CLAIMS

1. A composition for topical application comprising:

a primary active agent for topical treatment of the skin, and

a user adherence-improving skin barrier restoring combination of:

1.0 to 5%w/w of nicotinamide

1.0 to 5%w/w of polyhydroxy acid

10 to 60%w/w of a partition coefficient enhancer (PC enhancer), having a structure of the general formula: $C_nH_{2n+2}O_2$ where n represents an integer from 3 to 5 inclusive,

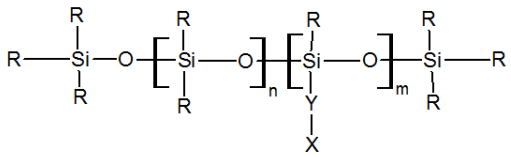
a diffusion coefficient enhancer (DC enhancer) selected from the group consisting of a C_{12} to C_{14} straight chain fatty acid and a C_{14} straight chain primary alcohol,

a first dimethicone macromer mixture including a dimethicone macromer and a hydrocarbyl methyl siloxane emollient selected from the group consisting of an alkyl methyl siloxane, an aryl methyl siloxane and an alkyl aryl methyl siloxane, and

a second dimethicone macromer mixture including a methyl siloxane compound and a cross-linked dimethicone macromer;

in which the composition comprises less than 15 % water by weight.

2. A composition according to Claim 1, in which the first dimethicone macromer mixture includes a polyglycol dimethicone macromer, generally comprising a compound of the following structure:



where R represents H or hydrocarbyl group, in particular C1 to C6 alkyl group;

Y represents a hydrocarbyl group in particular C1 to C6 alkyl group;

X represents an amine, a quaternary amino group or acid functionality.

M and n independently represent an integer from 1 to 50.

3. A composition according to Claim 1 or 2, in which the composition comprises 5 to 45%w/w first dimethicone macromer mixture, typically 10 to 40%w/w, generally 20 to 30%w/w, and/or comprising 5 to 45%w/w second dimethicone macromer mixture, typically 10 to 40%w/w, generally 20 to 30w%w/w, suitably in which the first dimethicone macromer mixture includes a dimethicone macromer having a number average molecular weight of more than 1000 (typically more than 2000) and a hydrocarbyl methyl siloxane emollient (generally an alkyl methyl siloxane) having a number average molecular weight of less than 500.

4. A composition according to Claim 1, 2 or 3, in which the first dimethicone macromer mixture includes:

(a) a polyglycol dimethicone macromer cross-linked with a polyalkylene oxide compound (generally a polyethylene glycol compound, a polypropylene glycol compound or a copolymer of ethylene oxide and propylene oxide) or cross-linked with a diene, generally in which the first dimethicone macromer mixture includes a polyglycol dimethicone macromer selected from the group consisting of PEG dimethicone PPG crosspolymer and PEG dimethicone bis-isoalkyl PPG crosspolymer; or

(b) a polyglycol dimethicone macromer comprising one or more pendant groups from the dimethicone backbone, the pendant group(s) being a polyalkylene oxide group (generally a polyethylene glycol compound, a polypropylene glycol compound or a copolymer of ethylene oxide and propylene oxide), generally in which the polyglycol dimethicone macromer includes a polyethylene glycol pendant group and a polypropylene glycol pendant group from the dimethicone backbone.

5. A composition according to any preceding claim, comprising a pyrrolidone carboxylic acid functionalized dimethicone macromer.

6. A composition according to any preceding claim, in which:

(a) the second dimethicone macromer mixture includes a methyl siloxane compound having a number average molecular weight of less than 1000 and a cross-linked polyalkylsiloxane diol dimethicone macromer having a number average molecular weight of more than 1000, generally of more than 2000; and/or

(b) the first dimethicone macromer mixture comprises 5 to 30%w/w polyglycol dimethicone macromer, typically 10-20%w/w generally 12-19%w/w; and/or where the second dimethicone macromer mixture comprises 5 to 30%w/w cross-linked dimethicone macromer, typically 10-20%w/w generally 12-19%w/w.

7. A composition according to any preceding claim, including less than 0.05% w/w water or substantially no water.

8. A composition according to any preceding claim, in which the polyhydroxy acid is selected from lactobionic acid, gluconolactone or galactose and any mixture of these.

9. A composition according to any preceding claim, comprising a second mutually miscible PC enhancer/cosolvent selected from the group consisting of an alcohol, ether-alcohol, diol, triol or alkyl pyrrolidone, suitably selected from the group consisting of a diol of the general formula $C_nH_{2n+2}O_2$ where n represents an integer greater than 6; an alcohol of the general formula $C_nH_{2n+2}O$, where n represents an integer 2 or 3; an ether-alcohol of the general formula $C_nH_{2n+2}O_3$ or $C_nH_{2n+2}O_2$ where n represents an integer from 1 to 10 or an alkyl pyrrolidone; generally in which the second mutually miscible PC enhancer/cosolvent is glycerol or N-methyl pyrrolidone.

10. A composition according to any preceding claim, including:

(a) 25 to 45%w/w PC enhancer; and/or including less than 10%w/w diffusion coefficient enhancer, generally less than 5%w/w, optimally 0.5-2%w/w; and/or

(b) 25 to 45%w/w PC enhancer; and/or including less than 0.5-2%w/w diffusion coefficient enhancer, generally less than 0.25%%w/w, optimally 0.01-0.25%, for example; where retention of the primary active in the stratum corneum is required; and/or

(c) a highly volatile solvent selected from the group consisting of hexamethyldisiloxane, octamethyltrisiloxane, cyclopentacyloxane, ethanol, isopropyl alcohol and water.

11. A composition according to any preceding claim, in which the product pH is in the range 4.4-6.00 and /or the equilibrium pH is in the range pH 3-4.

12. A composition according to any preceding claim, in which the active agent is selected from:

(a) the group consisting of retinoids, retinoic acid metabolic blocking agents (RAMBAs), cannabinoids including tetrahydrocannabinol and cannabidiol, alpha and beta hydroxy acids and polymers and derivatives thereof especially lactobionic acid and gluconolactone, immune response modifier compounds, tranexamic acid, vitamin D analogues including calcipotriol (aka calcipotriene), Vitamin B3 analogues, including nicotinamide, corticosteroids, anabolic steroids, estrogens, anti-rosacea, agents, antihistamines, antibacterial agents, antiacne agents, antifungal agents, antiviral agents, cytotoxic agents for use in actinic keratoses, basal cell and squamous cell cancers and melanoma, psoralens, anti-alopecia agents, anti-androgens, anti-pruritic agents, keratolytic agents, skin lightening and depigmenting agents, dithranol, antiseptics, anaesthetics, analgesics, neuropathics, non-steroidal anti-inflammatory agents, vasoactive agents and agents to combat dry and ageing skin; or

(b) a PARP-1 inhibitor, preferably nicotinamide, for use in the treatment of inflammatory a condition selected from skin diseases such as eczema, psoriasis, acne, bullous pemphigoid and rosacea; or

(c) a PARP-1 inhibitor, preferably nicotinamide, for use in the chemoprevention of a condition selected from actinic keratoses, basal cell and squamous cell skin cancers and melanoma; or

(d) a PARP-1 inhibitor, preferably nicotinamide in combination with a broad-spectrum inorganic or hydrophilic UV-block, for use in the chemoprevention of a condition selected from actinic keratoses, basal cell and squamous cell skin cancers and melanoma; or

(e) a PARP-1 inhibitor, preferably nicotinamide, for use in the treatment of a condition selected from actinic keratoses, basal cell and squamous cell skin cancers and melanoma; or

(f) a PARP-1 inhibitor, preferably nicotinamide in combination with a broad spectrum inorganic or hydrophilic UV-block, for use in the treatment of a condition selected from actinic keratoses, basal cell and squamous cell skin cancers and melanoma; or

(g) a PARP-1 inhibitor, preferably nicotinamide, for use in the chemoprevention of radiation dermatitis; or

(h) a melanosome transfer inhibitor, preferably nicotinamide, for use in the treatment of skin pigmentation; or

(i) nicotinamide at 5-10% by weight.

13. A composition according to any preceding claim, in which the primary active is not tranexamic acid in combination with nicotinamide 1-5% by weight and PHA 1-5% by weight.

14. A composition according to any preceding claim for use in therapy.

15. A composition according to any of Claims 1 to 13 for use in the prevention, alleviation or treatment of a medical condition of the human or animal body in which the medical condition is caused by or associated with one or more of pain and/or inflammation, pigmentation, pruritus, acne, eczema, psoriasis, rosacea, skin blistering diseases such as bullous pemphigoid, nappy rash, dry skin, microbial conditions including fungal and/or bacterial conditions such as skin infections including yeast infections and dermatophyte infections, viral infections of the skin or mucosa, warts, dry or ageing skin, hypoandrogenism, immunological conditions, sun spots, actinic keratosis, basal cell and squamous cell skin cancers and melanoma, alopecia and dermatitis due to radiation therapy.

16. Use of a composition according to any of Claims 1 to 13 in the preparation of a medicament for the treatment or prevention of a medical condition of the human or animal body in which the medical condition is caused by or associated with one or more of pain and/or inflammation, pigmentation, pruritus, acne, eczema, psoriasis, rosacea, skin blistering diseases such as bullous pemphigoid, nappy rash, dry skin, microbial conditions including fungal and/or bacterial conditions such as skin infections including yeast infections and dermatophyte infections, viral infections of the skin or mucosa, warts, dry or ageing skin, hypoandrogenism, immunological conditions, sun spots, actinic keratosis, basal cell and squamous cell skin cancers and melanoma, alopecia and dermatitis due to radiation therapy.