[0014] FIG. 5 illustrates the amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene delivered into the receiving fluid over 72 hours from Formulations 12 and 21.

[0015] FIG. 6 illustrated the percent change of mRNA Cyp1A1 in human ex vivo skin after Th17 stimulation for Formulations 12, 17, 21 and 22.

[0016] FIG. 7 illustrates the amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene delivered into skin of Gottingen mini pigs after 7 days of repeat dosing.

[0017] FIG. 8 illustrates the amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene in the plasma of Gottingen mini pigs after 7 days of repeat dosing. Formulation in FIGs. 7 and 8 correspond to Formulations 12 and 22.

SUMMARY OF THE INVENTION

[0018] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion composition is homogeneous.

[0019] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion composition is uniform.

[0020] The present disclosure provides for formulations which effectively solubilize 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene, or a pharmaceutically acceptable salt thereof, resulting in a homogeneous and uniform emulsion. Homogeneity and uniformity can be determined using microscopy, hot stage optical microscopy, XRD, IR microscopy and fluorescent microscopy and by analyzing transmission profile, droplet size, droplet shape, viscosity and/or stability index.

[0021] In another example, the active is solubilized in the oil phase of the emulsion composition. In another example, the oil phase contains mineral oil and/or petrolatum. In another example, if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1 % petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester or an ester of

glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride.

[0022] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising an effective amount of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the emulsion composition is homogeneous and the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum then a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1% petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or and ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride.

[0023] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the active is solubilized in the oil phase of the emulsion composition. In another example, the emulsion composition is homogeneous.

[0024] In another example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion composition is homogeneous and/or the active is solubilized in the oil phase of the emulsion composition.

[0025] In another example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water

phase, a surfactant, and an antioxidant, and wherein the average the average droplet size of the discontinuous phase is about 0.1 micron to about 35 microns. In another example, the average the average droplet size of the discontinuous phase is about 0.1 micron to about 25 microns. In another example, the average the average droplet size of the discontinuous phase is about 0.1 micron to about 15 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 10 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 5 microns. In another example, the average droplet size of the discontinuous phase is about or is about 0.1 micron to about 1 micron. In another example, the average droplet size of the discontinuous phase is from about 0.1 to about 0.75 microns. In another example, the average droplet size of the discontinuous phase is about 0.5 microns.

[0026] In another example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the average particle size of the oil phase is about 0.1 micron to about 35 microns, and the emulsion composition is homogeneous and/or the active is solubilized in the oil phase of the emulsion composition.

[0027] In another example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the average particle size of the oil phase is about 0.1 micron to about 10 microns, and the emulsion composition is homogeneous and/or the active is solubilized in the oil phase of the emulsion composition.

[0028] In another example, the disclosure provides a method of treating a dermatological condition or disorder in a patient in need thereof, the method comprising administering to said patient a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion composition is homogeneous.

[0029] In another example, the disclosure provides a method of treating a dermatological condition or disorder in a patient in need thereof, the method comprising administering to said patient a topical pharmaceutical emulsion composition comprising the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable

salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion composition is uniform.

[0030] In another example, the active is solubilized in the oil phase of the emulsion composition. In another example, the oil phase contains mineral oil and/or petrolatum. In another example, if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1 % petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride.

[0031] In another example, the disclosure provides a method of treating a dermatological condition or disorder in a patient in need thereof, the method comprising administering to said patient a topical pharmaceutical emulsion composition comprising an effective amount of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1% petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum then at least a third oil phase component is present which comprises an ester and/or an ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride. In one example, the dermatological condition or disorder is an inflammatory dermatological condition or disorder. In another example, the inflammatory dermatological condition or disorder is atopic dermatitis and/or psoriasis, and/or acne.

[0032] In another example, the disclosure relates to the use of a topical pharmaceutical emulsion composition comprising an effective amount of the active ingredient 3,5-Dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion is homogeneous, for use in the treatment or prophylaxis of a dermatological condition or disorder in a human patient.

[0033] In another example, the disclosure relates to the use of a topical pharmaceutical emulsion composition comprising an effective amount of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase comprises mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1% petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride.

[0034] In another example, the disclosure relates to a topical pharmaceutical emulsion composition comprising an effective amount of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present for use in the treatment or prophylaxis of a dermatological condition or disorder in a human patient. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1% petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin such as a medium

chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or and ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride.

[0035] In another example, the disclosure relates to a method of reducing irritancy in a topical pharmaceutical emulsion composition containing the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof in use in a patient in need thereof, the method comprising administering to the patient a pharmaceutical emulsion composition comprising an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1% petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin, such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride.

[0036] In one example, the emulsion composition of the instant disclosure is compared to that of Formulation 1 or 12 (with comparable % w/w active).

[0037] In another example, the disclosure relates to a method of improving the residency time of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof in the skin of a patient in need thereof, the method comprising administering to said patient a pharmaceutical emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the emulsion composition is homogeneous.

[0038] In another example, the disclosure relates to a method of improving the residency time of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbenc or a pharmaceutically acceptable salt thereof in the skin of a patient in need thereof, the method comprising administering to said patient a pharmaceutical emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically

acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1 % petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is which is an ester and/or an ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In one example, the emulsion composition of the instant disclosure is compared to that of the Formulation 1 or 12 (with comparable% w/w of active ingredient).

[0039] In another example, the disclosure relates to a method of improving the residency time of the active ingredient 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof in the skin of a patient in need thereof, the method comprising administering to said patient a pharmaceutical emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion is homogeneous and/or the active is solubilized in the oil phase. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 35 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 5 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 1 micron.

[0040] In another example, the disclosure relates to a method of reducing side effects in a patient who is administered a composition containing 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, the method comprising administering to the patient a pharmaceutical emulsion composition comprising an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the emulsion is homogeneous and/or the active is solubilized in the oil phase. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 35 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about

5 microns. In another example, the average droplet size of the discontinuous phase is about 0.1 micron to about 1 micron.

[0041] In another example, the disclosure relates to a method of reducing side effects in a patient who is administered a composition containing 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, the method comprising administering to the patient a pharmaceutical emulsion composition comprising an oil phase, a water phase, a surfactant, and an antioxidant, and wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and provided that if the oil phase contains mineral oil or petrolatum, then a second oil phase component is present, and if the oil phase contains both mineral oil and petrolatum than a third oil phase component is present. In one example, the oil phase is substantially free from petrolatum. In another example, the oil phase contains ≤ 3%, or ≤ 2%, or ≤ 1 % petrolatum. In another example, if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present which is an ester and/or and ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In another example, if the oil phase contains mineral oil then a second oil phase component is present which is an ester and/or and ester of glycerin, suitably an ester of glycerin such as a medium chain triglyceride. In one example, the emulsion composition of the instant disclosure is compared to that of Formulation 1 or 12, or a similar formulation with equivalent active ingredient present.

[0042] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3, 5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition. In one example, the oil phase contains mineral oil and/or petrolatum. In another example, if the oil phase contains mineral oil, then a second oil phase component other than petrolatum is present in the composition. In another example, if the oil phase contains petrolatum, then a second oil phase component other than mineral oil is present in the composition. In any of these examples it is preferable that the resulting emulsion does not contain non-uniform areas or waxy regions upon storage.

[0043] In one example, the present disclosure provides for a topical pharmaceutical emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water

phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and wherein if the oil phase contains mineral oil, then a second oil phase component other than petrolatum is present in the composition.

[0044] In an example, the disclosure provides for a topical pharmaceutical emulsion composition comprising 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and wherein if the oil phase contains mineral oil then a second oil phase component other than petrolatum is present in the composition, or if the oil phase contains both mineral oil and petrolatum at least a third oil phase component is present. In another example, the oil phase is substantially free from mineral oil and/or petrolatum.

[0045] In one example, the present disclosure provides for a topical pharmaceutical O/W emulsion composition comprising an effective amount of 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or a pharmaceutically acceptable salt thereof, an oil phase, a water phase, a surfactant, and an antioxidant, wherein the 3,5-Dihydroxy-4-isopropyl-*trans*-stilbene or pharmaceutically acceptable salt thereof is solubilized in the oil phase of the emulsion composition, and the composition is formulated as a cream or lotion. In another example, the cream or lotion is homogeneous and uniform in appearance.

[0046] In certain examples, the topical pharmaceutical oil-in-water emulsion composition comprises: about 0.1% to about 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof, an oil phase in an amount of about 5% to about 35% by weight, based on the total weight of the composition and is selected from the group consisting of cocoyl caprylocaprate, isostearyl isostearate, octyldodecanol, jajoba oil, sesame oil, walnut oil, isopropyl palmitate, isopropyl myristate, safflower oil, mineral oil, olive oil, almond oil, and combinations thereof, a water phase in an amount of about 25% to about 85% by weight, based on the total weight of the composition, a surfactant in an amount of about 0.1% to about 20% by weight, based on the total weight of the composition, and an antioxidant.

[0047] In certain examples, the topical pharmaceutical oil-in-water emulsion composition comprises: about 0.1% to about 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof, mineral oil in an amount of about 5% to about 15% by weight, based on the total weight of the composition, a co-solvent in an

amount of about 1% to about 30% by weight, based on the total weight of the composition, a water phase in an amount of 25% to about 85% by weight, based on the total weight of the composition, a surfactant in an amount of about 0.1% to about 20% by weight, based on the total weight of the composition, comprising a mixture of polysorbate 80, nonionic emulsifying wax (Polawax NF), Steareth 2, and Steareth 20, and an antioxidant.

[0048] In certain examples, the topical pharmaceutical oil-in-water emulsion composition comprises: about 0.1% to about 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof, an oil phase in an amount of about 5% to about 45% by weight, based on the total weight of the composition, a water phase in an amount of about 25% to about 85% by weight, based on the total weight of the composition, a surfactant in an amount of about 1% to about 20% by weight, based on the total weight of the composition and is selected from the group consisting of oleoyl polyoxyl-6 glycerides, PEG32 Stearate, PEG 75, PEG 20 cetostearyl ether, ceteareth-12, ceteareth-15, ethylene glycol palmitostearate, cetostearyl alcohol, glycerol monostearate, stearyl alcohol, cetyl alcohol, steareth-2, steareth-20, steareth-21, and combinations thereof, and an antioxidant.

[0049] In certain examples, the topical pharmaceutical oil-in-water emulsion composition comprises: about 0.1% to about 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof, an oil phase in an amount of about 5% to about 45% by weight, based on the total weight of the composition, a water phase in an amount of about 25% to about 85% by weight, based on the total weight of the composition, a surfactant in an amount of about 0.1% to about 20% by weight, based on the total weight of the composition, an antioxidant, and a co-solvent in an amount of greater than 30% by weight, based on the total weight of the composition.

[0049a] In an aspect, the present disclosure provides a topical pharmaceutical oil-in-water emulsion composition comprising:

0.1% to 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof,

an oil phase in an amount of 5% to 45% by weight, based on the total weight of the composition,

a water phase in an amount of 25% to 85% by weight, based on the total weight of the composition,

a surfactant in an amount of 0.1% to 20% by weight, based on the total weight of the composition,

an antioxidant, and

a co-solvent in an amount of greater than 30% by weight, based on the total weight of the composition.

[0049b] In another aspect, the present disclosure provides use of the topical pharmaceutical emulsion composition as defined herein in the manufacture of a medicament for treating a dermatological condition or disorder in a patient in need thereof, wherein the medicament is to be administered to said patient.

[0049c] In another aspect, the present disclosure provides the topical pharmaceutical emulsion composition as defined herein for use in therapy.

DETAILED DESCRIPTION OF THE INVENTION

[0050] In addition to creating a physically and chemically stable pharmaceutical formulation, the present invention also provides for a pharmaceutical formulation which is non-irritating to the skin upon application and use, or is one which is less irritating than any previous formulations used in the development of the active ingredient to date. Another aspect of the invention is a formulation that not only has superior skin penetration and target engagement of the appropriate receptors, but also has significant non-systemic exposure of the active ingredient to the patient upon application and use.

CLAIMS

1. A topical pharmaceutical oil-in-water emulsion composition comprising:

0.1% to 5% by weight of 3,5-dihydroxy-4-isopropyl-trans-stilbene or a pharmaceutically acceptable salt thereof,

an oil phase in an amount of 5% to 45% by weight, based on the total weight of the composition,

a water phase in an amount of 25% to 85% by weight, based on the total weight of the composition,

a surfactant in an amount of 0.1% to 20% by weight, based on the total weight of the composition,

an antioxidant, and

a co-solvent in an amount of greater than 30% by weight, based on the total weight of the composition.

2. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the surfactant is selected from the group consisting of non-ionic surfactants, ethoxylated fatty alcohol ethers, PEG castor oils, PEG esters, propylene glycol esters, polymeric ethers, fatty alcohols, emulsifying waxes, and mixtures thereof.

3. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the oil phase is selected from the group consisting of fatty acids, esters, esters of glycerin, fatty alcohols, waxes, sterols, unsaponifiables, siloxanes, silanes, lanolin, hydrocarbons, essential oils, vegetable oils, mineral oils, animal oils, edible oils, and mixtures thereof

4. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the antioxidant is in an amount of 0.001% to 5%.

5. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the antioxidant is selected from the group consisting of butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), tocopherol, propyl gallate, vitamin E TPGS and tert-Butylhydroquinone (TBHQ), and mixtures thereof.

6. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the pH of the composition is 4 to 7.

7. The topical pharmaceutical oil-in-water emulsion composition of claim 1, further comprising one or more additional dermatologically acceptable excipients selected from the group consisting of pH adjusting agent, a chelating agent, a preservative, a co-solvent, a penetration enhancer, a humectant, a thickening agent, a gelling agent, a viscosity building agent, a fragrance, a colorant, and combinations thereof.

8. The topical pharmaceutical oil-in-water emulsion composition of claim 11, wherein the viscosity is 10,000 mPa.s to 300,000 mPa.s.

9. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the composition has a droplet size having a D90 of 0.1 μm to 35μm.

10. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the composition has a droplet size having a D50 of 0.1 μm to 35μm.

11. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the composition has an in vitro skin permeation profile of 10 ng/cm^2 to 65 ng/cm^2.

12. The topical pharmaceutical oil-in-water emulsion composition of claim 11, wherein the composition has an in vitro penetration into the epidermis profile of 500 ng to 5,200 ng.

13. The topical pharmaceutical oil-in-water emulsion composition of claim 1, wherein the composition has an in vitro penetration into the dermis profile of 1,800 ng to 12,000 ng.

14. Use of the topical pharmaceutical emulsion composition of any one of claims 1 to 13 in the manufacture of a medicament for treating a dermatological condition or disorder in a patient in need thereof, wherein the medicament is to be administered to said patient.

15. The topical pharmaceutical emulsion composition of any one of claims 1 to 13 for use in therapy.