illustrated later in the  
specification, the composition for use in accordance with

the invention can either be employed as a "leave-on" product, in which case it is intended to be applied to the skin and left in place, or it can be employed as a "rinse-off" or "wipe-off" product, usually for cleansing the skin, in which case it will normally be rinsed or wiped from the skin shortly after application, e.g., after washing. Thus for "leave-on" products, the most preferred amount of hydroxyalkanoate derivative will be from 0.1 to 2%, whereas, for "rinse-off" or "wipe-off" products, the corresponding preferred amount will be from 0.1 to 20% or more, in both instances expressed in terms of percentage by weight of the composition.

#### Cleansing Compositions

A significant form of this invention is therefore a cleansing composition containing from 5 to 40% by weight of an acyl derivative of a hydroxyalkanoate, having the above structure (1) in which  $R^3$  represents -H or a metallic, ammonium or alkanolammonium counterion, while  $R^1$

represents  $C_xH_yO_zN_w-C(=O)-$ , preferably  $C_xH_yC(=O)-$ . Such a cleansing composition generally also contains water.

In a related aspect, the invention provides a method for cleaning the skin or the hair which comprises the steps of

- (i) applying to the skin or hair cleansing composition as specified above;
- (ii) forming a lather on the skin or hair by massaging in the presence of added water, thereby to cleanse the skin or hair; and
- (iii) subsequently rinsing the lather from the skin or hair with water.

#### Cosmetically Acceptable Vehicles

The hydroxyalkanoate derivatives, as herein described,

will in use normally be applied to human skin in the form of a composition that also comprises a cosmetically acceptable vehicle, that is intended to facilitate the distribution of the hydroxyalkanoate derivative on and  
5 over the skin surface at an appropriate concentration.

The composition can thus be solid, semi-solid or liquid in nature, dependent upon the choice of vehicle. The vehicle itself can be inert or it can possess beneficial  
10 physiological properties of its own.

The selection of a vehicle for this purpose presents a wide range of possibilities depending on the required product form of the composition. Suitable vehicles can be  
15 classified as described hereinafter.

Vehicles are therefore substances that can act as diluents, dispersants, or solvents for the hydroxy alkanoate derivative which ensures that it can be applied  
20 to and distributed evenly over the skin at an appropriate concentration. The vehicle is preferably one which can aid penetration of the hydroxy alkanoate derivative deep into the epidermis, to enable it more readily to influence the condition of the skin.

25 Compositions according to the invention can include water as a vehicle, and/or at least one cosmetically acceptable vehicle other than water.

30 Vehicles other than water can include liquid or solid emollients, solvents, humectants, thickeners and powders. Examples of each of these types of vehicle, which can be used singly or as mixtures of one or more vehicles, are as follows:

35 Emollients, such as stearyl alcohol, glyceryl monoricinoleate, mink oil, cetyl alcohol, isopropyl

isostearate, stearic acid, isobutyl palmitate, isocetyl  
stearate, oleyl alcohol, isopropyl laurate, hexyl laurate,  
decyl oleate, octadecan-2-ol, isocetyl alcohol, eicosanyl  
alcohol, behenyl alcohol, cetyl palmitate, silicone oils  
5 such as dimethylpolysiloxane, di-n-butyl sebacate,  
isopropyl myristate, isopropyl palmitate, isopropyl  
stearate, butyl stearate, polyethylene glycol, triethylene  
glycol, lanolin, cocoa butter, corn oil, cotton seed oil,  
olive oil, palm kernel oil, rapeseed oil, safflower seed  
10 oil, evening primrose oil, soybean oil, sunflower seed  
oil, avocado oil, sesame seed oil, coconut oil, arachis  
oil, castor oil, acetylated lanolin alcohols, petroleum  
jelly, mineral oil, squalane, squalene, butyl myristate,  
isostearic acid, palmitic acid, isopropyl linoleate, decyl  
15 oleate, myristyl myristate;

Propellants for aerosols, such as propane, butane,  
isobutane, dimethyl ether, carbon dioxide, nitrous oxide;

20 Solvents, such as ethyl alcohol, methylene chloride,  
isopropanol, acetone, ethylene glycol monoethyl ether,  
diethylene glycol monobutyl ether, diethylene glycol  
monoethyl ether, dimethyl sulphoxide, dimethyl formamide,  
tetrahydrofuran;

25 Powders, such as chalk, talc, fullers earth, kaolin,  
starch, gums, colloidal silica sodium polyacrylate, tetra  
alkyl and/or trialkyl aryl ammonium smectites, chemically  
modified magnesium aluminium silicate, organically  
30 modified montmorillonite clay, hydrated aluminium  
silicate, fumed silica, carboxyvinyl polymer, sodium  
carboxymethyl cellulose, ethylene glycol monostearate,  
ethylene glycol distearate;

35 The cosmetically acceptable vehicle will usually form from  
10 to 99.99%, preferably from 10 to 99% and most  
preferably from 50 to 99% by weight of the composition,

and can, in the absence of other cosmetic adjuncts, form the balance of the composition.

OPTIONAL SKIN BENEFIT MATERIALS AND COSMETIC ADJUNCTSPenetration Enhancer

5 The composition for use according to the invention can also optionally comprise a penetration enhancer which can potentiate the benefit of the hydroxy alkanoate derivative by improving its delivery through the stratum corneum to its site of action deep in the epidermis.

10

The penetration enhancer can accordingly function in a variety of ways. It can for example, improve the distribution of the hydroxy alkanoate derivative on the skin surface, or it can increase its partition into the stratum corneum and beyond from the composition when applied topically, so aiding its passage to a lower level within the epidermis. Other mechanisms enhancing the benefit of the hydroxy alkanoate derivative may also be involved.

20

Examples of penetration enhancers include:

2-methyl propan-2-ol

Propan-2-ol

25 Hexan-2,5-diol

POE(2) ethyl ether

Di(2-hydroxypropyl) ether

Pentan-2,4-diol

POE(2) methyl ether

30 Propan-1-ol

1,4 Dioxane

Butan-1,4-diol

Propylene glycol dipelargonate

Polyoxypropylene 15 stearyl ether

35 Octyl alcohol

POE ester of oleyl alcohol

Oleyl alcohol

- Lauryl alcohol
- Dioctyl adipate
- Dicapryl adipate
- Diisopropyl adipate
- 5 Diisopropyl sebacate
- Dibutyl sebacate
- Diethyl sebacate
- Dimethyl sebacate
- Dioctyl sebacate
- 10 Dibutyl suberate
- Dioctyl azelate
- Dibenzyl sebacate
- Dibutyl phthalate
- Dibutyl azelate
- 15 Ethyl myristate
- Dimethyl azelate
- Butyl myristate
- Dibutyl succinate
- Didecyl phthalate
- 20 Decyl oleate
- Ethyl caproate
- Ethyl salicylate
- Isopropyl myristate
- Isopropyl palmitate
- 25 Ethyl laurate
- 2-ethyl-hexyl pelargonate
- Isopropyl isostearate
- Butyl laurate
- Benzyl benzoate
- 30 Butyl benzoate
- Hexyl laurate
- Ethyl caprate
- Ethyl caprylate
- Butyl stearate
- 35 Benzyl salicylate
- 2-Pyrrolidone
- 1-Methyl-2-pyrrolidone

5-Methyl-2-pyrrolidone  
1,5-Dimethyl-2-pyrrolidone  
1-Ethyl-2-pyrrolidone  
Sugar esters  
5 Tetrahydrofurfural alcohol  
Urea  
Diethyl-m-toluamide, and  
1-Dodecylazacycloheptan-2-one

- 10 The amount of penetration enhancer, when employed in accordance with the invention, will normally be from 0.1 to 50%, preferably from 0.5 to 25% and most preferably from 0.5 to 10% by weight of the composition.

15 Emulsions and Oily Materials

The composition according to the invention can optionally comprise one or more oils or other materials having the properties of an oil.

20

- A composition in accordance with the invention may be formulated as an emulsion having both aqueous and oil phases. This applies particularly to leave-on products which are frequently formulated as emulsions. In an  
25 emulsion, an oil or oily material will normally be present, together with an emulsifier to provide either a water-in-oil emulsion or an oil-in-water emulsion, depending largely on the average hydrophilic-lipophilic balance (HLB) of the emulsifier employed.

30

Examples of suitable oils include mineral oils and vegetable oils, silicone oils and oily materials such as those already proposed herein as emollients.

- 35 The quantity of oil, if present, is often at least 5% by weight, often remains a minority of the composition, in other words 5 to 50% by weight. Preferred are at least

10% and/or not more than 30% by weight.

The oil or oily material, when present for the purposes for forming an emulsion, may form up to 90%, e.g.

5 preferably from 10 to 80% by volume of the composition.

#### Emulsifier

The composition according to the invention can also  
10 optionally comprise one or more emulsifiers the choice of which will normally determine whether a water-in-oil or and oil-in-water emulsion is formed. Duplex emulsions, ie water-in-oil-in-water or oil-in-water-in-oil, can also be formed.

15

When a water-in-oil emulsion is required, the chosen emulsifier or emulsifiers should normally have an average HLB value of from 1 to 6. When an oil-in-water emulsion is required, a chosen emulsifier or emulsifiers should  
20 have an average HLB value of >6.

Examples of suitable emulsifiers are set below in Table 1 in which the chemical name of the emulsifiers is given together with an example of a trade name as commercially  
25 available, and the average HLB value.

TABLE 1

| 30 | Chemical Name         | Trade Name | HLB Value |
|----|-----------------------|------------|-----------|
|    | of Emulsifier         |            |           |
|    | Sorbitan trioleate    | Arlacel 85 | 1.8       |
|    | Sorbitan tristearate  | Span 65    | 2.1       |
| 35 | Glycerol monooleate   | Aldo MD    | 2.7       |
|    | Glycerol monostearate | Atmul 84S  | 2.8       |
|    | Glycerol monolaurate  | Aldo MC    | 3.3       |

|    |                              |                  |        |
|----|------------------------------|------------------|--------|
|    | Sorbitan sesquioleate        | Arlacel 83       | 3.7    |
|    | Sorbitan monooleate          | Arlacel 80       | 4.3    |
|    | Sorbitan monostearate        | Span 60          | 4.7    |
|    | Cetyl dimethicone copolyol   | Abil EM-90       | 4 to 6 |
| 5  | Poloxyethylene (2)           |                  |        |
|    | stearyl ether                | Brij 72          | 4.9    |
|    | Poloxyethylene sorbitol      |                  |        |
|    | beeswax derivative           | G-1702           | 5      |
|    | PEG 200 dilaurate            | Emerest 2622     | 6.3    |
| 10 | Sorbitan monopalmitate       | Arlacel 40       | 6.7    |
|    | Polyoxyethylene (3.5)        |                  |        |
|    | nonyl phenol                 | Emulgen 903      | 7.8    |
|    | PEG 200 monostearate         | Tegester PEG     |        |
|    |                              | 200 MS           | 8.5    |
| 15 | Sorbitan monolaurate         | Arlacel 200      | 8.6    |
|    | PEG 400 dioleate             | Tegester PEG     |        |
|    |                              | 400-DO           | 8.8    |
|    | Polyoxyethylene (5)          |                  |        |
|    | monostearate                 | Ethofat 60-16    | 9.0    |
| 20 | Polyoxyethylene (4) sorbitan |                  |        |
|    | monostearate                 | Tween 61         | 9.6    |
|    | Polyoxyethylene (4) lauryl   |                  |        |
|    | ether                        | Brij 30          | 9.7    |
|    | Dimethicone copolyol         | Abil B 8842      | >10    |
| 25 | Polyoxyethylene (5) sorbitan |                  |        |
|    | monooleate                   | Tween 81         | 10.0   |
|    | PEG 300 monooleate           | Neutronyx 834    | 10.4   |
|    | Polyoxyethylene (20)         |                  |        |
|    | sorbitan tristearate         | Tween 65         | 10.5   |
| 30 | Polyoxyethylene (20)         |                  |        |
|    | sorbitan trioleate           | Tween 85         | 11.0   |
|    | Polyoxyethylene (8)          |                  |        |
|    | monostearate                 | Myrj 45          | 11.1   |
|    | PEG 400 monooleate           | Emerest 2646     | 11.7   |
| 35 | PEG 400 monostearate         | Tegester PEG 400 | 11.9   |
|    | Polyoxyethylene 10           |                  |        |
|    | monooleate                   | Ethofat 0/20     | 12.2   |

|    |                             |                  |      |
|----|-----------------------------|------------------|------|
|    | Polyoxyethylene (10)        |                  |      |
|    | stearyl ether               | Brij 76          | 12.4 |
|    | Polyoxyethylene (10)        |                  |      |
|    | cetyl ether                 | Brij 56          | 12.9 |
| 5  | Polyoxyethylene (9.3)       |                  |      |
|    | octyl phenol                | Triton X-100     | 13.0 |
|    | Polyoxyethylene (4)         |                  |      |
|    | sorbitan monolaurate        | Tween 21         | 13.3 |
| 10 | PEG 600 monooleate          | Emerest 2660     | 13.7 |
|    | PEG 1000 dilaurate          | Kessco           | 13.9 |
|    | Polyoxyethylene sorbitol    |                  |      |
|    | lanolin derivative          | G-1441           | 14.0 |
|    | Polyoxyethylene (12)        |                  |      |
| 15 | lauryl ether                | Ethospense LA-12 | 14.4 |
|    | PEG 1500 dioleate           | Pegospense 1500  | 14.6 |
|    | Polyoxyethylene (14)        |                  |      |
|    | laurate                     | Arosurf HFL-714  | 14.8 |
|    | Polyoxyethylene (20)        |                  |      |
| 20 | sorbitan monostearate       | Tween 60         | 14.9 |
|    | Polyoxyethylene 20 sorbitan |                  |      |
|    | monooleate                  | Tween 80         | 15.0 |
|    | Polyoxyethylene (20)        |                  |      |
|    | stearate                    | Myrj 49          | 15.0 |
| 25 | Polyoxyethylene (20)        |                  |      |
|    | stearyl ether               | Brij 78          | 15.3 |
|    | Polyoxyethylene (20)        |                  |      |
|    | sorbitan monopalmitate      | Tween 40         | 15.6 |
|    | Polyoxyethylene (20) cetyl  |                  |      |
| 30 | ether                       | Brij 58          | 15.7 |
|    | Triethanolamine stearate    |                  | >16  |
|    | Polyoxyethylene (25)        |                  |      |
|    | oxypropylene                |                  |      |
|    | monostearate                | G-2162           | 16.0 |
| 35 | Polyoxyethylene (20)        |                  |      |
|    | sorbitol monolaurate        | Tween 20         | 16.7 |
|    | Polyoxyethylene (23)        |                  |      |

25

|   |                       |                 |      |
|---|-----------------------|-----------------|------|
|   | lauryl ether          | Brij 35         | 16.9 |
|   | Polyoxyethylene (50)  |                 |      |
|   | monostearate          | Myrj 53         | 17.9 |
|   | PEG 4000 monostearate | Pegospense 4000 |      |
| 5 |                       | MS              | 18.7 |

-----

The foregoing list of emulsifiers is not intended to be limiting and merely exemplifies selected emulsifiers which are suitable for use in accordance with the invention.

It is to be understood that two or more emulsifiers can be employed if desired.

The amount of emulsifier or mixtures thereof, to be incorporated in the composition of the invention, when appropriate is from 1 to 50%, preferably from 2 to 20% and most preferably from 2 to 10% by weight of the composition.

20

#### Retinoids

The composition for use according to the invention optionally can also comprise a retinoid, such as retinoic acid or retinol (Vitamin A) and/or derivative thereof, further to enhance the benefits to skin.

25

In addition to retinol itself, examples of derivatives of retinol include:

30

Retinyl acetate  
Retinyl butyrate  
Retinyl propionate  
Retinyl octanoate  
35 Retinyl laurate  
Retinyl palmitate  
Retinyl oleate

Retinyl linoleate, and  
Retinyl linolenate.

The amount of retinoid, when present in the composition  
5 according to the invention is from 0.01 to 10% and  
preferably 0.1 to 5% by weight of the composition.

#### Tocopherol and Tocopheryl Esters

10 The composition for use according to the invention  
optionally can also comprise a tocopherol (vitamin E  
group), as an antioxidant for the composition, and to  
limit oxidative damage to skin. The vitamin E group  
comprises  $\alpha$ -tocopherol,  $\beta$ -tocopherol,  $\gamma$ -tocopherol and  $\delta$ -  
15 tocopherol. The composition according to the invention  
optionally can also comprise a tocopheryl ester, such as  
tocopheryl acetate.

The amount of a tocopherol, or ester thereof, when present  
20 in the composition according to the invention, is from  
0.0001 to 20%, preferably from 0.0001 to 10% by weight of  
the composition.

#### Water

25 The composition of the invention can also comprise water,  
usually up to 90%, preferably from 5 to 80% by volume.  
Water can function as the cosmetically acceptable vehicle.

30 Preferred is that the vehicle contains water, or aqueous  
ethanol, in an amount which is a majority of the  
composition, that is to say over 50%. If ethanol is  
present, the amount will generally remain a minority of  
the composition, such as from 10 to 50%. Even when  
35 ethanol is included, the quantity of water will generally  
be substantial, amounting to a majority of the composition  
or nearly so, such as at least 40% of the composition.

### Surfactants

A composition for use in accordance with the invention may contain one or more surfactants notably at least 1% thereof, in addition to the hydroxy alkanoate derivatives, which are cosmetically acceptable and suitable for topical application to the skin. This applies particularly when the composition is a cleansing composition containing an acyl derivative of hydroxyalkanoate as surfactant. Such compositions may contain a co-surfactant, for example in an amount up to 30% by weight of the composition, preferably from 5% or 10% to 25% or 20% by weight.

A co-surfactant may assist in providing a good lather when the composition is used. Examples of possible skin cleansing surfactants are now given.

### Anionic surfactant

The composition of the invention can comprise soap or a non-soap anionic surfactant which is preferably chosen from alkyl sulphate, alkyl ether sulphate, alkyl sulphonate, alkyl aryl sulphonate, olefin sulphonate, acyl sarcosinate, acyl tauride, acyl isethionate, monoalkyl sulphosuccinate, dialkylsulphosuccinate, N-acylated  $\alpha$ -amino acid, alkyl carboxylate, monoalkyl phosphate and dialkyl phosphate.

Specific examples of anionic surfactants include:

alkyl sulphates, such as sodium lauryl sulphate [eg. EMPICOL CX available from Albright & Wilson], and triethanolamine lauryl sulphate [e.g. EMPICOL TL40/T, available from Albright & Wilson].

alkylether sulphates, such as sodium lauryl ether sulphate [eg. EMPICOL ESB70, available from Albright & Wilson].

alkyl sulphonates, such as sodium alkane (C<sub>13-18</sub>)  
sulphonate [eg. HOSTAPUR SAS 30, available from Hoechst].

alkylaryl sulphonates, such as sodium alkyl benzene  
5 sulphonate [eg. TEEPOL CM44, available from Shell].

olefin sulphonates, such as sodium olefin sulphonate (C<sub>5-18</sub>) [eg. HOSTAPUR OS, available from Hoechst].

10 acyl sarcosinates, having the structure: (51)

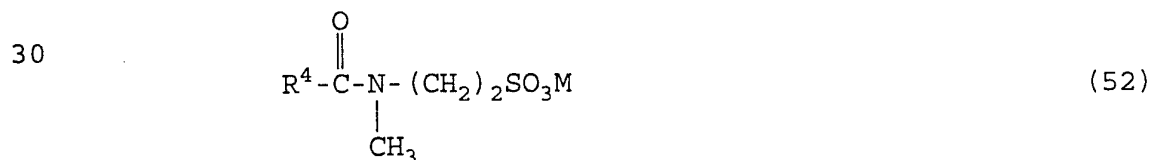


where R<sup>3</sup> is chosen from C<sub>6-14</sub> alkyl, and

20 M is a counterion chosen from alkali metals, ammonium and substituted ammonium such as alkanolammonium.

An example of an acyl sarcosinate having the structure  
(51), is sodium lauryl sarcosinate [eg. HAMPOSYL L-95,  
25 available from Grace].

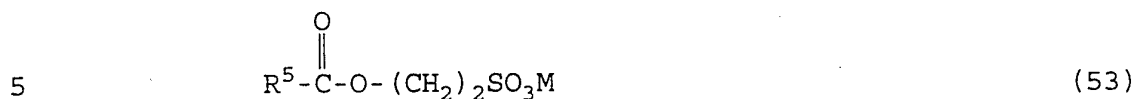
acyl taurides, having the structure (52):



35 where R<sup>4</sup> is chosen from C<sub>8-18</sub> alkyl

An example of an acyl tauride having the structure (52) is  
coconut methyl taurine [eg. FENOPEN TC 42, available from  
International Spaicalty Products].

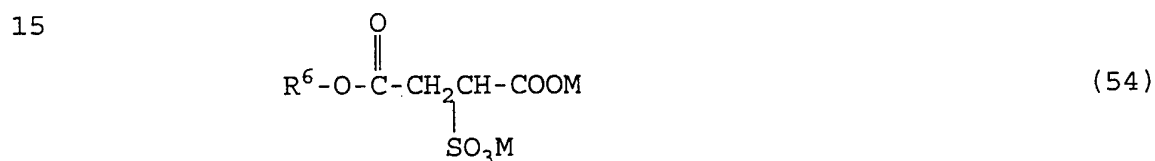
acyl isethionates, having the structure (53):



where  $\text{R}^5$  is chosen from  $\text{C}_{8-18}$  alkyl.

An example of an acyl isethionate having the structure (53) is sodium acyl isethionate [eg. JORDAPON C1, available from Jordon].

monoalkyl sulphosuccinates, having the structure (54):



where  $\text{R}^6$  is chosen from  $\text{C}_{10-20}$  alkyl.

Examples of monoalkyl sulphosuccinates having the structure (54) include:

sodium lauryl sulphosuccinate [eg. EMPICOL SLL, available from Albright & Wilson].

magnesium alkyl sulphosuccinate [eg. ELFANOL 616 Mg, available from AKZO].

sodium lauryl ethoxysulphosuccinate [eg. EMPICOL SDD, available from Albright & Wilson].

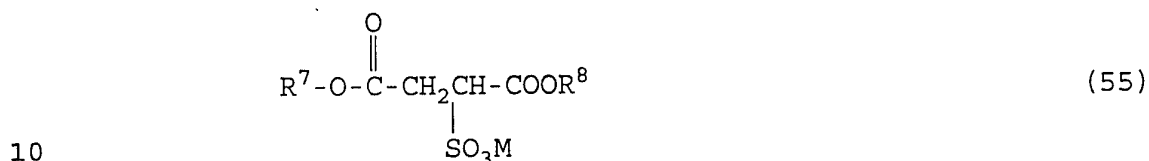
coconut monoethanolamide ethoxysulphosuccinate [eg. EMPICOL SGG].

disodium lauryl polyglycolether sulphosuccinate [eg. SURTAGENE S30, available from CHEM-Y].

polyethyleneglycol sulphosuccinate [eg. REWOPOL SBFA 30, available from REWO].

dialkyl sulphosuccinates, having the structure (55):

5



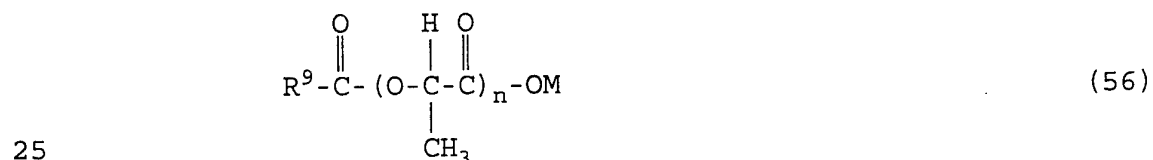
10

where  $\text{R}^7$  and  $\text{R}^8$  are the same or different, and are chosen from  $\text{C}_{6-14}$  alkyl.

15 An example of a dialkyl sulphosuccinate having the structure (55) is sodium dilauryl sulphosuccinate [eg. EMCOL 4500, available from Witco].

acyl lactylates, having the structure (56):

20



25

where  $\text{R}^9$  is chosen from  $\text{C}_{6-16}$  alkyl,

and  $n$  is 1 or 2.

30

An example of an acyl lactylate having the structure (56) is decanoyl lactylate [eg. PATIONIC 122a, available from Patterson, CJ].

35 N-acylated  $\alpha$ -amino acids, such as sodium lauroyl glutamate [eg. ACYLGLUTAMATE LS-11, available from Ajinomoto Co. Inc].

alkyl ether carboxylates, such as

40  $\text{C}_{12-14}\text{O}(\text{EO})_4\text{OCH}_2\text{CO}_2\text{Na}$  [eg. AKYPO RLM 38, available from Akzo].

monoalkyl phosphates and dialkyl phosphates, such as dioctyl phosphate.

Cationic surfactant

5

The composition of the invention can also comprise a cationic surfactant. Suitable cationic surfactants are those with the structure (57):

10



15

where  $R^1$ ,  $R^2$ ,  $R^3$  and  $R^4$  each represents alkyl or aryl groups,  
and X represents a halogen counterion.

20 Preferred cationic surfactants in accordance with structure (57) include:

Hexadecyl trimethyl ammonium chloride, such as Arquad 16, available from Akzo.

25

Dihydrogenated tallow dimethyl ammonium chloride, such as Arquad 2HT, available from Akzo.

30 Dodecyl benzyl dimethyl ammonium bromide, such as Amoxyl BR 1244, available from Seppic.

Cocoamidopropyl trimethyl ammonium chloride, such as Empigen CSC, available from Albright & Wilson.

Amphoteric surfactant

The composition of the invention can also comprise an amphoteric surfactant. Suitable amphoteric surfactants are derivatives of aliphatic quaternary ammonium, phosphonium and sulphonium compounds, wherein the aliphatic radicals contain from 8 to 18 carbon atoms, and may be straight chain or branched, and further contain an anionic water-solubilising group, such as carboxyl, sulphonate, sulphate, phosphate or phosphonate.

Preferred amphoteric surfactants include:

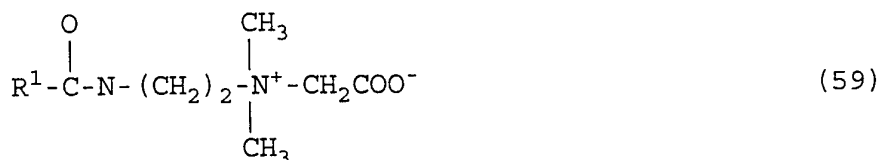
Alkyl betaines, having the structure (58):



where  $\text{R}^1$  is  $\text{C}_{1-16}$  alkyl.

An example of an alkyl betaine having the structure (58) is lauryldimethyl betaine [eg. EMPIGEN BB, available from Albright & Wilson].

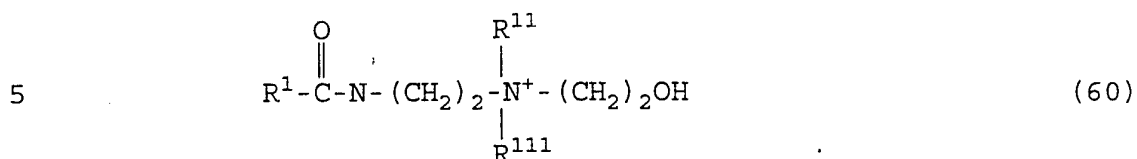
Alkylamidopropyl betaines, having the structure (59):



An example of an alkylamidopropyl betaine having the structure (59) is cocamidopropyl betaine [eg. TEGOBETAIN L7, available from Goldschmidt].

Alkylamphoglycinates or Alkylamphopropionates having the

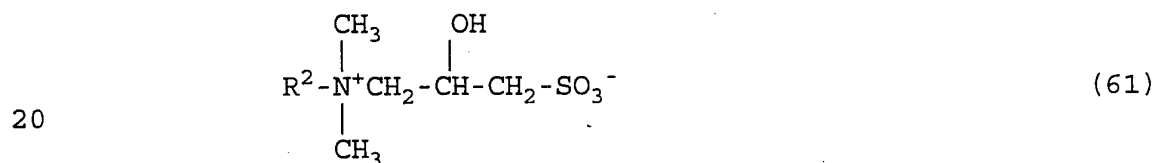
structure (60):



where  $\text{R}^{11}$  is chosen from H,  $\text{CH}_2\text{COO}^-$  and  $(\text{CH}_2)_2\text{COO}^-$ , and  
 $\text{R}^{111}$  is chosen from  $\text{CH}_2\text{COO}^-$  and  $(\text{CH}_2)_2\text{COO}^-$

Suitable examples of compounds (60) are cocoamphoglycinate (available from GAF), and cocoamphopropionate.

Sultaines, having the structure (61):



where  $\text{R}^2$  is chosen from  $\text{C}_{12-16}$  alkyl alkylamido groups.

An example of a sultaine having the structure (61) is cocamidopropylhydroxysultaine [eg. CYCLOTERIC BET-CS, available from Alcolac).

The most preferred amphoteric surfactant are lauryl dimethyl betaine and cocamidopropyl betaine.

Such amphoteric surfactants can contribute to the foaming of the skin cleansing composition, while ameliorating the harshness of the anionic surfactant.

#### Nonionic surfactant

The composition of the invention can also comprise alkoxyated or glycosidic nonionic surfactant having an HLB of 8 or more. Above this value nonionics generally

form clear isotropic solutions in combination with the other surfactants in the ranges defined above. Preferred nonionic surfactants are polyoxyethylene alkyl esters and polyoxyethylene alkyl ethers and alkyl polyglycosides.

5

A suitable example of a polyoxyethylene alkyl ester is that having the CTFA designation Polysorbate 80 which is a mixture of oleate esters of sorbitol and sorbitol anhydrides, condensed with approximately 20 moles of ethylene oxide. Also suitable is Polysorbate 20 which is a mixture of laurate esters of sorbitol and sorbitol anhydrides condensed with approximately 20 moles of ethylene oxide.

15 Polysorbate 80 and Polysorbate 20 are available commercially as TWEEN 80 and TWEEN 20 respectively, from ICI Americas.

Also suitable for use in the compositions of the invention is the polyethylene glycol ether of C<sub>9-11</sub> alcohol with an average of 8 ethoxy units, which is available commercially as NONIDET LE-8T or as SYNPERONIC 91-8T, and the polyethylene glycol ether of C<sub>12-15</sub> alcohol with an average of 9 ethoxy units which is available commercially as DOBANOL 25-9.

Particularly useful alkyl polyglycosides include the glycosides of glucose or glucose oligomers where the alkyl chain can be C<sub>8-16</sub> and the average number of glucose units is 1 to 2. A suitable example is ORAMIX NS 10 which is the glucoside of C<sub>10-12</sub> fatty alcohol with an average of about 1.5 glucose units.

Also suitable for use in compositions of the invention are high molecular weight silicone surfactants, such as a high molecular weight polymer of dimethyl polysiloxane with polyoxyethylene and/or polyoxypropylene side chains having

a molecular weight from 10,000 to 50,000.

The dimethyl polysiloxane polymer is conveniently provided as a dispersion in a volatile siloxane, the dispersion  
5 comprising, for example, from 1 to 20% by volume of the polymer and from 80 to 99% by volume of the volatile siloxane. Ideally, the dispersion consists of a 10% by volume of the polymer dispersed in the volatile siloxane.

10 Examples of the volatile siloxanes in which the polysiloxane polymer can be dispersed include polydimethyl siloxane (pentamer and/or hexamer).

A particularly preferred silicone surfactant is  
15 cyclomethicone and dimethicone copolyol, such as DC 3225C Formulation Aid available from DOW CORNING. Another is laurylmethicone copolyol, such as DC Q2-5200, also available from Dow Corning.

20 The amount of silicone surfactant, when present in the composition will normally be up to 25%, preferably from 0.5 to 15% by weight of the emulsion.

#### Other Cosmetic Adjuncts

25

Examples of other cosmetic adjuncts which can optionally be employed in the composition for use according to the invention include preservatives, such as para-hydroxy benzoate esters; antioxidants, such as butyl hydroxy  
30 toluene; humectants, such as glycerol, sorbitol, 2-pyrrolidone-5-carboxylate, dibutylphthalate, gelatin, polyethylene, glycol, preferably PEG 200-600; buffers, such as lactic acid together with a base such as triethanolamine or sodium hydroxide; ceramides of  
35 synthetic, animal or plant origin; pseudoceramides; phospholipids; vitamins, such as 1,25 dihydroxy cholecalciferol; waxes, such as beeswax, ozokerite wax,

- paraffin wax, plant extracts, such as Aloe vera, cornflower, witch hazel, elderflower, cucumber, thickeners; activity enhancers; colourants; perfumes; and sunscreen materials such as ultrafine titanium dioxide and organic sunscreens such as p-aminobenzoic acid and esters thereof, ethylhexyl p-methoxycinnamate, 2-ethoxyethyl p-methoxycinnamate and butyl methoxydibenzoylmethane, and mixtures thereof.
- 10 In a further preferred composition, the hydroxy alkanoate derivative is combined with ceramides, pseudoceramides, polyol fatty acid polyesters, sterols, particularly cholesterol, galactosyldiacyl-glycerols, glycosphingolipids, fatty acids and esters thereof and mixtures thereof and other ingredients, such as mevalonic acid, hexadecylsuccinic acid monobehenyl ester ethoxylate (7.3 EO) and/or derivatives thereof to produce a liposomal dispersion.
- 15 20 A further preferred composition may also contain in combination with the hydroxy alkanoate derivative and optional additional ingredients disclosed above, an organic acid component chosen from hydroxy alkanoic acids, such as alpha, beta and omega hydroxyacids, especially glycolic acid, lactic acid, citric acid, tartaric acid, tartronic acid and 2-hydroxyoctanoic acid, and keto alkanoic acids, esters thereof and mixtures thereof.

Cosmetic adjuncts can form the balance of the composition.

30

#### pH

- The composition of the invention will normally have a pH value of from 4 to 9, preferably from 4.5 to 8.5. The pH can be adjusted as necessary by the addition of an alkali or acid as a pH adjustant, and/or by the addition of a buffer, such as a citrate buffer or a phosphate buffer.
- 35

PRESERVATION OF THE COMPOSITION

The composition for use in accordance with the invention is preferably preserved against microbial attack in such a manner that it will enjoy an extended shelf life following  
5 manufacture and prior to sale and use. Ideally the composition will have an indefinite shelf life.

Examples of the methods that can be employed to achieve  
10 preservation of the composition, includes the following:

(i) Sterilisation

The composition according to the invention can be  
15 preserved by sterilisation to remove or kill substantially all viable microbial contaminants. This can be achieved for example by irradiation using a lethal dose of gamma rays, by heat sterilisation or by ultrafiltration using techniques that are well established in the pharmaceutical  
20 industry.

(ii) Chemical Preservative

The composition according to the invention can also be  
25 preserved by including in it a chemical preservative which functions to prevent the growth of or kill bacteria, fungi or other microorganisms.

Examples of chemical preservatives include ethanol,  
30 benzoic acid, sodium benzoate, sorbic acid, potassium sorbate, sodium propionate and the methyl, ethyl, propyl and butyl esters of p-hydroxybenzoic acid. The amount of chemical preservative that can be incorporated in the composition according to the invention will generally be  
35 from 0.05 to 5%, preferably from 0.1 to 2% by weight, the amount chosen being sufficient to arrest microbial proliferation.

(iii) Water activity depressants

The composition according to the invention can also be preserved by the inclusion of a water activity depressant  
5 such as glycerol, propylene glycol, sorbitol, sugars and salts, for examples alkali metal halides sulphates and carboxylates. When employing a water activity depressant, sufficient should be incorporated in the composition according to the invention to reduce the water activity  
10 ( $\alpha_w$ ) from 1 to  $< 0.9$ , preferably to  $< 0.85$  and most preferably  $< 0.8$ , the lowest of these values being that at which yeasts, moulds and fungi will not proliferate.

PROCESS

15 The invention also provides a process for preparing a composition according to the invention which comprises the steps of mixing an effective amount of an hydroxy alkanooate derivative, as herein defined, together with a  
20 cosmetically acceptable carrier for the derivative.

Product Form and Container

The composition of the invention can be formulated as  
25 liquids, for example as a lotion, shampoo, milk or cream for use in conjunction with an applicator such as roll-ball applicator, or a spray device such as an aerosol can containing propellant, or a container fitted with a pump to disperse the liquid product. Alternatively, the  
30 compositions of the invention can be solid or semi-solid, for example sticks, creams or gels, for use in conjunction with a suitable applicator or simply a tube, bottle or lidded jar, or as a liquid-impregnated fabric such as a tissue wipe.

35 The invention accordingly also provides a closed container containing a composition as herein defined.

USE OF THE COMPOSITION

The acyl (and/or alkyl) derivatives of hydroxyalkanoate,  
5 when applied to the stratum corneum, will penetrate into  
the epidermis or cutaneous appendages, such as eccrine,  
apocrine and sebaceous glands, where hydrolysis by  
endogenous skin or microbial esterases will cleave the  
10 molecule to release in situ the corresponding hydroxy  
alkanoate, together with the fatty acid or fatty alcohol  
that forms the residue of the applied hydroxy alkanoate  
derivative.

As stated earlier, the composition as applied to the skin  
15 surface can either be a "leave-on" product or a "rinse-  
off" or "wipe-off" product. When the composition is a  
leave-on product, such as a cream or lotion, it can be  
applied to the skin from a suitable container and spread  
over a desired area of skin, such as the face and neck,  
20 shoulders, arms and legs, and then rubbed in using the  
hands and fingers, or using an applicator. The  
hydroxyalkanoate derivative being lipophilic in nature,  
will penetrate into and through the stratum corneum, by  
virtue of the lipid materials that normally reside in that  
25 region close to the skin surface. On reaching the strata  
below the superficial stratum corneum cells, or  
penetration into the cutaneous appendages, esterases are  
encountered that hydrolyse the hydroxy alkanoate  
derivative to release the desired hydroxyalkanoate.

30

Repeated application of such leave-on products, for  
example at night and in the morning on a daily basis, will  
provide a continuous supply of hydroxyalkanoate to the  
epidermis, which will thereby benefit by its improving  
35 ability to retain moisture i.e. to become moisturised.  
Other attributes of the skin will also improve,  
particularly elasticity, disappearance of fine lines and

wrinkles, and the skin will altogether become more healthy with improved tone and condition.

When the composition for use in accordance with the invention is a "rinse-off" product, it will generally function as a skin cleanser. A suitable amount, for example 5 to 10 ml of the skin cleanser comprising the hydroxy alkanoate derivative, which can itself have surfactant properties, but is preferably accompanied by a co-surfactant, is applied to the skin and formed into a lather in the presence of water. After cleansing the skin, surplus product is generally rinsed from the skin and the skin is then dried. The rinse-off product can also be used for washing the hair or for cleansing the entire body surface, for example in the shower.

Although when using a rinse-off cleansing product, it would be expected that little or no product would remain on the skin, we have surprisingly found that a significant amount of the hydroxy alkanoate derivative is retained by the skin after each successive wash. This enables the skin to retain moisture to a greater extent than with other "rinse-of" products.

For this reason a hydroxyalkanoate derivative in accordance with this invention might be included as part of a composition for washing dishes by hand, thereby to enhance its mildness.

When the composition is a wipe-off product, it will also generally function as a skin cleanser, especially for removing make-up. A suitable amount, for example 0.5 to 5ml of the skin cleanser comprising the hydroxy alkanoate derivative can be applied to the skin, particularly where make-up is to be removed, and rubbed-in. The area of treated skin can then be wiped with a cloth, tissue or with cotton wool to remove surplus of the composition

together with make-up that has been loosened from the skin.

Particularly preferred examples of both "rinse-off" and  
5 "leave-on" products in accordance with the invention and  
those that are used as part of the normal shaving process,  
namely as a pre-shave product, or as an after-shave  
product. Both products in use are intended to moisturise  
or otherwise condition the skin, prior to or after  
10 shaving, so as to enhance the shaving process, and this  
can be achieved by delivery to the epidermis of an hydroxy  
alkanoate, in the manner described hereinbefore.

Shaving treatment products such as these can be employed  
15 either by men to remove unwanted facial hair or beard, or  
by women to remove unwanted hair from other parts of the  
body surface, particularly the legs. Wherever such  
products are used, they possess the ability to enhance the  
moisturisation of the skin, so improving its condition  
20 after the shaving process.

Because men's shaving products are used regularly, they  
can serve to provide regular delivery of hydroxyalkanoate  
to the skin.

25 According to a particularly preferred embodiment of this  
aspect of the invention, after-shave products contain as a  
cosmetically acceptable vehicle, more than about 85% by  
weight of ethanol and water. Additionally, such shaving  
30 products can contain other cosmetic adjuncts such as  
glycerine, perfume, perfume solubilisers to promote  
product clarity, vitamins and derivatives thereof such as  
vitamin E acetate and Vitamin A palmitate, thickeners such  
as Carbopol 980, triethanolamine and other adjuncts as  
35 conventionally used in pre- or after-shave products.

EXAMPLESExample 1. Synthesis of 2-(stearoyl)octanoic acid

Stearic acid was dissolved under reflux in sodium-dried  
5 diethyl ether and oxalyl chloride added and further  
refluxed for 2½ hours to complete the reaction to stearoyl  
chloride. Excess ether and oxalyl chloride were first  
removed by warm distillation, and then, last traces of  
oxalyl chloride were removed by pumping under vacuum.

10

2-hydroxy octanoic acid was dissolved in pyridine  
(potassium hydroxide dried) and chloroform (ethanol free,  
anhydrous sodium sulphate/ $\text{Al}_2\text{O}_3$  column dried) and then  
stearoyl chloride added rapidly to the 2-hydroxy octanoic  
15 acid solution and shaken vigorously. The reaction vessel  
was left for 60 hours with occasional shaking.

The whole reaction mixture was then dissolved in diethyl  
ether and transferred to a separating funnel at  $-10^\circ\text{C}$ .  
20 The ether solution was washed free of pyridine/salts with  
four aliquots of 0.5N hydrochloric acid cooled to  $0^\circ\text{C}$ .  
The ether solution was then washed with three aliquots of  
ice cold distilled water before drying over anhydrous  
sodium sulphate.

25

The solvent was then carefully removed in a dry nitrogen  
stream with heating at  $35^\circ\text{C}$ . Further purification of the  
stearoyl 2-hydroxy octanoic acid was then achieved by  
chromatography on a gel column made up and eluted with  
30 petroleum spirit (boiling range  $40-60^\circ\text{C}$ ).

Example 2

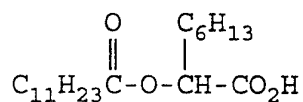
A similar reaction was carried out using lauryl (i.e. dodecanoyl) chloride. It was added to 2-hydroxyoctanoic acid in pyridine and dry chloroform over 1 hour at 0°C.

- 5 The reaction mixture was stirred for one further hour at 0°C, then allowed to warm to 20°C and allowed to stand for 48 hours.

The product was extracted as in Example 1, then its  
10 solution in a small volume of ether was neutralised to pH 7 with sodium hydroxide solution at 0°C. The solution was frozen and freeze dried.

The nmr spectrum of the product in deuteriochloroform  
15 corresponded with information in the literature.

A sample of this substituted octanoate was acidified, extracted into ether and converted to its methyl ester by reaction in diazo methane. This was subjected to glc.  
20 The material eluting from the glc column was identified by mass spectroscopy, which confirmed the expected molecular weight and also showed fragments corresponding to loss of CH<sub>3</sub>O and COOCH<sub>3</sub>. Lauroyl fragments were also observed, confirming that the preparation had led to the intended 2-  
25 (dodecanoyloxy)octanoic acid of structure



30

The above preparation was also carried out using <sup>14</sup>C radiolabelled 2-hydroxyoctanoic acid. The resulting radiolabeled 2-(decanoyloxy)octanoic acid had a specific  
35 activity of about 2.5 μCi. mg<sup>-1</sup>, which is about 900 mCi. mole<sup>-1</sup>. It was neutralised to its sodium salt and diluted to an aqueous solution with a concentration of 55.6 mM, corresponding to 2.0 % by weight.

Three pieces of full thickness skin, taken from pig ear, were cut to 4 x 4cm and pinned out on a polystyrene foam support. 30 $\mu$ l aliquots of the above solution were applied to four of the test pieces with a pipette and spread over the entire surface using the pipette tip. The fifth piece was left untreated.

After 15 minutes the first test piece was swabbed with dry cotton wool to remove excess liquid. Ten pieces of Desquame tape, available from Diastron, were applied to the skin and then removed. Each piece strips cells from the skin. The later pieces of tape thus strip cells from further into the skin than the earlier pieces.

Each strip of tape was placed in a scintillation vial with 1ml of phosphate buffer (pH 7).

The other two pieces of skin were treated similarly, but the test solution was left on them for one hour, or two hours before drying with cotton wool and tape stripping.

At the end of the experiment, 10ml scintillation fluid was added to each vial, and the amount of radio label was determined (as disintegrations per minute) using a scintillation counter. These results are set out in the following table, and show penetration of the 2-(decanoyloxy)octanoate to a considerable depth into the skin.

| TAPE NO. | DPM at stated time after application |        |         |
|----------|--------------------------------------|--------|---------|
|          | 15 MIN                               | 1 HOUR | 2 HOURS |
| 1        | 341.8                                | 474.3  | 374.8   |
| 2        | 145.3                                | 205.9  | 236.9   |
| 3        | 99.6                                 | 168.4  | 193.9   |
| 4        | 105.8                                | 115.5  | 153.2   |
| 5        | 95.8                                 | 98.8   | 68.7    |
| 6        | 51.5                                 | 81.4   | 93.3    |
| 7        | 56.3                                 | 63.2   | 92.6    |
| 8        | 45.4                                 | 49.9   | 48.9    |
| 9        | 24.0                                 | 48.8   | 44.3    |
| 10       | 13.3                                 | 49.6   | 32.5    |

In a similar experiment nine tape strips were taken after six hours. The first three strips were incubated in 3ml of phosphate buffer. The next three strips and the final three strips were likewise incubated. After 30 minutes the buffer solutions were spotted onto a thin-layer chromatography plate (bearing silica gel as the stationary phase).

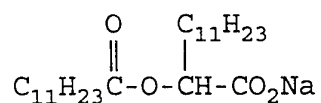
The plate was eluted with 80:20:2 hexane:ether:acetic acid mixture. The spots on the plate were detected and quantified by their emitted radiation. Each lane on the plate displayed two spots, one corresponding to hydrolysis products of the octanoate and a second spot corresponding to the substituted octanoate itself. The results (mean of five repeats) were:

|    |              | <u>% of Total label</u> |
|----|--------------|-------------------------|
|    | Tapes 1 to 3 |                         |
|    | Peak 1       | 8.1                     |
|    | Peak 2       | 91.9                    |
| 5  |              |                         |
|    | Tapes 4 to 6 |                         |
|    | Peak 1       | 54.4                    |
|    | Peak 2       | 45.6                    |
| 10 |              |                         |
|    | Tapes 7 to 9 |                         |
|    | Peak 1       | 99.5                    |
|    | Peak 2       | 0.5                     |

These results show that hydrolysis of the 2-(dodecanoyloxy)octanoate had occurred in each instance, and had proceeded almost to completion for the material which had penetrated furthest into the skin.

### Example 3

The dodecanoyl derivative of 2-hydroxy dodecanoic acid, incorporating  $^{14}\text{C}$  radiolabel, was prepared in analogous manner to the preceding example. It had specific activity of  $4.17\mu\text{Ci. mg}^{-1}$ . It was neutralised to its sodium salt of formula:



and a 56mM solution was tested on pig skin, taking tape strips after 15 minutes, 1 hour and 2 hours as in the previous example. The results, set out in the following table, again show penetration to considerable depth into the skin. For tapes numbered 4 onwards there was more radiolabel after 1 hour than after 15 minutes. The final line in the table shows the amount of radiolabel removed onto the cotton wool used to remove liquid from the pig skin before taking tape strips.

| TAPE NO.    | DPM at stated time after application |        |         |
|-------------|--------------------------------------|--------|---------|
|             | 15 MIN                               | 1 HOUR | 2 HOURS |
| 1           | 519800                               | 593000 | 354500  |
| 2           | 374500                               | 344200 | 151500  |
| 3           | 236700                               | 176100 | 104000  |
| 4           | 105400                               | 198000 | 93730   |
| 5           | 69770                                | 137700 | 66770   |
| 6           | 60100                                | 101000 | 75590   |
| 7           | 54510                                | 103700 | 50530   |
| 8           | 41870                                | 60280  | 53910   |
| 9           | 28690                                | 58830  | 65890   |
| 10          | 30590                                | 65690  | 45630   |
| Cotton wool | 701000                               | 56920  | 92080   |

The invention is further illustrated by the following examples of formulations.

Example 4 - Water-in-oil skin cream

| <u>Ingredients</u>              | <u>% w/w</u> |
|---------------------------------|--------------|
| Silicone oil                    | 20.00        |
| Sodium chloride                 | 2.00         |
| Sodium 2-(octanoyloxy)butanoate | 1.00         |
| Whitener                        | 0.15         |
| Preservatives                   | 0.36         |
| Sodium hydroxide                | 1.00         |
| Water                           | to 100.00    |

Example 5 - Water-in-oil skin cream

|    | <u>Ingredients</u>           | <u>% w/w</u> |
|----|------------------------------|--------------|
|    | Silicones                    | 20.50        |
| 5  | Whitener                     | 0.20         |
|    | Preservatives                | 0.30         |
|    | Perfume                      | 0.15         |
|    | Ammonium hydroxide           | 7.95         |
|    | 2-(Decanoyloxy)hexanoic acid | 1.00         |
| 10 | Humectant                    | 10.00        |
|    | Ammonium chloride            | 2.00         |
|    | Water                        | to 100.00    |

15 Example 6 - Water-in-oil skin cream with sunscreens

|    | <u>Ingredients</u>                   | <u>% w/w</u> |
|----|--------------------------------------|--------------|
|    | Silicones                            | 24.00        |
|    | Whitener                             | 0.10         |
| 20 | Preservatives                        | 0.01         |
|    | Potassium 2-(dodecanoyloxy)octanoate | 1.50         |
|    | Potassium chloride                   | 1.50         |
|    | Humectants                           | 5.00         |
|    | Evening primrose oil                 | 3.00         |
| 25 | Sunscreens                           | 4.00         |
|    | Bactericides                         | 0.30         |
|    | Water                                | to 100.00    |

Example 7 - Oil-in-water skin cream

|    | <u>Ingredients</u>          | <u>% w/w</u> |
|----|-----------------------------|--------------|
|    | Emulsifier                  | 10.00        |
| 5  | Silicone oil                | 8.00         |
|    | Thickener                   | 0.50         |
|    | Whitener                    | 0.10         |
|    | Preservatives               | 0.10         |
|    | 2-(Octanoyloxy)butyric acid | 2.00         |
| 10 | Humectant                   | 10.00        |
|    | Evening primrose oil        | 2.00         |
|    | Sunscreens                  | 3.00         |
|    | Bactericides                | 0.30         |
|    | Triethanolamine             | 3.10         |
| 15 | Water                       | to 100.00    |

Example 8 - Face mask

|    |                                         |              |
|----|-----------------------------------------|--------------|
| 20 | <u>Ingredients</u>                      | <u>% w/w</u> |
|    | Kaolin                                  | 35.00        |
|    | Bentonite                               | 5.00         |
|    | Cetyl alcohol                           | 2.00         |
|    | Potassium 2-(tetradecanoyloxy)octanoate | 5.25         |
| 25 | Glycerol                                | 10.00        |
|    | Methyl paraben                          | 0.10         |
|    | Potassium dodecyl sulphate              | 2.00         |
|    | Perfume                                 | 0.75         |
|    | Water                                   | to 100.00    |

Example 9 - Cleansing Cream

|    | <u>Ingredients</u>                 | <u>% w/w</u> |
|----|------------------------------------|--------------|
|    | Lanette wax SX                     | 16.00        |
| 5  | Mineral oil                        | 20.00        |
|    | Microcrystalline wax               | 3.00         |
|    | Glycerol                           | 5.00         |
|    | Sodium 2-(isostearoyloxy)octanoate | 1.00         |
|    | Water                              | 55.00        |
| 10 | Perfume                            |              |
|    | Preservative                       |              |

Example 10 - Cleansing Milk

|    |                                 |              |
|----|---------------------------------|--------------|
| 15 | <u>Ingredients</u>              | <u>% w/w</u> |
|    | Mineral oil                     | 10.00        |
|    | Cetyl alcohol                   | 0.50         |
|    | Stearic acid                    | 3.00         |
| 20 | Sodium 2-(hexanoyloxy)octanoate | 1.00         |
|    | TEA                             | 1.80         |
|    | Water                           | 83.7         |
|    | Perfume                         |              |
|    | Preservative                    |              |

Example 11 - Cleansing Mousse

|    | <u>Ingredients</u>                           | <u>% w/w</u> |
|----|----------------------------------------------|--------------|
|    | Sodium lauryl ether sulphate (28%)           | 18.00        |
| 5  | Sodium cocoamidopropyl betaine               | 7.50         |
|    | Sodium 2-( $\gamma$ -linolenoyloxy)octanoate | 1.00         |
|    | Glycerol                                     | 10.00        |
|    | Ethanol                                      | 5.00         |
|    | Vitamin E acetate                            | 0.10         |
| 10 | Cremophore RH410                             | 0.50         |
|    | Redoderm LIS 80                              | 1.00         |
|    | Preservative                                 | 0.26         |
|    | Ammonium hydroxide (29%) to pH 7.00          |              |
|    | Colourant                                    |              |
| 15 | Perfume                                      |              |
|    | Propane/Butane                               | 3.00         |
|    | Water                                        | to 100.00    |

20 Example 12 - Mild Facial Cleanser

|    | <u>Ingredients</u>                               | <u>% w/w</u> |
|----|--------------------------------------------------|--------------|
|    | TEA 2-(linoleoyloxy)octanoate                    | 20.00        |
|    | Glycerol                                         | 10.00        |
| 25 | Sodium cocoyl isethionate                        | 7.00         |
|    | Cocamidopropyl betaine                           | 4.00         |
|    | Polyoxeyethylene (EO) 20 sorbitan<br>monolaurate | 3.00         |
|    | Hydroxypropyl methylcellulose                    | 0.20         |
| 30 | Preservative                                     | 0.20         |
|    | Perfume                                          | 0.10         |
|    | Citric acid to pH 6.50                           |              |
|    | Water                                            | to 100.00    |

Example 13 - Liquid Soap

|    | <u>Ingredients</u>                     | <u>% w/w</u> |
|----|----------------------------------------|--------------|
|    | Potassium 2-(dodecanoyloxy)butanoate   | 15.00        |
| 5  | Triethanolammonium N-lauroyl glutamate | 9.00         |
|    | Cocoamidopropyl betaine                | 4.00         |
|    | Propyleneglycol hydroxy isostearate    | 1.00         |
|    | Trisodium citrate                      | 7.00         |
|    | Preservative                           | 0.26         |
| 10 | Perfume                                | 0.15         |
|    | Triethanolamine to pH 7.00             |              |
|    | Water                                  | to 100.00    |

15 Example 14 - Cleansing Beauty Bar

|    | <u>Ingredients</u>             | <u>% w/w</u> |
|----|--------------------------------|--------------|
|    | Sodium n-myristoyl dilactylate | 15.00        |
|    | TEA 2-(mandeloyloxy)octanoate  | 15.00        |
| 20 | Sodium n-stearoyl aspartate    | 10.00        |
|    | Glycerol                       | 8.00         |
|    | Diglycerol                     | 1.00         |
|    | Perfume                        | 0.50         |
|    | Preservatives                  | 0.26         |
| 25 | Colourant                      | 0.10         |
|    | Water                          | to 100.00    |

Example 15 - Deep Cleansing Gel

|    | <u>Ingredients</u>                   | <u>% w/w</u> |
|----|--------------------------------------|--------------|
|    | Mineral oil                          | 35.00        |
| 5  | Lanolin                              | 10.00        |
|    | Coco diethanolamide                  | 4.00         |
|    | Stearic acid                         | 2.43         |
|    | Oleic acid                           | 3.64         |
|    | Sodium 2-(12-hydroxy octadecanoyloxy |              |
| 10 | butanoate                            | 1.00         |
|    | Sodium hydroxide                     | 0.38         |
|    | Water                                | 43.29        |
|    | Colourant                            |              |
|    | Perfume                              |              |
| 15 | Preservative                         | 0.26         |

Example 16 - Moisturising Lotion

|    |                                        |              |
|----|----------------------------------------|--------------|
| 20 | <u>Ingredients</u>                     | <u>% w/w</u> |
|    | Glycerol                               | 5.00         |
|    | TEA                                    | 1.00         |
|    | TEA 2-(cocoamidopropanoyloxy(butanoate | 1.00         |
|    | Magnesium aluminium silicate           | 4.00         |
| 25 | Glyceryl monostearate                  | 0.70         |
|    | Mineral oil                            | 3.00         |
|    | Stearic acid                           | 2.50         |
|    | Cetyl alcohol                          | 0.30         |
|    | Cerasynt IP                            | 1.50         |
| 30 | Silicone oil                           | 1.00         |
|    | Preservative                           | 0.26         |
|    | Perfume                                | 0.25         |
|    | Carbopol 934 (2%)                      | 3.00         |
|    | Water                                  | to 100.00    |

Example 17 - Skin Cream

|    | <u>Ingredients</u>                     | <u>% w/w</u> |
|----|----------------------------------------|--------------|
|    | Lanette wax SX                         | 10.00        |
| 5  | Cetyl alcohol                          | 4.00         |
|    | Mineral oil                            | 4.00         |
|    | Glycerol                               | 6.00         |
|    | Ammonium 2-(pyroglutamoyloxy)octanoate | 1.00         |
|    | Preservative                           | 0.26         |
| 10 | Perfume                                |              |
|    | Water                                  | to 100.00    |

Example 18 - Dry Skin Cream

|     |                                        |              |
|-----|----------------------------------------|--------------|
| 15  | <u>Ingredients</u>                     | <u>% w/w</u> |
|     | Mineral oil                            | 8.00         |
|     | Petrolatum                             | 4.50         |
|     | Ceresin wax                            | 1.75         |
| 20  | Candilla wax                           | 1.00         |
|     | Glyceryl monostearate                  | 1.75         |
|     | Stearic acid                           | 2.25         |
|     | Cetyl alcohol                          | 1.40         |
|     | Isopropyl palmitate                    | 6.00         |
| 25  | Laureth - 23                           | 0.36         |
|     | Sorbitan oleate                        | 1.40         |
|     | Preservative                           | 0.26         |
|     | Glycerol                               | 3.00         |
|     | Sodium isostearoyl lactylate           | 1.00         |
| 30. | Potassium 2-(cholesteroyloxy)butanoate | 1.00         |
|     | TEA                                    | 0.60         |
|     | Carbopol 934 (2%)                      | 10.00        |
|     | Trisodium EDTA                         | 0.03         |
|     | Perfume                                | 0.30         |
| 35  | Water                                  | to 100.00    |

Example 19 - Barrier Cream

|    | <u>Ingredients</u>             | <u>% w/w</u> |
|----|--------------------------------|--------------|
|    | Stearic Acid                   | 6.00         |
| 5  | Cetyl alcohol                  | 3.00         |
|    | Lanolin                        | 3.00         |
|    | Soft paraffin                  | 2.00         |
|    | TEA 2-(n-octanoyloxy)butanoate | 0.50         |
|    | Sodium hydroxide               | 0.65         |
| 10 | Kaolin                         | 18.00        |
|    | Perfume                        |              |
|    | Colourant                      |              |
|    | Preservative                   |              |
|    | Water                          | to 100.00    |
| 15 |                                |              |

Example 20 - Anti-ageing Eye Gel

|    | <u>Ingredients</u>               | <u>% w/w</u> |
|----|----------------------------------|--------------|
| 20 | Glycerol                         | 3.00         |
|    | Potassium 2-(acetyloxy)octanoate | 0.50         |
|    | Vitamin E acetate                | 0.10         |
|    | Aloe vera gel                    | 0.25         |
|    | TEA to pH 7.00                   |              |
| 25 | Carbopol 934 (2%)                | 25.00        |
|    | Preservative                     | 0.15         |
|    | Perfume                          |              |
|    | Colourant                        |              |
|    | Water                            | to 100.00    |

Example 21 - Aftershave Lotion

|   | <u>Ingredients</u>                  | <u>% w/w</u> |
|---|-------------------------------------|--------------|
|   | Ethanol                             | 40           |
| 5 | Glycerin                            | 2            |
|   | Sodium 2-(iso-stearoyloxy)butanoate | 0.5          |
|   | PEG hydrogenated castor oil         | 5            |
|   | Perfume                             | 3            |
|   | Water                               | to 100       |

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Example 22. Aftershave Gel

|    | <u>Ingredients</u>                  | <u>% w/w</u> |
|----|-------------------------------------|--------------|
| 15 | Ethanol                             | 30           |
|    | Glycerin                            | 2            |
|    | Sodium 2-(iso-stearoyloxy)octanoate | 0.1          |
|    | PEG hydrogenated castor oil         | 0.55         |
|    | Vitamin E acetate                   | 0.1          |
| 20 | Emollient oil                       | 1            |
|    | Carbopol 980                        | 1            |
|    | Triethanolamine                     | 2            |
|    | Perfume                             | 0.4          |
|    | Perfume solubiliser                 | 0.5          |
| 25 | Water                               | to 100       |

Example 23. Skin Cleansing Milk

|    | <u>Ingredients</u>           | <u>% w/w</u> |
|----|------------------------------|--------------|
|    | PEG-20 Sorbitan Monostearate | 1.80         |
| 5  | Sorbitan monostearate        | 1.50         |
|    | Mineral Oil                  | 39.9         |
|    | Butyl 2-hydroxyoctanoate     | 5.00         |
|    | Triethanolamine              | 0.70         |
|    | Stearic Acid                 | 1.40         |
| 10 | Porpylparaben                | 0.10         |
|    | Polyethylene glycol          | 8.00         |
|    | Methyl paraben               | 0.10         |
|    | Ethylhydroxyethyl cellulose  | 0.54         |
|    | Sorbic acid                  | 0.002        |
| 15 | Water                        | to 100       |

Example 24. Dry Skin Cream

|    | <u>Ingredients</u>              | <u>% w/w</u> |
|----|---------------------------------|--------------|
| 20 | Mineral Oil                     | 5.00         |
|    | Isostearyl 2-hydroxyhexanoate   | 3.00         |
|    | Cerasin Wax                     | 1.75         |
|    | Petroleum jelly                 | 4.50         |
|    | Glyceryl monostearate           | 1.75         |
| 25 | Candelilla Wax                  | 1.00         |
|    | Stearic acid                    | 2.25         |
|    | Cetyl alcohol                   | 1.40         |
|    | Isopropyl palmitate             | 6.00         |
|    | Laureth 23                      | 0.36         |
| 30 | Sorbitan oleate                 | 1.40         |
|    | Propyl paraben                  | 0.10         |
|    | Glycerol                        | 3.00         |
|    | Triethanolamine                 | 0.60         |
|    | Methyl paraben                  | 0.15         |
| 35 | Carbopol CC-122 (2% dispersion) | 10.0         |
|    | Imidazolidinyl urea             | 0.20         |
|    | Water                           | to 100       |

Example 25. Sunscreen

|    | <u>Ingredients</u>                       | <u>% w/w</u> |
|----|------------------------------------------|--------------|
|    | Propyl paraben                           | 0.10         |
| 5  | Dea-cetyl phosphate                      | 1.00         |
|    | Benzophenone-3/oxobenzene                | 6.00         |
|    | PVP/eicosene copolymer                   | 2.50         |
|    | Stearic acid                             | 4.00         |
|    | Tocopherol acetate                       | 0.10         |
| 10 | Dimethicone                              | 1.00         |
|    | Stearyl 2-hydroxyoctanoate               | 1.50         |
|    | Petroleum Jelly                          | 0.25         |
|    | Octyl methoxycinnamate ethylhexyl P-ME   | 7.50         |
|    | Triethanolamine                          | 1.40         |
| 15 | DMDM hydantoin                           | 0.25         |
|    | Carbopol 2% dispersion                   | 5.00         |
|    | Magnesium aluminium silicate             | 0.20         |
|    | Glycerol                                 | 5.00         |
|    | Methyl paraben                           | 0.15         |
| 20 | Aloe Vera Gel                            | 0.05         |
|    | Disodium EDTA                            | 0.05         |
|    | Simethicone                              | 0.01         |
|    | Cetyl alcohol                            | 0.70         |
|    | Octyl salicylate/2 ethylhexyl salicylate | 5.00         |
| 25 | Water                                    | to 100       |

Example 26. Moisturising Facial Cleanser

|    | <u>Ingredients</u>        | <u>% w/w</u> |
|----|---------------------------|--------------|
|    | Mineral Oil               | 5.00         |
|    | Lauryl 2-hydroxyoctanoate | 4.00         |
| 5  | Sorbitan stearate         | 1.50         |
|    | Polysorbate 60            | 1.80         |
|    | Methyl paraben            | 0.20         |
|    | Propyl paraben            | 0.10         |
|    | PEG 550                   | 8.00         |
| 10 | Triethanolamine           | 1.06         |
|    | Stearic acid              | 1.40         |
|    | BHT                       | 0.05         |
|    | Phenoxyethanol            | 0.40         |
|    | Carbopol 2% dispersion    | 5.00         |
| 15 | Glycerol                  | 5.00         |
|    | Water                     | to 100       |

Example 27. Rinsable Cream Cleanser

|    |                             |              |
|----|-----------------------------|--------------|
| 20 | <u>Ingredients</u>          | <u>% w/w</u> |
|    | Mineral Oil                 | 30.00        |
|    | Myristyl 2-hydroxydecanoate | 10.00        |
|    | Beeswax                     | 2.30         |
| 25 | Cerasin                     | 0.50         |
|    | Propyl paraben              | 0.10         |
|    | PEG-16 soya sterol          | 5.00         |
|    | PEG-8 dilaurate             | 2.00         |
|    | Cetearyl alcohol            | 0.80         |
| 30 | Behenic acid                | 0.80         |
|    | Methyl paraben              | 0.15         |
|    | Disodium EDTA               | 0.05         |
|    | Sodium borate               | 0.80         |
|    | Carpobol 2% dispersion      | 16.00        |
| 35 | Water                       | to 100       |

Example 28. Smoothing Shaving Foam

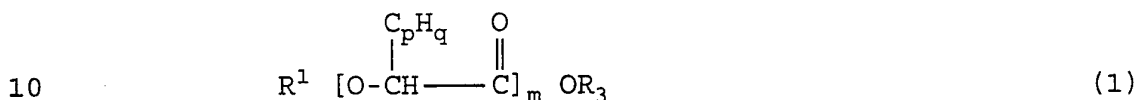
|    | <u>Ingredients</u>                                                                                                                         | <u>% w/w</u> |
|----|--------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 5  | Stearic acid                                                                                                                               | 3.27         |
|    | Palmitic acid                                                                                                                              | 3.51         |
|    | Lauric acid                                                                                                                                | 0.76         |
|    | Triethanolamine                                                                                                                            | 3.01         |
|    | Potassium hydroxide                                                                                                                        | 0.28         |
| 10 | Glycerol                                                                                                                                   | 4.61         |
|    | Decyl 2-hydroxyoctanoate                                                                                                                   | 1.30         |
|    | Tween 20                                                                                                                                   | 0.96         |
|    | Tocopherol acetate                                                                                                                         | 0.05         |
|    | Isostearyl lactylate                                                                                                                       | 0.10         |
| 15 | Silicone Fluid DC2-1865                                                                                                                    | 1.50         |
|    | Silicone Fluid DC193                                                                                                                       | 0.77         |
|    | CAP 48                                                                                                                                     | 4.00         |
|    | Water                                                                                                                                      | to 100       |
| 20 | The above formulation can be modified by replacing the ester of 2-hydroxyalkanoic acid with an equal amount of sodium 2-decyloxyoctanoate. |              |

25 Example 29. Aftershave Balm

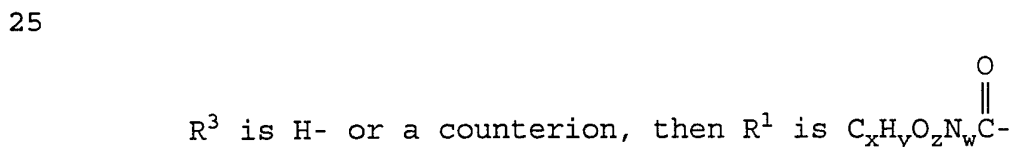
|    | <u>Ingredients</u>                                                                                                                         | <u>% w/w</u> |
|----|--------------------------------------------------------------------------------------------------------------------------------------------|--------------|
|    | Ethanol                                                                                                                                    | 60.0         |
|    | Cetyl 2-hydroxyhexanoate                                                                                                                   | 0.40         |
| 30 | Glycerol                                                                                                                                   | 2.00         |
|    | Perfume                                                                                                                                    | 0.40         |
|    | Benzophenone-11                                                                                                                            | 0.02         |
|    | Water                                                                                                                                      | to 100       |
| 35 | The above formulation can be modified by replacing the ester of 2-hydroxyalkanoic acid with an equal amount of sodium 2-octyloxyhexanoate. |              |

CLAIMS

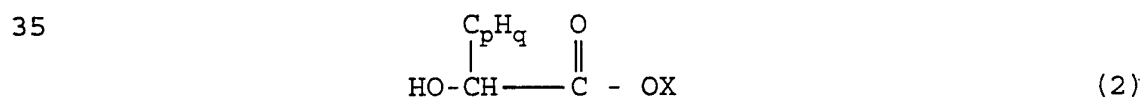
1. The use of an effective amount of at least 0.001% by weight based on the total composition of a hydroxyalkanoate derivative having the structure (1):



- where  $R^1$  represents H- or  $C_x H_y O_z N_w - \overset{\overset{O}{||}}{C}-$   
 $R^3$  represents H-,  $C_x H_y O_z N_w -$  or a metallic, ammonium or alkanolammonium counterion,  
 p is an integer from 2 to 22,  
 q is an integer from 5 to 45,  
 x is an integer of from 1 to 20,  
 y is an integer of from 3 to 41,  
 z is 0, or an integer of from 1 to 10,  
 w is 0, or an integer of from 1 to 5, and  
 m is an integer of from 1 to 5  
 provided that when  $R^1$  is H-, then  $R^3$  is  $C_x H_y O_z N_w -$ , and when



- to deliver to the epidermis, as a moisturiser for the skin, the corresponding 2-hydroxyalkanoate having the structure (2):



- where X represents -H or a counterion;

in a composition intended for topical application to human skin; said compositions also comprising a cosmetically

acceptable vehicle.

2. A method for delivering to the epidermis a 2-hydroxy alkanooate having the structure (2):



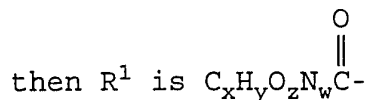
where  $p$  is an integer of from 2 to 20,  
 $q$  is an integer of from 5 to 41, and  
 $X$  represents H-, or a counterion,

which comprises the steps of

i) applying topically to the skin a composition comprising the corresponding hydroxy alkanooate derivative having the structure (1):



the values of  $R^1$ ,  $R^3$ ,  $p$ ,  $q$ ,  $m$  and  $X$  being as defined in claim 1;  
 provided that when  $R^1$  is H-, then  $R^3$  is  $\text{C}_x\text{H}_y\text{O}_z\text{N}_w-$ , and when  $R^3$  is H- or a counterion,

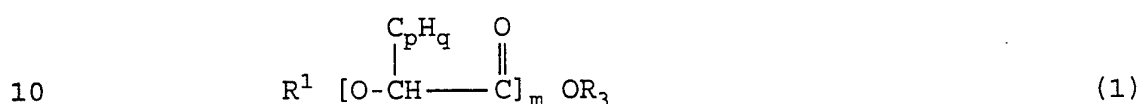


ii) leaving the composition in contact with the skin for at least 10 seconds to permit the hydroxy alkanooate derivative to penetrate through the stratum corneum to reach the lower strata of the epidermis, and

iii) cleaving the hydroxy alkanooate derivative in the epidermis by contact with esterases to provide the 2-hydroxy alkanooate.

3. A composition suitable for topical application to the skin, hair, nails, mucosae and other epithelial tissue, which composition comprises:

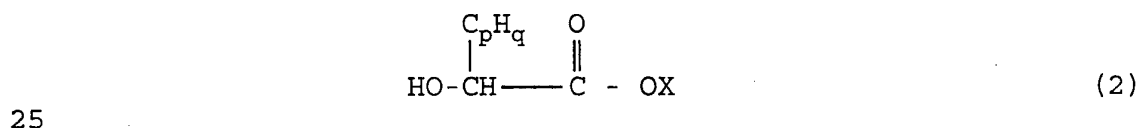
- 5 i) a hydroxy alkanoate derivative having the structure (1):



- ii) a cosmetically acceptable vehicle for the hydroxy alkanoate derivative;

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the hydroxyalkanoate derivative possessing the ability of penetrating the stratum corneum and hydrolysing by enzymic cleavage within the epidermis to yield the corresponding hydroxyalkanoate having the structure (2):



thereby to moisturise the epithelial tissue; the value of  $R^1$ ,  $R^3$ ,  $p$ ,  $q$ ,  $m$  and  $X$  being as defined in claim 1.

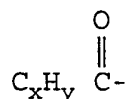
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4. The use, method or composition according to claim 1, 2 or 3 respectively, in which  $C_p H_q$  is an alkyl or alkenyl group such that  $q = 2p \pm 1$ .

35

5. The use, method or composition according to claim 4, in which the alkanoate derivative is an acyl hydroxy alkanoate where  $R^1$  in structure (1) represents the acyl group

40



wherein  $C_xH_y$  is a straight or branched alkyl or alkenyl chain

m is 1 to 5, and

5  $R^3$  represents -H, or an alkali metal, an alkaline earth metal ammonium or an alkanolammonium counterion.

6. The use, method or composition according to claim 5, in which  $R^1$  is an acyl group chosen from:

10

n-propionyl

n-butanoyl

n-hexanoyl

n-octanoyl

15 n-decanoyl

n-dodecanoyl

n-tetradecanoyl

n-hexadecanoyl

n-octadecanoyl

20 n-linoleoyl

n-linolenoyl

$\gamma$ -linolenoyl

n-arachidonoyl

columbinoyl

25 iso-butanoyl

iso-hexanoyl

iso-octanoyl

iso-octadecanoyl

iso-butanoyl

30 iso-octanoyl

iso-octadecanoyl

iso-dodecanoyl

ethylglycoloyl

leucoyl and

35 mandeloyl.

7. The use, method or composition according to any one

of claims 1 to 4, in which the hydroxyalkanoate derivative is an alkyl hydroxyalkanoate where  $R^1$  in structure (1) represents H-,

5  $R^3$  represents  $C_xH_y-$ , and  
m is 1.

8. The use, method or composition according to claim 7, in which the alkyl hydroxy alkanoate is chosen from:

10

methyl 2-hydroxybutanoate  
n-butyl 2-hydroxybutanoate  
n-hexyl 2-hydroxybutanoate  
n-octyl 2-hydroxybutanoate  
15 n-decyl 2-hydroxybutanoate  
n-dodecyl 2-hydroxybutanoate  
n-octadecyl 2-hydroxybutanoate  
ethyl 2-hydroxyhexanoate  
ethyl 2-hydroxyoctanoate, and  
20 n-dodecanyl 2-hydroxyoctanoate.

9. The use, method or composition according to any preceding claim, in which the amount of hydroxyalkanoate derivative present in the composition as an effective  
25 amount, is from 0.001 to 50%, preferably from 0.1 to 30%, and most preferably from 0.5 to 20% by weight of the composition.

10. The use, method or composition according to any  
30 preceding claim, in which the composition further comprises a penetration enhancer.

11. The use, method or composition according to any preceding claim, in which the composition further  
35 comprises a retinoid chosen from

retinyl acetate

retinyl butyrate  
retinyl propionate  
retinyl octanoate  
retinyl laurate  
5 retinyl palmitate  
retinyl oleate  
retinyl linoleate, and  
retinyl linolenate, and/or further comprises  
tocopherol and/or a tocopheryl ester.

10

12. The use, method or composition according to any preceding claim, in which the composition is a leave-on product chosen from creams, lotions, milks, gels.

15 13. The use, method or composition according to any preceding claim, in which the composition is an emulsion containing both an aqueous phase and an oil phase.

14. The use, method or composition according to any  
20 preceding claim in which the cosmetically acceptable vehicle includes water or aqueous ethanol in an amount which is more than 50% by weight of the composition, the amount of ethanol, if any, not exceeding 50% by weight of the composition.

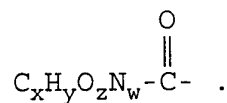
25

15. The use, method or composition according to any preceding claim in which the composition includes water-immiscible oil in an amount exceeding the amount of hydroxyalkanoate derivative.

30

16. The use, method or composition according to any of claims 1 to 7, in which the composition is a cleaning composition containing water and from 5 to 40% by weight of a said hydroxyalkanoate derivative of structure (1)  
35 wherein  $R^3$  represents -H, or a metallic, ammonium or alkanolammonium counterion while  $R^1$  represents

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- 5     17. The use, method or composition according to claim 16  
in which the composition also contains from 5 to 30% by  
weight of one or more co-surfactants.
- 10    18. A method for cleaning the skin or the hair which  
comprises the steps of
- (i) applying to the skin or hair cleansing  
composition as defined in claims 16 or 17;
  - (ii) forming a lather on the skin or hair by  
massaging in the presence of added water,  
15        thereby to cleanse the skin or hair; and
  - (iii) subsequently rinsing the lather from the skin or  
hair with water.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 94/02666

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 6 A61K7/50 A61K7/48

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 6 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)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|------------------------------------------------------------------------------------|-----------------------|
| X          | EP,A,0 261 812 (UNILEVER) 30 March 1988<br><br>see the whole document<br>---       | 1-4,7-9,<br>12-15,17  |
| A          | EP,A,0 007 785 (UNILEVER) 6 February 1980<br>cited in the application<br>---       |                       |
| A          | US,A,4 105 783 (YU ET AL.) 8 August 1978<br>cited in the application<br>-----      |                       |

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Further documents are listed in the continuation of box C.

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Patent family members are listed in annex.

## \* Special categories of cited documents :

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Date of the actual completion of the international search

25 November 1994

Date of mailing of the international search report

28. 12. 94

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# INTERNATIONAL SEARCH REPORT

I International Application No

PCT/EP 94/02666

| Patent document.<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|--------------------------------------------|---------------------|----------------------------|---------------------|
| EP-A-0261812                               | 30-03-88            | AU-B- 598020               | 14-06-90            |
|                                            |                     | AU-A- 7739587              | 03-03-88            |
|                                            |                     | DE-A- 3772139              | 19-09-91            |
|                                            |                     | JP-A- 63068519             | 28-03-88            |
|                                            |                     | US-A- 4839161              | 13-06-89            |
| -----                                      |                     |                            |                     |
| EP-A-0007785                               | 06-02-80            | AU-A- 4914079              | 07-02-80            |
|                                            |                     | US-A- 4424234              | 03-01-84            |
| -----                                      |                     |                            |                     |
| US-A-4105783                               | 08-08-78            | US-A- 4021572              | 03-05-77            |
|                                            |                     | US-A- 4363815              | 14-12-82            |
|                                            |                     | US-A- 4380549              | 19-04-83            |
|                                            |                     | US-A- 4197316              | 08-04-80            |
| -----                                      |                     |                            |                     |