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- (71) Applicant: **CRODA INTERNATIONAL PLC** [GB/GB];
Cowick Hall, Snaith, Goole, Yorkshire DN14 9AA (GB).
- (72) Inventors: **CHAVAN, Bhaven**; 10 Coppicewood Grove,
Bradford, Yorkshire BD7 2JB (GB). **BARNES, Alun**; 7
Lime Tree Drive, Whitley, Goole, Yorkshire DN14 0GF
(GB).
- (74) Agents: **CRAVEN, Ian** et al.; Croda Europe Limited, In-
tellectual Property, Cowick Hall, Snaith, Goole Yorkshire
DN14 9AA (GB).
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(54) Title: COMPOSITION

(57) Abstract: A composition contains at least one C10 to C30 mono- and/or di-ester phosphate, at least one C10 to C30 fatty alcohol, and an organic medium. The composition can be used as the, or as part of, the oil phase of an emulsion, particularly in the form of an Aqueous Cream BP. The composition and emulsion are suitable for application to the skin and maintain skin barrier properties, water content of the skin, and/or stratum corneum thickness, even after prolonged use.



WO 2013/167866 A2

Composition

Field of Invention

5 The present invention relates to a composition comprising a phosphate ester and a fatty alcohol, an emulsion comprising the composition, and in particular in the form of an Aqueous Cream BP.

Background

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Aqueous Cream BP is a light paraffin-based emulsion which is officially registered in the British Pharmacopoeia and is a widely prescribed emollient for the treatment of dry skin conditions. It can be used as a topical external medicine and as an emollient moisturizer in health care and personal care applications.

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Aqueous Cream BP normally contains sodium lauryl sulphate (SLS) which is a known skin irritant. Thus, there is a need to produce an aqueous cream or emulsion which does not contain SLS and does not act as an irritant to the skin. There is also a need to produce compositions which do not act as an irritant to the skin and can be used in a wide range of health care and personal care products, including Aqueous Cream BP.

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There is also a need for such compositions and emulsion to exhibit improved properties, particularly after prolonged application to the skin, such as maintaining (i) skin barrier properties, (ii) water content of the skin, and/or (iii) stratum corneum thickness.

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Summary of the Invention

We have now surprisingly discovered a composition and/or emulsion which overcomes or significantly reduces at least one of the aforementioned problems.

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Accordingly, the present invention provides a composition comprising, consisting essentially of, or consisting of (i) 0.1 to 30% by weight at least one C10 to C30 mono- and/or di-ester phosphate, (ii) 1 to 60% by weight at least one C10 to C30 fatty alcohol, and (iii) 20 to 98.9% by weight of an organic medium, all based on the total weight of the composition.

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The invention also provides a pre-mixture consisting of 4 to 20% by weight of at least one C10 to C30 mono- and/or di-ester phosphate and 80 to 96% by weight of at least one C10 to C30 fatty alcohol, both based upon the total weight of the mixture.

The invention further provides a method of forming a composition which comprises (i) pastillating or flaking a mixture comprising at least one C10 to C30 mono- and/or di-ester phosphate and at least one C10 to C30 fatty alcohol, (ii) adding the pastilles or flake formed in (i) to organic medium, and (iii) heating to melt the pastilles or flake and form a uniform mixture.

The invention yet further provides a an emulsion comprising an aqueous phase and an oil phase comprising at least one C10 to C30 mono- and/or di-ester phosphate and at least one C10 to C30 fatty alcohol.

The invention still further provides the use of (a) a composition comprising (i) 0.1 to 30% by weight at least one C10 to C30 mono- and/or di-ester phosphate, (ii) 1 to 60% by weight at least one C10 to C30 fatty alcohol, and (iii) 20 to 98.9% by weight of an organic medium, all based on the total weight of the composition, or (b) an emulsion comprising the composition in (i), to maintain skin barrier properties, water content of the skin, and/or stratum corneum thickness when applied to the skin as an emollient treatment.

The monoester phosphate suitably comprises, consists essentially of, or consists of compounds of formula $R^1-O-P(=O)(OH)_2$. The diester phosphate suitably comprises, consists essentially of, or consists of compounds of formula $R^1-O-P(=O)(OR^1)(OH)$. R^1 is suitably a C10 to C30 hydrocarbyl group, preferably an alkyl group. R^1 may be saturated or unsaturated, linear or branched, but is preferably saturated, and more preferably linear. R^1 is preferably a C12 to C24, more preferably C14 to C20, particularly C16 to C18, and especially C16 hydrocarbyl group, particularly alkyl group. It is not necessary that each R^1 group in the diester phosphate be the same, and thus the diester phosphates may be asymmetrically substituted.

The molar ratio of monoester phosphate to diester phosphate present in a composition according to the present invention may be in the range from 0 to 100%:0 to 100%, but is preferably 40 to 95%:5 to 60%, more preferably 50 to 85%:15 to 50%, especially 60 to 75%:25 to 40%, and especially 65 to 70%:30 to 35%.

The concentration of phosphate ester present in a composition according to the present invention is preferably in the range from 1 to 20%, more preferably 1.5 to 10%, particularly 2 to 5%, and especially 2.5 to 3.5% by weight based upon the total weight of the composition.

The phosphate esters used in the present invention may be suitably formed, as is known in the art, by reacting a fatty alcohol, e.g. of formula R^1OH , wherein R^1 is as defined above, with a phosphorylating agent such polyphosphoric acid, phosphorus pentoxide, oxychloride or

trichloride. In one embodiment, phosphorus pentoxide is preferred. The reaction can produce a statistical mixture of mono-, di- and tri-ester products and the proportions can be controlled to produce the desired ratio of esters, e.g. monoester:diester ratio, for example by varying the proportions of the starting materials. Suitable linear fatty alcohols include cetyl alcohol, stearyl alcohol, oleyl alcohol, lauryl alcohol, cocoyl alcohol, tetradecanol, arachidyl alcohol, behenyl alcohol and lignoceryl alcohol. Suitable branched fatty alcohols include isostearyl alcohol, isotetradecanol, isocetyl alcohol, isoarachidyl alcohol, isobehenyl alcohol and isolignoceryl alcohol; neo-alcohols such as neocapric alcohol; and/or anti-iso alcohols. Linear fatty alcohols are preferred, particularly cetyl alcohol and/or stearyl alcohol, and especially cetyl alcohol.

The fatty alcohol component in the composition according to the present invention is suitably of formula R^2OH wherein R^2 is preferably a C12 to C24, more preferably C14 to C22, particularly C16 to C20, and especially C16 to C18 hydrocarbyl group, particularly alkyl group. The hydrocarbyl group may be saturated or unsaturated, linear or branched, but is preferably saturated, and more preferably linear. Suitable linear fatty alcohols include cetyl alcohol, stearyl alcohol, oleyl alcohol, lauryl alcohol, cocoyl alcohol, tetradecanol, arachidyl alcohol, behenyl alcohol and lignoceryl alcohol. Suitable branched fatty alcohols include isostearyl alcohol, isotetradecanol, isocetyl alcohol, isoarachidyl alcohol, isobehenyl alcohol and isolignoceryl alcohol; neo-alcohols such as neocapric alcohol; and/or anti-iso alcohols. Linear fatty acids are preferred.

In one preferred embodiment, R^2 is a mixture of linear C16 and C18 alkyl groups, i.e. the fatty alcohol is cetyl alcohol and stearyl alcohol (cetostearyl alcohol), preferably present at a weight ratio of stearyl alcohol:cetyl alcohol in the range from 0.3 to 10:1, more preferably 1 to 5:1, particularly 1.5 to 3.5:1, and especially 2 to 2.8:1.

The concentration of fatty alcohol present in a composition according to the present invention is preferably in the range from 9 to 40%, more preferably 16.5 to 35%, particularly 23 to 30%, and especially 25.5 to 28.5% by weight based upon the total weight of the composition.

The ratio by weight of fatty alcohol to phosphate ester present in a composition according to the present invention is preferably in the range from 1 to 40:1, more preferably 5 to 20:1, especially 8 to 12:1, and especially 9.5 to 10.5:1.

In one embodiment, the phosphate ester and fatty alcohol components are pre-mixed prior to combining with the organic medium to form the composition according to the present invention.

The concentration of fatty alcohol present in the fatty alcohol/phosphate ester mixture is preferably in the range from 70 to 99%, more preferably 80 to 96%, particularly 86 to 94%, and especially 88 to 92% by weight based upon the total weight of the mixture.

- 5 The concentration of phosphate ester present in the fatty alcohol/phosphate ester mixture is preferably in the range from 1 to 30%, more preferably 4 to 20%, particularly 6 to 14%, and especially 8 to 12% by weight based upon the total weight of the mixture.

10 In one embodiment, the mixture of phosphate ester and fatty alcohol is pastillatable and/or flakable. If the mixture is too gummy or pasty it will not be amenable to flaking or pastillation. Further, it will often not flow through the transfer line and will be difficult to heat or cool due to poor heat transfer. Flakes or pastilles are desired because they are easily handled and incorporated into the composition according to the present invention.

- 15 The mixture of phosphate ester and fatty alcohol is preferably a free-flowing liquid above their melting points, making it easy to manufacture and to transfer and pump through transfer lines to flaking or pastillation equipment where it is chilled below its melting point and either broken up into easy to handle flakes or dispensed into pastilles and cooled. The melting point of the mixture generally needs to be below 100°C in order to facilitate the transfer to the flaking or
20 pastillation lines whilst maintaining the integrity of the blend. More preferably, the melting point of the mixture is below 95°C, and particularly below 90°C.

Whether a mixture is flakable is measured by pouring a relatively thin film (1/16" – 1/8") of the heated mixture onto a metal sheet and allowing it to cool. The cooled film is then "crumbled"
25 or "scraped" into small flakes by any type of mechanical process. Thus, a flakeable mixture must possess two properties. Firstly, the mixture must possess the property of being easily pourable onto the sheet, thus forming a thin film. Secondly, once the mixture is allowed to cool, it must break up into flakes after crumbling or scraping. These flakes are consequently easily stored and re-melted as necessary.

30 Pastillation is a process in which small amounts of the desired mixture are dispensed into pastilles. These pastilles are then allowed to cool, forming a product, which is in solid form, but easily returned to a liquid state. Whether a mixture is capable of pastillation is measured by distributing small amounts of the heated mixture into pastilles. These pastilles are then
35 allowed to cool. The pastilles must be easily melted without great amounts of heat, preferably below the boiling point of water.

Thus in one preferred embodiment, the composition according to the present invention is formed by (i) pastillating or flaking the mixture of phosphate ester and fatty alcohol defined

herein, (ii) adding the pastilles or flake formed in (i) to organic medium as defined herein, and (iii) heating to melt the pastilles or flake and form a uniform mixture.

The organic medium used in the present invention is preferably a cosmetically acceptable material, for example an oil of the type widely used in personal care or cosmetic products, such as those registered as solvents by the Cosmetics Toiletries and Fragrance Association.

The organic medium preferably comprises, consists essentially of, or consists of one or more oily materials, such as those selected from the group consisting of glycols, glyceride oils, vegetable oils, ester oils, fatty alcohol alkoxylates, alkyl carbonates, lanolin, mineral oils and silicone oils, and mixtures thereof. Suitable silicone oils or siloxane fluids include a cyclic oligomeric dialkylsiloxane, such as the cyclic pentamer of dimethylsiloxane known as cyclomethicone. Alternative siloxane fluids include dimethylsiloxane linear oligomers or polymers having a suitable fluidity and phenyltris(trimethylsiloxy)silane (also known as phenyltrimethicone).

Specific examples of suitable organic media materials include avocado oil, C12-15 alkyl benzoate, C12-15 alkyl ethylhexanoate, C12-15 alkyl lactate, C12-15 alkyl salicylate, C13-14 isoparaffin, C18-36 acid glycol ester, C18-36 acid triglyceride, caprylic/capric glycerides, caprylic/capric triglyceride, caprylic/capric/lauric triglyceride, caprylic/capric/linoleic triglyceride, caprylic/capric/myristic/stearic triglyceride, caprylic/capric/stearic triglyceride, castor oil, castor oil-silicone ester, cetearyl ethylhexanoate, cetearyl isononanoate, cetearyl palmitate, cetearyl stearate, cetyl dimethicone, cetyl dimethicone copolyol, cetyl ethylhexanoate, cetyl glycol isostearate, cetyl isononanoate, cetyl lactate, cetyl myristate, cetyl oleate, cetyl palmitate, cetyl ricinoleate, cetyl stearate, cocoglycerides, coconut oil, cyclomethicone, cyclopentasiloxane, cyclotetrasiloxane, decyl isostearate, decyl oleate, decyl polyglucoside, dibutyl adipate, diethylhexyl dimer dilinoleate, diethylhexyl malate, diisopropyl adipate, diisopropyl dimer dilinoleate, diisostearyl trimethylolpropane siloxy silicate, diisostearyl adipate, diisostearyl dimer dilinoleate, diisostearyl malate, diisostearyl trimethylolpropane siloxy silicate, dilauryl trimethylolpropane siloxy silicate, dilauryl trimethylolpropane siloxy silicate, dimethicone, dimethicone copolyol, dimethicone propyl PG-betaine, dimethiconol, dimethyl isosorbide, dioctyl maleate, dioctylododecyl dimer dilinoleate, ethylhexyl benzoate, ethylhexyl cocoate, ethylhexyl dimethyl PABA, ethylhexyl ethylhexanoate, ethylhexyl hydroxystearate, ethylhexyl hydroxystearate benzoate, ethylhexyl isononanoate, ethylhexyl isopalmitate, ethylhexyl isostearate, ethylhexyl laurate, ethylhexyl methoxycinnamate, ethylhexyl myristate, ethylhexyl neopentanoate, ethylhexyl oleate, ethylhexyl palmitate, ethylhexyl salicylate, ethylhexyl stearate, glyceryl caprate, glyceryl caprylate, glyceryl caprylate/caprate, glyceryl cocoate, glyceryl dilaurate, glyceryl dioleate, glyceryl hydroxystearate, glyceryl isostearate, glyceryl laurate, glyceryl oleate, glycol oleate,

glycol ricinoleate, helianthus annuus (hybrid sunflower) seed oil, helianthus annuus (sunflower) seed oil, homosalate, isoamyl laurate, isoamyl p-methoxycinnamate, isocetyl alcohol, isocetyl behenate, isocetyl ethylhexanoate, isocetyl isostearate, isocetyl laurate, isocetyl linoleoyl stearate, isocetyl myristate, isocetyl palmitate, isocetyl salicylate, isocetyl stearate, isocetyl stearoyl stearate, isohexadecane, isononyl isononanoate, isopropyl C12-15-pareth-9 carboxylate, isopropyl isostearate, isopropyl lanolate, isopropyl laurate, isopropyl linoleate, isopropyl methoxycinnamate, isopropyl myristate, isopropyl oleate, isopropyl palmitate, isopropyl PPG-2-isodeceth-7 carboxylate, isopropyl ricinoleate, isopropyl stearate, isostearic acid, isostearyl alcohol, isostearyl ethylhexanoate, isostearyl isononanoate, isostearyl isostearate, isostearyl lactate, isostearyl myristate, isostearyl neopentanoate, isostearyl palmitate, isostearyl stearoyl stearate, jojoba oil, lanolin (lanolin oil), maleated soybean oil, myristyl isostearate, myristyl lactate, myristyl myristate, myristyl neopentanoate, myristyl stearate, octocrylene, octyldecanol, octyldodecanol, oenothera biennis (evening primrose oil), paraffinum liquidum (mineral oil), PCA dimethicone, pentaerythrityl tetraisononanoate, pentaerythrityl tetraisostearate, perfluoropolymethylisopropyl ether, persea gratissima (avocado oil), phenyl trimethicone, PPG-15 stearyl ether, propylene glycol ceteth-3 acetate, propylene glycol dicaprylate, propylene glycol dicaprylate/dicaprate, propylene glycol dipelargonate, propylene glycol distearate, propylene glycol isoceteth-3 acetate, propylene glycol isostearate, propylene glycol laurate, propylene glycol ricinoleate, propylene glycol stearate, prunus dulcis (sweet almond oil), squalane, squalene, tricaprylin, tricaprylyl citrate, tridecyl ethylhexanoate, tridecyl neopentanoate, tridecyl stearoyl stearate, triethylhexanoin, triethylhexyl citrate, trihydroxystearin, triisocetyl citrate, triisostearin, triisostearyl citrate, trimethylolpropane triisostearate, trimethylsiloxysilicate, triticum vulgare (wheat germ oil), vitis vinifera (grape) seed oil, and mixtures thereof.

One preferred organic medium comprises, consists essentially of, or consists of at least one mineral oil, particularly paraffin wax, light mineral oil or liquid paraffin, especially medicinal grade liquid paraffin, and mixtures thereof.

The concentration of organic medium in a composition according to the present invention is preferably in the range from 40 to 90%, more preferably 55 to 82%, particularly 65 to 75%, and especially 68 to 72% by weight based on the total weight of the composition.

In one embodiment, the composition according to the invention is substantially anhydrous. The term "anhydrous" as used in this specification means compositions containing less than 10%, preferably less than 5% water by weight based on the weight of the composition. More preferably, the composition is substantially water free, i.e. contains less than 2%, particularly less than 1% water by weight. However, it will be appreciated that components of the

composition may contain small amounts of residual water (moisture) which will be present in the composition.

5 The composition according to the present invention is suitably stable, preferably for greater than one month, more preferably greater than two months, particularly greater than three months, and especially greater than four months at 5°C, at ambient temperature (23°C), and/or at 43°C. The stability at even higher temperatures can also be important, and therefore the composition is suitably stable for greater than one week, preferably greater than two weeks, more preferably greater than 3 weeks, particularly greater than one month, and
10 especially greater than two months at 50°C. Stability was assessed by observing the composition after storage cold at 5°C, at ambient temperature (23°C), and under elevated temperature storage at 43°C and 50°C. The composition is stable if there are no visible signs of coalescence, creaming or sedimentation.

15 In one embodiment of the present invention, the composition comprises, consists essentially of, or consists of (i) 0.1 to 30% by weight of cetyl phosphate and/or di-cetyl phosphate, (ii) 1 to 60% by weight of cetostearyl alcohol, and (iii) 20 to 98.9% by weight of paraffin wax and/or liquid paraffin, all based on the total weight of the composition.

20 The composition according to the present invention may be used as an ointment, an ointment base, or as a component of an emulsion. The composition may be present in an oil-in-water emulsion or water-in-oil emulsion, preferably an oil-in-water emulsion.

The concentration of the oil phase in the emulsion is suitably in the range from 1 to 80%,
25 preferably 10 to 50%, more preferably 20 to 40%, particularly 25 to 35%, and especially 28 to 32% by weight based on the total weight of the emulsion.

The oil phase of the emulsion comprises, consists essentially of, or consists of the composition defined herein, i.e. the oil phase may comprise components additional to those
30 present in the composition.

The concentration of the composition defined herein present in the emulsion is suitably in the range from 1 to 80%, preferably 10 to 50%, more preferably 20 to 40%, particularly 25 to 35%, and especially 28 to 32% by weight based on the total weight of the emulsion.

35 The concentration of the phosphate ester present in the oil phase of the emulsion is suitably in the range from 0.1 to 30%, preferably 1 to 20%, more preferably 1.5 to 10%, particularly 2 to 5%, and especially 2.5 to 3.5% by weight based upon the total weight of the oil phase.

The concentration of the fatty alcohol present in the oil phase of the emulsion is suitably in the range from 1 to 60%, preferably 9 to 40%, more preferably 16.5 to 35%, particularly 23 to 30%, and especially 25.5 to 28.5% by weight based upon the total weight of the oil phase.

- 5 The concentration of organic medium in the oil phase of the emulsion is suitably in the range from 20 to 98.9%, preferably 40 to 90%, more preferably 55 to 82%, particularly 65 to 75%, and especially 68 to 72% by weight based on the total weight of the oil phase.

- 10 The concentration of the aqueous phase in the emulsion is suitably in the range from 20 to 99%, preferably 50 to 90%, more preferably 60 to 80%, particularly 65 to 75%, and especially 68 to 72% by weight based on the total weight of the emulsion.

- 15 In addition to water, the aqueous phase may also comprise up to 20%, preferably in the range from 1 to 15%, and more preferably 5 to 10% by weight of alcohol based upon the total weight of the aqueous phase. Suitable alcohols are C1 to C6 alcohols such as those selected from the group consisting of methanol, ethanol, propanol, isopropanol, butanol, isobutanol, tert-butanol, n-pentanol, iso-pentanol, n-hexanol, isohexanol, glycol, glycerol, 1,2-pentanediol, 1,5-pentanediol, 1,2-hexanediol and 1,6-hexanediol.

- 20 The emulsion according to the present invention may also contain other surfactant materials, in addition to the phosphate ester described herein, which form part of the emulsifier system. Other suitable surfactants include relatively hydrophilic surfactants, e.g. having a HLB value of greater than 10, preferably greater than 12, and relatively hydrophobic surfactants e.g. having a HLB value of less than 10, preferably less than 8. Relatively hydrophilic surfactants include alkoxylate surfactants with an average in the range from about 10 to about 100
25 alkylene oxide, particularly ethylene oxide residues; and relatively hydrophobic surfactants include alkoxylate surfactants preferably with an average in the range from about 3 to about 10 alkylene oxide, particularly ethylene oxide residues.

- 30 The amount of surfactant, including phosphate ester, in an emulsion according to the present invention is preferably in the range from 0.1 to 5% by weight based on the total weight of the emulsion.

- 35 Emulsions can be divided by viscosity into milks and lotions, which preferably have a low shear viscosity (measured at shear rates of about 0.1 to 10 s^{-1} as is typically used in Brookfield viscometers) of up to $10,000\text{ mPa.s}$, and creams which preferably have a low shear viscosity of more than $10,000\text{ mPa.s}$. Milks and lotions preferably have a low shear viscosity in the range from 100 to $10,000$, more preferably 200 to $5,000$, and particularly 300 to $1,000\text{ mPa.s}$. Creams preferably have a low shear viscosity of at least $20,000$, more

preferably in the range from 30,000 to 80,000, and particularly 40,000 to 70,000 mPa.s, although even higher viscosities e.g. up to about 10^6 mPa.s, may also be used.

- 5 The emulsions of the invention may be made by conventional emulsification and mixing methods. For example, the surfactant may be added to (i) the oil phase, which is then added to the aqueous phase, or (ii) both the combined oil and water phases, or (iii) the water phase, which is then added to the oil phase. Method (i) is preferred. In all of these methods, the resulting mixture can then be emulsified using standard techniques. It is preferred to either
- 10 heat the aqueous and oil phases usually above about 60°C, e.g. to about 70 to 85°C, or to subject the aqueous phase to high intensity mixing at lower, e.g. about ambient, temperature. Vigorous mixing and the use of moderately elevated temperatures can be combined if desired. The heating and/or high intensity mixing can be carried out before, during or after addition of the oil phase.
- 15 The emulsions can also be made by inverse emulsification methods, whereby the surfactant is added to either the oil phase or the aqueous phase, and the aqueous phase is mixed into the oil phase to initially form a water-in-oil emulsion. Aqueous phase addition is continued until the system inverts to form an oil-in-water emulsion. A substantial amount of aqueous phase will generally be needed to effect inversion and so this method is not likely to be used
- 20 for high oil phase content emulsions. Vigorous mixing and the use of moderately elevated temperatures can be combined if desired. Heating can be carried out during or after addition of the aqueous phase and before, during or after inversion. High intensity mixing can be carried out during or after addition of the aqueous phase, and before or during inversion
- 25 The emulsions may for example be microemulsions or nanoemulsions, having a mean droplet size over a wide range, preferably in the range from 10 to 10,000 nm. In one embodiment, the emulsion droplet size may be reduced, for example by high pressure homogenisation, preferably to a value in the range from 100 to 1,000 nm, more preferably 300 to 600 nm.
- 30 The emulsion according to the present invention is suitably stable, preferably for greater than one month, more preferably greater than two months, particularly greater than three months, and especially greater than four months at 5°C, at ambient temperature (23°C), and/or at 43°C. The stability at even higher temperatures can also be important, and therefore the
- 35 emulsion is suitably stable for greater than one week, preferably greater than two weeks, more preferably greater than 3 weeks, particularly greater than one month, and especially greater than two months at 50°C. Stability was assessed by observing the emulsion after storage cold at 5°C, at ambient temperature (23°C), and under elevated temperature storage

at 43°C and 50°C. The emulsion is stable if no separation of the components or phases or creaming occurs.

The compositions and emulsions of the present invention are particularly suitable to be included in health care, personal care or cosmetic formulations. The compositions and emulsions may be incorporated into both milk and cream health care and personal care products. The compositions and emulsions may include many other components, which may be oil soluble, water soluble or non-soluble. Examples of such materials include:

(i) preservatives such as those based on parabens (alkyl esters of 4-hydroxybenzoic acid), phenoxyethanol, substituted ureas and hydantoin derivatives e.g. those sold commercially under the trade names Germaben II Nipaguard BPX and Nipaguard DMDMH, when used usually in a concentration of from 0.5 to 2% by weight based on the total weight of the composition/emulsion;

(ii) perfumes, when used typically at a concentration of from 0.1 to 10% more usually up to about 5% and particularly up to about 2% by weight based on the total weight of the composition/emulsion;

(iii) humectants or solvents such as alcohols, polyols such as glycerol and polyethylene glycols, when used typically at a concentration of from 1 to 10% by weight based on the total weight of the composition/emulsion;

(iv) sunfilter or sunscreen materials including chemical sunscreens and physical sunscreens including those based on titanium dioxide or zinc oxide; when used typically at from 0.1% to 15% by weight based on the total weight of the composition/emulsion;

(v) alpha hydroxy acids such as glycolic, citric, lactic, malic, tartaric acids and their esters;

(vi) self-tanning agents such as dihydroxyacetone;

(vii) antimicrobial, particularly anti-acne components such as salicylic acid;

(viii) vitamins and their precursors including:

a) Vitamin A e.g. as retinyl palmitate and other tretinoin precursor molecules,

b) Vitamin B e.g. as panthenol and its derivatives,

c) Vitamin C e.g. as ascorbic acid and its derivatives,

d) Vitamin E e.g. as tocopheryl acetate,

e) Vitamin F e.g. as polyunsaturated fatty acid esters such as gamma-linolenic acid esters;

(ix) skin care agents such as ceramides either as natural materials or functional mimics of natural ceramides;

(x) phospholipids;

(xi) vesicle-containing formulations;

(xii) botanical extracts with beneficial skin care properties;

(xiii) skin whiteners such as dioic acid, for example O.D.A. white™ (ex Sederma), hydroquinone, kojic acid, arbutin and similar materials;

(xiv) skin repair compounds actives such as Allantoin and similar series;

5 (xv) caffeine and similar compounds;

(xvi) cooling additives such as menthol or camphor;

(xvii) insect repellents such as N,N-diethyl-3-methylbenzamide (DEET) and citrus or eucalyptus oils;

(xviii) essential oils; and

10 (xix) pigments, including microfine pigments, particularly oxides and silicates, e.g. iron oxide, particularly coated iron oxides, and/or titanium dioxide, and ceramic materials such as boron nitride, or other solid components, such as are used in make up and cosmetics, to give suspoemulsions, preferably used in an amount of from 1 to 15%, more preferably at least 5%, and particularly at least 10% by weight based on the total weight of the emulsion.

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In one preferred embodiment, the compositions and emulsions of the present invention comprise a sunscreen. The sunscreen may be one or more organic sunscreens and/or inorganic sunscreens such as metal oxides, but preferably comprises at least one particulate titanium dioxide and/or zinc oxide, particularly included in the composition in the form of an aqueous and/or organic dispersion available commercially from Croda under the trade marks
20 Tioveil, Solaveil Clarus and Solaveil SpeXtra (all titanium dioxide) and Spectraveil (zinc oxide). In addition, organic sunscreens may be used, preferably together with the preferred metal oxide sunscreens, and include p-methoxy cinnamic acid esters, salicylic acid esters, p-amino benzoic acid esters, non-sulphonated benzophenone derivatives, derivatives of
25 dibenzoyl methane and esters of 2-cyanoacrylic acid. Specific examples of useful organic sunscreens include benzophenone-1, benzophenone-2, benzophenone-3, benzophenone-6, benzophenone-8, benzophenone-12, isopropyl dibenzoyl methane, butyl methoxy dibenzoyl methane, ethyl dihydroxypropyl PABA, glyceryl PABA, octyl dimethyl PABA, octyl methoxycinnamate, homosalate, octyl salicylate, octyl triazone, octocrylene, etocrylene,
30 menthyl anthranilate, 4-methylbenzylidene camphor, benzophenone 4, and phenyl benzimidazole sulphonic acid.

The compositions and emulsions according to the present invention are suitable for use in a wide range of personal care formulations and end-use applications, such as cream,
35 emulsion, lotion, gel and oil for the skin (for example hands, face, feet), soap, for example toilet soap and deodorant soap, bath and shower preparation in the form of salt, foam, oil, gel, depilatories, deodorant and anti-perspirant, shaving product in the form of creams,

moisturizer, sunscreen, after sun product, body butter, and high perfume containing products, skin whitening products, and anti-wrinkle products; products intended for application to the lips; products intended for care of the teeth and the mouth; products for nail care and make up; and products for external intimate hygiene.

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Suitable pharmacological formulations include medicine, quasi-drug and medical products. Medical products includes adhesive plaster, bandage, dressing. The form of the pharmacological formulation is not limited as long as it can be applied to the skin, mucosa, hair, nails, scalp or wounds of the skin. Suitable forms include liquid, milky lotion, powder, suspension, cream, ointment, mousse, gel, jelly, paste, solid stick, aerosol, spray, liniment, serum, impregnated into bandage, dressing, patch or adhesive plaster and needle free jet injection.

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Examples of suitable applications areas for the pharmacological formulation include treatment of wounds. Types of wounds include burns (first, second and third degree) caused by sun exposure or scalding and wounds caused by cuts. Other examples include use in sanitising gels and lotions for application to the skin. Suitable application areas for a dermatological formulation include treatment of skin disorders, for example eczema, dermatitis and furuncles, in particular treatment of both adult and child dermatitis, such as treatment of atopic dermatitis and diaper dermatitis for babies and toddlers.

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The invention is illustrated by the following non-limiting examples.

Examples

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Example 1

659 g phosphorus pentoxide was added in small portions to 3000 g of cetyl alcohol in a jacketed reaction vessel equipped with a high shear mixer at a rate so as to maintain the temperature between 65 and 70°C. Mixing was continued for a further 6 hours at 75°C.

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240.4 g of the resultant material was then mixed with 2500 g of cetostearyl alcohol. The mixture was neutralised with 110.3 g of 50% aqueous potassium hydroxide and the product was pastillated by dripping molten material from a pipette onto a chilled metal surface to form pastilles.

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Example 2

600 g of the pastilles formed in Example 1 were added to 400 g liquid paraffin and 1000 g white soft paraffin in a vessel and heated to above 75°C in a water bath, and mixed until uniform to form an emulsifying ointment.

Example 3

Formulation Y was produced from the components listed in Table 1.

Table 1: Emulsion formulation

<u>Phase</u>	<u>Component</u>	<u>Formulation Y</u> <u>(% w/w)</u>
A	White Soft Paraffin	15
A	Liquid Paraffin	6
A	Pastilles produced in Example 1	9
B	Phenoxyethanol	1
B	Water	69

The pastilles produced in Example 1 were added to the remaining Phase A components in a vessel and heated to above 75°C in a water bath and mixed until uniform to form the oil phase (A) of the emulsion. In a separate vessel, the Phase B components (aqueous phase) were mixed and heated in a water bath to above 75°C. The Phase A mixture was slowly added to the Phase B mixture while stirring at approximately 300 rpm and then homogenized using an Ultra-Turrax dispenser stirring at approximately 11,000 rpm. The resulting emulsion was then cooled to room temperature whilst gently stirring at approximately 150 rpm. The pH of the resulting mixture was then measured, and if required, adjusted to be between 5 and 5.5 using triethanolamine.

Example 4

An in vivo assessment of stratum corneum thickness and skin barrier integrity was carried out. 6 volunteers participated in the study. All were healthy, had no history of skin disease and did not suffer from any dermatological conditions at the time of the study. The mid-volar forearm region was the experimental site and both arms were tested. An imagined vertical line from the elbow to the wrist was used to divide the arm into 2 sites, the treated site and the untreated site. In the morning, to the treated sites of both arms, 1 ml of Formulation Y produced in Example 3 was applied homogenously. The formulation was left on for 10 minutes and the excess material removed with soft tissues. This process was repeated in the afternoon and evening, i.e. in total there were 3 applications per day, for a period of 4 weeks.

The application of Formulation Y was discontinued after 4 weeks. 24 hours later, the volunteers were acclimatized in a humidity controlled room (50% $\pm$ 5% relative humidity, 21 °C $\pm$ 1 °C) for 20 minutes. Water loss measurements (trans epidermal water loss (TEWL)) of the

skin were then taken from both the treated and untreated sites of the arm using a Biox AquaFlux AF200. The results are shown in Table 2.

5 Sequential tape stripping was then carried out. This involved the sequential attachment and removal of adhesive discs (D-Squame sampling discs) onto the treated and untreated sites of the arms with each removal of the disc being followed by water loss measurements. This process was repeated until either 30 discs were removed or when a water loss reading of 70 grams/m²/hour was reached, whichever came first.

10 The absorption of each adhesive disc at 850 nm was carried out using a SquameScan 850A spectrophotometer. This allowed the determination of the amount of protein removed with each disc by using the following equation:

$$\text{Protein amount removed } (\mu\text{g}/\text{cm}^2) = (1.366 \times \text{absorbance at 850 nm}) - 1.557$$

15 Using the calculated protein amount removed, the weight of stratum corneum removed ($\mu\text{g}/\text{cm}^2$) could be determined as described in M. Tsang and R.H Guy, British Journal of Dermatology, 2010, volume 163. Assuming that 1 gram of stratum corneum equates to 1 cm³ of skin removed, the depth of stratum corneum removed with each disc could be calculated.

20 The total stratum corneum depth was be calculated by plotting 1/TEWL vs. cumulative depth of stratum corneum removed. The intercept on the x-axis represents the total thickness of the stratum corneum. The results are shown in Table 2.

25 Table 2: Stratum corneum thickness and TEWL values

	<u>Untreated Site</u>	<u>Formulation Y Site</u>
Mean stratum corneum thickness (μm)	10.7	9.8
Change in stratum corneum thickness from untreated site (μm)	-	-0.9
Percentage change in stratum corneum thickness from untreated site	-	-8.0%
Mean TEWL ($\text{g}/\text{m}^2/\text{hr}$)	13.2	13.8
Change in TEWL from untreated site ($\text{g}/\text{m}^2/\text{hr}$)	-	0.6

Percentage change in TEWL from untreated site	-	5.1%
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The results show that after 4 weeks application of Formulation Y, 3 times per day, the stratum corneum thins out by 0.9 μm (8.0%) compared to the untreated site. This decrease of 0.9 μm is not statistically different ($p>0.05$) to the untreated site showing that application of Formulation Y does not reduce the thickness of the stratum corneum. In addition, the skin barrier integrity was also maintained throughout the application of Formulation Y as an increase in water loss of 0.6 $\text{g/m}^2/\text{hr}$ (5.1%) was obtained, which again is not statistically different to the untreated site ($p>0.05$).

The above results demonstrate that the application of Formulation Y does not thin the stratum corneum and also maintains the water holding capability of the skin.

Example 5

Formulation I was produced from the components listed in Table 3.

Table 3: Emulsion formulation

<u>Phase</u>	<u>Component</u>	<u>Formulation I</u> (% w/w)
A	PPG-15 Stearyl Ether	20
A	Pastilles produced in Example 1	10
B	Phenoxyethanol	1
B	Water	69

The pastilles produced in Example 1 were added to the remaining Phase A components in a vessel and heated to above 75 °C in a water bath and mixed until uniform to form the oil phase (A) of the emulsion. In a separate vessel, the Phase B components (aqueous phase) were mixed and heated in a water bath to above 75 °C. The Phase A mixture was slowly added to the Phase B mixture while stirring at approximately 300 rpm and then homogenised using an Ultra-Turrax dispenser stirring at approximately 11,000 rpm. The resulting emulsion was then cooled to room temperature whilst gently stirring at approximately 150 rpm. The pH of the resulting mixture was then measured, and if required, adjusted to be between 5 and 5.5 using triethanolamine.

Example 6

Formulation II was produced from the components listed in Table 4.

5 Table 4: Emulsion formulation

<u>Phase</u>	<u>Component</u>	<u>Formulation II</u> (% w/w)
A	Caprylic/Capric Triglyceride	20
A	Pastilles produced in Example 1	10
B	Phenoxyethanol	1
B	Water	69

The pastilles produced in Example 1 were added to the remaining Phase A components in a vessel and heated to above 75°C in a water bath and mixed until uniform to form the oil phase (A) of the emulsion. In a separate vessel, the Phase B components (aqueous phase) were mixed and heated in a water bath to above 75°C. The Phase A mixture was slowly added to the Phase B mixture while stirring at approximately 300 rpm and then homogenised using an Ultra-Turrax dispenser stirring at approximately 11,000 rpm. The resulting emulsion was then cooled to room temperature whilst gently stirring at approximately 150 rpm. The pH of the resulting mixture was then measured, and if required, adjusted to be between 5 and 5.5 using triethanolamine.

Example 7

Formulation III was produced from the components listed in Table 5.

20 Table 5: Emulsion formulation

<u>Phase</u>	<u>Component</u>	<u>Formulation III</u> (% w/w)
A	Isopropyl Palmitate	20
A	Pastilles produced in Example 1	10
B	Phenoxyethanol	1
B	Water	69

The pastilles produced in Example 1 were added to the remaining Phase A components in a vessel and heated to above 75°C in a water bath and mixed until uniform to form the oil phase (A) of the emulsion. In a separate vessel, the Phase B components (aqueous phase) were mixed and heated in a water bath to above 75°C. The Phase A mixture was slowly added to the Phase B mixture while stirring at approximately 300 rpm and then homogenised using an Ultra-Turrax dispenser stirring at approximately 11,000 rpm. The resulting emulsion was then cooled to room temperature whilst gently stirring at approximately 150 rpm. The pH of the resulting mixture was then measured, and if required, adjusted to be between 5 and 5.5 using triethanolamine.

Example 8

Formulation IV was produced from the components listed in Table 6.

Table 6: Emulsion formulation

<u>Phase</u>	<u>Component</u>	<u>Formulation IV</u> (% w/w)
A	Isohexadecane	20
A	Pastilles produced in Example 1	10
B	Phenoxyethanol	1
B	Water	69

The pastilles produced in Example 1 were added to the remaining Phase A components in a vessel and heated to above 75°C in a water bath and mixed until uniform to form the oil phase (A) of the emulsion. In a separate vessel, the Phase B components (aqueous phase) were mixed and heated in a water bath to above 75°C. The Phase A mixture was slowly added to the Phase B mixture while stirring at approximately 300 rpm and then homogenised using an Ultra-Turrax dispenser stirring at approximately 11,000 rpm. The resulting emulsion was then cooled to room temperature whilst gently stirring at approximately 150 rpm. The pH of the resulting mixture was then measured, and if required, adjusted to be between 5 and 5.5 using triethanolamine.

CLAIMS

1. A composition comprising (i) 0.1 to 30% by weight of at least one C10 to C30 mono- and/or di-ester phosphate, (ii) 1 to 60% by weight of at least one C10 to C30 fatty alcohol,
5 and (iii) 20 to 98.9% by weight of an organic medium, all based on the total weight of the composition.
2. The composition according to claim 1 wherein the monoester phosphate is of formula $R^1-O-P(=O)(OH)_2$ and/or the diester phosphate is of formula $R^1-O-P(=O)(OR^1)(OH)$, and
10 R^1 is a C10 to C30 hydrocarbyl group.
3. The composition according to either one of claims 1 and 2 wherein the molar ratio of monoester phosphate to diester phosphate is 50 to 85%:15 to 50%.
- 15 4. The composition according to any one of the preceding claims wherein the concentration of mono- and/or di-ester phosphate is 1.5 to 10% by weight.
5. The composition according to any one of the preceding claims comprising a C12 to C24 fatty alcohol.
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6. The composition according to claim 5 comprising cetostearyl alcohol.
7. The composition according to any one of the preceding claims wherein the concentration of fatty alcohol is 16.5 to 35% by weight.
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8. The composition according to any one of the preceding claims wherein the organic medium comprises paraffin wax, light mineral oil and/or liquid paraffin.
9. The composition according to any one of the preceding claims wherein the
30 concentration of organic medium is 55 to 82% by weight.
10. A pre-mixture consisting of 4 to 20% by weight of at least one C10 to C30 mono- and/or di-ester phosphate and 80 to 96% by weight of at least one C10 to C30 fatty alcohol, both based upon the total weight of the mixture.
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11. A method of forming a composition which comprises (i) pastillating or flaking a mixture comprising at least one C10 to C30 mono- and/or di-ester phosphate and at least one C10 to C30 fatty alcohol, (ii) adding the pastilles or flake formed in (i) to organic medium, and (iii) heating to melt the pastilles or flake and form a uniform mixture.

12. An emulsion comprising an aqueous phase and an oil phase comprising at least one C10 to C30 mono- and/or di-ester phosphate and at least one C10 to C30 fatty alcohol.

5 13. The emulsion according to claim 12 comprising a composition according to any one of claims 1 to 9.

10 14. The emulsion according to either one of claims 12 and 13 comprising 10 to 50% by weight of the oil phase and 50 to 90% by weight of the aqueous phase, both based on the total weight of the emulsion.

15 15. The use of (a) a composition comprising (i) 0.1 to 30% by weight of at least one C10 to C30 mono- and/or di-ester phosphate, (ii) 1 to 60% by weight of at least one C10 to C30 fatty alcohol, and (iii) 20 to 98.9% by weight of an organic medium, all based on the total weight of the composition, or (b) an emulsion comprising the composition in (i), to maintain skin barrier properties, water content of the skin, and/or stratum corneum thickness when applied to the skin as an emollient treatment.

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