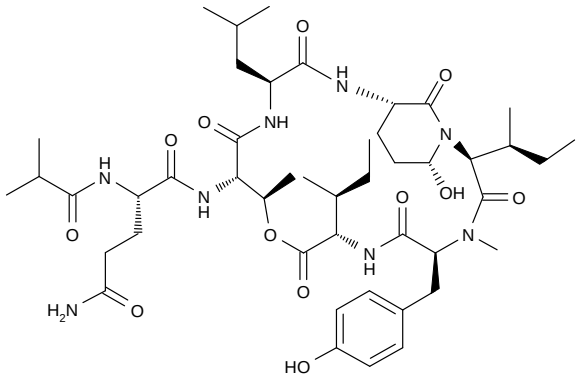
the word “contain”, or variations such as “contains” or “containing”, will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

It is further understood that the various embodiments, preferences and ranges of this invention, as provided / disclosed in the specification and claims may be combined with other specified features to provide further embodiments.

In a first aspect, the present invention provides a topical pharmaceutical composition comprising a cyclic depsipeptide of formula (II), a hydrophobic matrix and a consistency agent. It is typically a suspension type composition.

In another aspect, the present invention provides a topical pharmaceutical composition comprising a cyclic depsipeptide of formula (II)



(II),

a hydrophobic matrix and isopropyl myristate as a consistency agent.

The active agent has a tendency to degrade in hydrophilic environment such as water and polar organic solvents / co-solvents and is subject to hydrolysis in the presence of water.

It was found that topical pharmaceutical compositions comprising a cyclic depsipeptide of formula (II), a hydrophobic matrix and a consistency agent, allow the active agent to be formulated into stable compositions and allow for suitable penetration and permeation profile; especially in view of the fact that the active agent is suspended in the matrix and thus only a small fraction of molecules is dissolved and available for penetration. By the use of a consistency agent it is possible to increase the level of the active agent to a pharmaceutically beneficial level in the skin without skin irritation. However, permeation of

the active agent through the skin was very low, resulting in no systemic exposure or very low systemic exposure, thus minimizing the risk of side effects. Further, these compositions show good physical and chemical stability. This aspect of the invention shall be explained in further detail below:

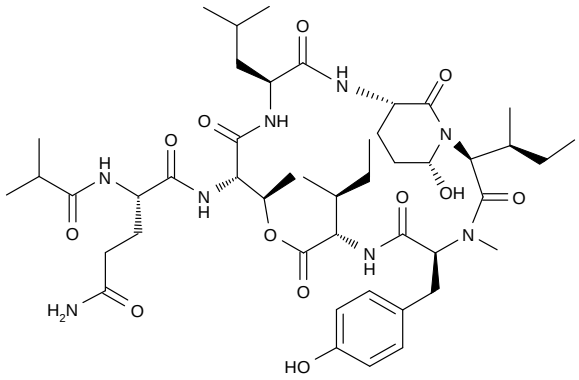
The active agent may be obtained according to the methods described in WO2009024527. Particularly suitable for the inventive compositions are active agents of the invention in micronized form (x90<20 micrometer). The amount of active agent in the inventive composition may vary over a broad range, it is typically provided in an effective amount. An effective amount refers to an amount of the active agent which, when administered to a mammal (preferably a human), is sufficient to effect a treatment as defined below. Suitable amounts for the active agent may be determined by the skilled person in routine experiments; typically they are in the range between 0.1 – 5 wt.%, preferably 0.5 – 2.0 wt.%, such as 0.5, 0.8 or 1.0 wt.%.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A topical pharmaceutical composition comprising a cyclic depsipeptide of formula (II)



(II),

a hydrophobic matrix and isopropyl myristate as a consistency agent.

2. A pharmaceutical composition according to claim 1, in form of a hydrophobic ointment.

3. A pharmaceutical composition according to claim 1 or 2, wherein the hydrophobic matrix includes one or more compounds selected from the group consisting of paraffines, vegetable oils, animal fats, synthetic glycerides, waxes, perflourcarbons, semiperflourcarbones and liquid polysiloxanes.

4. A composition according to any one of claims 1 to 3, wherein the hydrophobic matrix includes at least two types of hydrocarbons selected from mineral oil, petrolatum, and microcrystalline wax.

5. A composition according to any of claims 1 to 4 further comprising one or more excipients selected from the group consisting of antioxidants, gelling agents, pH adjusting agents / buffers, penetration enhancers, preservatives, (co-) solvents and stabilizers.

6. A composition according to any of claims 1 to 4 further comprising one or more penetration enhancer.

7. A composition according to any one of claims 1 to 6, wherein the cyclic depsipeptide of formula (II) is present in an amount between 0.1 – 5 wt.% of the total

composition, the consistency agent is present in an amount between 2.5 – 20 wt.% of the total composition and the hydrophobic matrix contains up to 66 wt.% mineral oil, up to 98 wt.% petrolatum, up to 25 wt.% microcrystalline wax.

8. A composition according to any of claims 1 to 7 for the treatment of, or for use in the treatment of inflammatory and/or hyperpoliferative and pruritic skin diseases such as acne, atopic dermatitis, psoriasis, pustular psoriasis, rosacea, keloids, hypertrophic scars, Netherton's syndrome or other pruritic dermatoses such as prurigo nodularis, unspecified itch of the elderly as well as other diseases with epithelial barrier dysfunction such as aged skin.

9. A composition according to any of claims 1 to 7 for the treatment of inflammatory and/or hyperpoliferative and pruritic skin diseases such as atopic dermatitis, psoriasis, pustular psoriasis, rosacea, keloids, hypertrophic scars, acne, Netherton's syndrome or other pruritic dermatoses such as prurigo nodularis, unspecified itch of the elderly as well as other diseases with epithelial barrier dysfunction such as aged skin.

~~10. A method of treatment of inflammatory and/or hyperpoliferative and pruritic skin diseases selected from atopic dermatitis, psoriasis, pustular psoriasis, rosacea, keloids, hypertrophic scars, acne, Netherton's syndrome or other pruritic dermatoses including prurigo nodularis, unspecified itch of the elderly, and diseases with epithelial barrier dysfunction including aged skin, said method comprising administering to a subject in need of such treatment an effective amount of a composition according to any of claims 1 to 7.~~

~~11~~10. Use of a composition according to any one of claims 1 to 7 in the manufacture of a medicament for the treatment of inflammatory and/or hyperpoliferative and pruritic skin diseases selected from atopic dermatitis, psoriasis, pustular psoriasis, rosacea, keloids, hypertrophic scars, acne, Netherton's syndrome or other pruritic dermatoses including prurigo nodularis, unspecified itch of the elderly, and diseases with epithelial barrier dysfunction including aged skin.