Compositions and methods for the treatment of dermal disease

Related Application

[001] This application claims priority to Australian Provisional Patent Application No 2024900656 filed 13 March 2024 which is herein incorporated by reference in its entirety.

Technical Field

[002] The invention relates to a topical composition comprising a water soluble substance and a water insoluble substance. The composition may further comprise a therapeutic agent for the treatment of a dermal disease. Also provided are methods of treating a dermal disease using the topical composition.

Background

[003] Eczema is a term used to describe a group of skin conditions that cause inflammation of the epidermis. The term is broadly applied to a range of persistent skin conditions characterised by one or more symptoms including redness, skin edema (swelling), itching and dryness, crusting, flaking, blistering, cracking, oozing, or bleeding. Itchy rash is particularly noticeable on the head and scalp, neck, inside of elbows, behind knees, and buttocks. There are several types of eczematous disorders, for example atopic eczema, asteatotic eczema, contact eczema, allergic contact eczema, seborrheic eczema, nummular eczema, dyshidrotic eczema, dermatitis herpetiformis, stasis dermatitis and neurodermatitis. The disorder often presents during infancy and sometimes disappears by adulthood. In some cases, it can present for the first time in adulthood.

[004] Although eczema is a common disease affecting 10-20% of children and 1-3% of adults in developed countries, the exact causes of the disease is unknown. It is thought to be associated with a disorder of the immune system and appears to have a genetic component, often occurring in a higher frequency in certain families and ethnic groups. It can cause considerable mental and physical distress such as constant itchiness, dry skin, unsightly rashes and, in the worst cases, can cause debilitation and require hospitalization.

[005] There is no known cure for eczema. The goal of treatment for eczema is to relieve and prevent itching. Treatments include moisturizing lotions, occlusive dressing for extremely dry patches, topical or oral anti-inflammatory corticosteroids and numbing agents. Over-the-counter strength preparations of these therapies usually have a minimal effect. While prescription strength corticosteroids are the most commonly prescribed therapies, they can have serious side effects. Topical corticosteroid use can lead to thin skin, red

lesions and acne, and oral corticosteroid use can lead to mood swings, glaucoma, weight gain, increased blood pressure, cataracts, and osteoporosis, often necessitating discontinuation of the treatment.

[006] Other eczema treatments include antihistamines, tar treatments, phototherapy, cyclosporine, and topical immunomodulators. Numbing agents and antihistamines provide minimal relief in the majority of moderate to severe clinical cases. UVB light therapy is commonly used to treat severe cases of eczema with a high rate of effectiveness, although undesirable side effects can occur such as an increased risk of developing skin cancer as well as undesirable phototoxic reactions. Topical immunomodulators may prevent eczema flare-ups but their use has also been linked with increased cancer risk.

[007] Despite the development of various products for the treatment of eczema, there still remains a need for effective compositions for the treatment of eczema that have minimal or no side effects.

Summary

[008] In a first aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and

a water insoluble substance.

[009] The composition may further comprise a therapeutic agent useful for the treatment of a dermal disease.

[010] In some embodiments, the organic acid comprised in the composition is selected from the group consisting of malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, propanedioic acid and lactic acid.

[011] In some embodiments, the metallic salt comprised in the composition is selected from the group consisting of sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium sulfate, sodium chloride, sodium fumarate, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate , potassium lactate, potassium tartrate, potassium maleate, potassium sulfate, potassium chloride, potassium fumarate, magnesium sulfate, magnesium chloride, calcium chloride, sodium ascorbate, and aluminum chloride.

[012] In some embodiments, the neutral substance comprised in the composition is selected from the group consisting of maltodextrin, mannitol, sorbitol, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, PEG

200 to PEG 20000, polyethylene-propylene glycol copolymer, docusate sodium, glyceryl monostearate, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate.

[013] In some embodiments, the composition is formulated as an ointment, beside the water soluble chemical it contains the water insoluble substance which is selected from the group consisting of glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil and fatty alcohol.

[014] In some embodiments, the composition is formulated as a powder, beside the water soluble chemical it contains the water insoluble substance, which is selected from the group consisting of talc, sublimed sulfur, sulfur, calamine, zinc oxide, calcium carbonate, microcrystalline cellulose, a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, tapioca starch and magnesium stearate.

[015] In some embodiments, the therapeutic agent is selected from the group consisting of a glucocorticoid steroid including amcinonide, beclometasone, betamethasone, clobetasol, ciclesonide, desonide, dexamethasone, fludrocortisone acetate, fluocinolone acetonide, fluocinonide, flunisolide, fluocortolone, fluticasone, halcinonide, halometasone, hydrocortisone, mometasone, prednisolone, tixocortol pivalate, and triamcinolone acetonide or a salt thereof, tacrolimus, pimecrolimus, and crisaborole, an antihistamine including doxepin hydrochloride, diphenhydramine, and loratadine, and a JAK1/JAK2 inhibitor including dalbitux, upadatinib, and ruxolitinib.

[016] In some embodiments, the composition is substantially anhydrous.

[017] In some embodiments, the composition comprises less than about 5% of water by weight of the total weight of the composition.

[018] In some embodiments, the composition comprises less than about 3% of water by weight of the total weight of the composition.

[019] In some embodiments, the composition comprises about 0.5% to about 99% of a water soluble substance by weight of the total weight of the composition.

[020] In some embodiments, the composition comprises about 10% to about 50% of a water soluble substance by weight of the total weight of the composition.

[021] In one embodiment, the composition is formulated as a powder, and the composition comprises about 0.5% to about 99% of a water soluble substance selected from an organic acid, a metallic salt and a neutral substance or a combination thereof, by weight of the total weight of the composition.

[022] In one embodiment, the composition comprises:

a water soluble substance selected from a metallic salt, an organic acid, and a neutral substance; and

a water insoluble substance selected from a sublimed sulfur, sulfur, calamine, zinc oxide, a starch, calcium carbonate, microcrystalline cellulose or a combination thereof,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as a powder.

[023] In some embodiments, the water soluble substance is an organic acid selected from the group consisting of malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, propanedioic acid and citric acid, or a combination thereof.

[024] In some embodiments, the water soluble substance is a metallic salt selected from the group consisting of sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium sulfate, sodium chloride, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium sulfate, potassium chloride, magnesium sulfate, magnesium chloride, calcium chloride, and aluminum chloride, or a combination thereof.

[025] In some embodiments, the water soluble substance is a neutral substance selected from the group consisting of maltodextrin, mannitol, sorbitol, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, PEG 200 to PEG 20000, polyethylene-propylene glycol copolymer, docusate sodium, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof.

[026] In one embodiment, the composition is formulated as an ointment, and the composition comprises:

a water soluble substance selected from the group consisting of a salt, an organic acid and a neutral substance; and

a water insoluble substance selected from a group consisting of glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil, fatty alcohol,

wherein the composition comprises less than about 5% of water by weight of the

total weight of the composition.

[027] In one embodiment, the composition is formulated as an ointment, and the composition comprises:

a water soluble substance selected from the group consisting of a salt, an organic acid and a neutral substance;

a therapeutic agent selecting from the group consisting of a glucocorticoid steroid including amcinonide, beclometasone, betamethasone, clobetasol, ciclesonide, desonide, dexamethasone, fludrocortisone acetate, fluocinolone acetonide, fluocinonide, flunisolide, fluocortolone, fluticasone, halcinonide, halometasone, hydrocortisone, mometasone, prednisolone, tixocortol pivalate, and triamcinolone acetonide or a salt thereof, tacrolimus, pimecrolimus, and crisaborole, an antihistamine including doxepin hydrochloride, diphenhydramine, and loratadine, and a JAK1/JAK2 inhibitor including dalbitux, upadatinib, and ruxolitinib; and

a water insoluble substance selected from a group consisting of glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil, fatty alcohol,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

[028] In some embodiments, the composition is formulated as a powder, and the water soluble substance is selected from the group consisting of magnesium sulfate, sodium chloride, sodium sulfate, sodium phosphate, maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, polyethylene-propylene glycol copolymer, docusate sodium, or a combination thereof, and wherein the water soluble substance is about 0.5% to about 50% by weight of the total weight of the composition.

[029] In some embodiments, the composition is formulated as a powder, and the water soluble substance is selected from the group consisting of a metallic salt including sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium sulfate, sodium chloride, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium sulfate, potassium chloride, magnesium sulfate, magnesium chloride, calcium chloride, and aluminum chloride, or a combination thereof and wherein the water soluble substance is about 0.5% to about 95% by weight of the total weight of the composition.

[030] In some embodiments, the composition is formulated as a powder, and the water

soluble substance is selected from the group consisting of an organic acid including malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, propanedioic acid and citric acid, or a combination thereof and wherein the water soluble substance is about 0.5% to about 95% by weight of the total weight of the composition.

[031] In some embodiments, the composition is formulated as a powder, and the water soluble substance is an organic acid.

[032] In a second aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from the group consisting of magnesium sulfate, sodium sulfate, sodium chloride, potassium chloride, potassium sulfate, polyethylene-propylene glycol copolymer, and PEG 200 to PEG 20000, or a combination thereof;

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

a glucocorticoid or a salt thereof,

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[033] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from the group comprising polyethylene-propylene glycol copolymer or PEG of molecular weight from 200 to PEG 20000, or a combination thereof;

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[034] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from the group comprising polysorbate of

molecular weight from Tween 20, Tween 40, Tween 60, to Tween 80, or a combination thereof;

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[035] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance including sodium sulfate, magnesium sulfate, Poloxamer,

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[036] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from the group comprising polyethylene-propylene glycol copolymer or PEG 200 to PEG 20000, or a combination thereof;

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

a glucocorticoid or a salt thereof,

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[037] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance selected from the group comprising polysorbate of

molecular weight from Tween 20, Tween 40, Tween 60, to Tween 80, or a combination thereof;

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

a glucocorticoid steroid or a salt thereof,

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[038] In another aspect, the invention relates to a topical composition comprising:

a water soluble substance including sodium sulfate, magnesium sulfate, Poloxamer,

a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

a glucocorticoid steroid or a salt thereof,

wherein the water soluble substance is about 0.5% to about 80% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

[039] In some embodiments, the glucocorticoid is selected from the group consisting of 0.1% mometasone, 0.1%-0.5% hydrocortisone, 0.1%-0.5% triamcinolone, 0.05% dexamethasone, 0.1% betamethasone, 0.05% halometasone, 0.025% fludrocortisone acetate, 0.02% clobetasol, 0.1% amcinonide, 0.05% desonide, 0.1% halcinonide, 0.05% fluticasone, and 0.5% prednisolone.

[040] In a third aspect, the invention relates to a method of treating a dermal disease in a subject comprising the steps of:

a) administering to the subject a topical therapeutic agent for the treatment of the dermal disease; and

b) administering to the subject an effective amount of the topical composition of the first aspect,

wherein the topical composition is formulated as a powder.

[041] In a fourth aspect, the invention relates to a method of treating a dermal disease in a subject comprising administering to the subject an effective amount of the topical composition of the first aspect or the second aspect.

[042] In one aspect, the invention relates to a method of treating a dermal disease in a subject comprising administering to the subject an effective amount of the topical composition comprising a water soluble substance in the form of a powder and or ointment.

[043] In some embodiments, the dermal disease is selected from the group consisting of eczema, atopic eczema, neurodermatitis, contact dermatitis, chronic eczema, infant eczema, miliaria, diaper rash, psoriasis and ulcer of diabetes mellitus.

[044] In a fifth aspect, the invention relates to use of a composition comprising a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and a water insoluble substance, in the manufacture of a topical medicament for the treatment of a dermal disease, wherein the medicament is substantially anhydrous.

[045] In one aspect, the invention relates to a topical composition comprising a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and a water insoluble substance.

Definitions

[046] The terms "eczema" and "dermatitis" are used interchangeably. As used herein, the term "eczema" refers to a group of skin conditions that present dry, swollen, irritated and/or itchy skin. Types of eczema to be treated with the compositions and methods of the present invention include, but are not limited to, atopic dermatitis, nummular dermatitis, seborrheic dermatitis, irritant contact dermatitis, allergic contact dermatitis, dyshidrotic dermatitis, hand dermatitis, neurodermatitis, occupational dermatitis, and stasis dermatitis. The term "dermal disease" as used herein include, but is not limited to, eczema, atopic eczema, neurodermatitis, contact dermatitis, chronic eczema, infant eczema, miliaria, diaper rash, psoriasis and ulcer of diabetes mellitus.

[047] The term "skin" is meant to include skin of the entire body including the scalp, the forehead, the head, neck, arms, legs, and so forth. The term "skin" is also meant to include various layers of the skin, such as stratum corneum, epidermis and dermis.

[048] The terms "disease", "disorder" and "condition" as used herein are used interchangeably to specify a state of a subject which is not the normal physiological state of a subject.

[049] The term "anhydrous" as used herein means that there is less than about 5% by weight of water in a composition based on the total weight of the composition. In some embodiments, the composition may include less than about 4%, less than about 3%, less than about 2%, less than about 1%, less than about 0.5%, or less than about 0.1% of water, or none at all.

[050] The terms "water soluble substance" and "water insoluble substance" are used here in a pragmatic sense. For example, "water soluble substance" need not necessarily imply that the substance form an aqueous "solution" within the technical meaning of "solution" as one might find in a chemistry textbook. If a more mathematically precise distinction is needed then the term "water soluble substance" refers to a substance that can be dissolved in water at a concentration of more than 1 wt-%, and the "water insoluble substance" refers to a substance that can be dissolved in water only to a concentration of less than 0.1 wt-%.

[051] All percentages, parts and ratios herein are based upon the total weight of the compositions of the present invention, unless otherwise indicated.

[052] The phrase "and/or" as used herein should be understood to mean "either or both" of the elements so conjoined, i.e., elements that are conjunctively present in some cases and disjunctively present in other cases.

[053] Throughout this specification, unless the context clearly requires otherwise, the word "comprise", or variations such as "comprises", "comprising", or "including", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

[054] Unless the context requires otherwise or specifically stated to the contrary, integers, steps, or elements of the technology recited herein as singular integers, steps or elements clearly encompass both singular and plural forms of the recited integers, steps or elements.

[055] In the context of the present specification, the terms "a" and "an" are used to refer to one or more than one (i.e., at least one) of the grammatical object of the article. By way of example, reference to "an element" means one element, or more than one element.

[056] In the context of the present specification, the term "about" means that reference to a figure or value is not to be taken as an absolute figure or value but includes margins of variation above or below the figure or value in line with what a skilled person would understand according to the art, including within typical margins of error or instrument limitation. In other words, use of the term "about" is understood to refer to a range or

approximation that a person or skilled in the art would consider to be equivalent to a recited value in the context of achieving the same function or result.

[057] The term "treating" or "treatment" of a dermal disease as used herein means: (1) preventing or delaying one or more symptoms of a dermal disease (e.g., eczema) from developing in a subject that may be predisposed to the dermal disease but does not yet experience or display symptoms, (2) inhibiting a dermal disease, i.e., arresting or reducing the development or progression of the dermal disease or at least one or more symptoms thereof, or (3) relieving a dermal disease, i.e., causing regression or reversing of the dermal disease or at least one of its symptoms. The benefit to a subject to be treated is either statistically significant or at least perceptible to the subject with the dermal disease and/or to the physician. Thus, the term "treating", or "treatment" and the like is to be considered in their broadest context and encompasses curing, ameliorating, or tempering the severity of a dermal disease or one or more of its associated symptoms. For the purposes of the present invention, "treating" or "treatment" may mean compared to the skin condition when not receiving treatment.

[058] "Effective amount" and "therapeutically effective amount" refer to an amount of a therapeutic agent (e.g., a glucocorticoid or antihistamine) or composition sufficient to produce a desired therapeutic or pharmacological effect in the subject being treated. The terms are synonymous and are intended to qualify the amount of each therapeutic agent or composition that will achieve the goal of improvement in disease severity and/or the frequency of incidence of disease while preferably avoiding or minimizing adverse side effects, including side effects typically associated with other therapies. The "effective amount" or "therapeutically effective amount" will vary depending on the therapeutic agent or composition, the disease severity, and the age, physical condition, and responsiveness of the individual to be treated.

[059] The terms "subject", "patient", and "individual" is used interchangeably and include any human or non-human mammal. Thus, in addition to being useful for human treatment, the methods and compositions of the present invention may also be useful for veterinary treatment of mammals, including companion animals and farm animals, such as, but not limited to dogs, cats, horses, cows, sheep, and pigs. In some embodiments the subject is a human.

[060] In the context of this specification, the term "administering" and variations of that term including "administer" and "administration", includes contacting, applying, delivering, or providing a therapeutic agent (e.g., a glucocorticoid or antihistamine) or a composition of the invention to a subject by any appropriate means.

[061] Any reference to or discussion of any document, act or item of knowledge in this specification is included solely for the purpose of providing a context for the present invention. It is not suggested or represented that any of these matters or any combination thereof formed, at the priority date, part of the common general knowledge, or was known to be relevant to an attempt to solve any problem with which this specification is concerned.

[062] Those skilled in the art will appreciate that the technology described herein is susceptible to variations and modifications other than those specifically described. It is to be understood that the technology includes all such variations and modifications. For the avoidance of doubt, the technology also includes all of the steps, features, and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more of said steps, features and compounds.

[063] In order that the present invention may be more clearly understood, preferred embodiments will be described with reference to the following drawings and examples.

Description of Embodiments

Compositions

[064] The present invention relates to topical compositions for the treatment of a dermal disease such as eczema and psoriasis. The compositions of the invention comprises a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and a water insoluble substance. In one embodiment, the topical composition further comprises a therapeutic agent (e.g., a glucocorticoid or a salt thereof, an antihistamine, or a JAK1/JAK2 inhibitor) for the treatment of a dermal disease. In some embodiments, the topical compositions of the invention is substantially free of water (i.e., anhydrous).

[065] In some embodiments, the compositions of the invention comprises a therapeutic agent known to be useful for the treatment of a dermal disease. In some embodiments, the compositions of the invention are formulated without a therapeutic agent known to be useful for the treatment of a dermal disease.

[066] The topical composition of the invention comprises a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof. In some embodiments, the organic acid may be malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, propanedioic acid or lactic acid, or any combination thereof. In some embodiments, the metallic salt of an acid may be sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium sulfate, sodium chloride, sodium fumarate, sodium phosphate, potassium

phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium sulfate, potassium chloride, potassium fumarate, magnesium sulfate, magnesium chloride, calcium chloride, or aluminum chloride, or any combination thereof. In some embodiments, the neutral substance may be maltodextrin, mannitol, sorbitol, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, PEG 200 to PEG 20000, polyethylene-propylene glycol copolymer, docusate sodium, glyceryl monostearate, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof.

[067] The topical composition of the invention comprises a water insoluble substance. In some embodiments, the water insoluble substance may be glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil, fatty alcohol, or any combination thereof. In some embodiments, the water insoluble substance may be talc, calcium carbonate, sublimed sulfur, calamine, zinc oxide, a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, tapioca starch or magnesium stearate, or any combination thereof.

[068] Topical compositions of the invention may be provided in several forms. Those skilled in the art may select a suitable water-soluble substance based on the desired form of application. For example, as a powder or an ointment.

[069] In some embodiments, the topical composition further comprises a therapeutic agent useful for the treatment of a dermal disease (e.g., eczema). For example, the therapeutic agent may be a glucocorticoid such as amcinonide, beclometasone, betamethasone, clobetasol, ciclesonide, desonide, dexamethasone, fludrocortisone acetate, fluocinolone acetonide, fluocinonide, flunisolide, fluocortolone, fluticasone, halcinonide, halometasone, hydrocortisone, mometasone, prednisolone, tixocortol pivalate, and triamcinolone acetonide or its salt thereof, tacrolimus, pimecrolimus, crisaborole, an antihistamine such as doxepin hydrochloride, diphenhydramine, and loratadine, or a JAK1/JAK2 inhibitor such as dalbitux, upadatinib, and ruxolitinib.

[070] The compositions of the invention may be formulated in a variety of suitable forms for topical administration. Standard pharmaceutical formulation techniques known by those skilled in the art may be used to prepare these formulations. Topical skin treatment compositions may be in any form including, for example, an emulsion including a microemulsion and a liposome formulation, oils, creams, ointments, powder, gels, lotions, pastes, moisturizers, skin patches, foam, spray, aerosol, and the like. Preferably, the topical composition is in the form of a powder or an ointment.

[071] In some embodiments, the topical compositions of the invention are substantially free of water (i.e., anhydrous). In some embodiments, the compositions of the invention comprise less than about 15% of water by weight of the total weight of the composition. In some embodiments, the compositions of the invention comprise less than about 10% of water by weight of the total weight of the composition. In some embodiments, the compositions comprise less than about 5%, about 4%, about 3%, about 2%, about 1%, or about 0.5% of water by weight of the total weight of the composition. Preferably, the composition comprises less than about 5% of water by weight of the total weight of the composition. Therefore, ointments and powder are preferable embodiments of the invention as they tend to be free of water.

[072] In some embodiments, the topical composition comprises about 0.5% to about 100% of a water-soluble substance by weight of the total weight of the composition. In some embodiments, the composition comprises about 0.5% to about 5%, about 5% to about 80%, about 10% to about 70%, about 10% to about 60%, about 10% to about 50%, about 10% to about 40%, about 10% to about 30%,or about 10% to about 20%, of a water soluble substance by weight of the total weight of the composition.

[073] In some embodiments, the amount of water soluble substance included in the composition will vary depending on the particular water soluble substance used and the severity of the dermal disease to be treated. Generally, the water-soluble substance in the composition will be present in an amount sufficient to cease itchiness of the skin of a subject suffering from a dermal disease (e.g., eczema or psoriasis). In some embodiments, the water soluble substance is in an amount ranging from about 10 mg to about 990 mg out of 1000 mg of the composition, thus accounting for about 1% to about 99% of the formulation. Preferably, the proportion is about 10% to about 80% of the total weight of the composition.

[074] In some embodiments, the water insoluble substance included in the composition is at least about 10 (w/w)%, at least about 20 (w/w)%, at least about 30 (w/w)% and up to about 98 (w/w)% of the composition. Thus, the total amount of water insoluble substance in the composition may range from about 10 (w/w)% to about 98 (w/w)% of the composition. In some embodiments, the total amount of water insoluble substance in the composition ranges from about 20 (w/w)% to about 80 (w/w)% of the composition. In some embodiments, the total amount of water insoluble substance in the composition ranges from about 50 (w/w)% to about 60 (w/w) % of the composition.

[075] In some embodiments, the composition of the invention may be formulated with a further substance such as a vehicle comprising one or more dermatologically acceptable

ingredients or carriers. The term "vehicle" as used herein is meant to define a liquid, solid or semi-solid base made of dermatologically acceptable excipients or carriers. The term "dermatologically acceptable" as used herein means that the carrier or vehicle so described are suitable for use in contact with human or animal keratinous tissue, in particular with respect to application to eczematous skin without undue toxicity, incompatibility, instability, allergic response, and the like. A variety of carrier materials are well known in the art for topical application, such as, for example, water, alcohols, aloe vera gel, allantoin, glycerin, vitamin A and E oils, mineral oil, propylene glycol, and the like can be used to prepare such formulations.

[076] In some embodiments, the composition is formulated as an anhydrous solution or ointment comprising a water soluble substance comprising an organic acid selected from malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, propanedioic acid, and lactic acid, a metallic salt selected from sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium chloride, sodium sulfate, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate , potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, magnesium sulfate, magnesium chloride, aluminum chloride, and calcium chloride, and a neutral substance selected from maltodextrin, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, PEG 200 to PEG 20000, polyethylene-propylene glycol copolymer, glyceryl monostearate, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof, Poloxamer (polyethylene-propylene glycol copolymer or polyoxyethylene-polyoxypropylene copolymer), and docusate sodium, alcohol, or a combination thereof, and a water insoluble substance selected from liquid paraffin, wax, petrolatum and lanolin. Preferably, the ointment composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

[077] In some embodiments, the composition is formulated as an anhydrous ointment comprising a glucocorticoid, a water soluble substance comprising an organic acid selected from malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, propanedioic acid and lactic acid, a metallic salt selected from sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium chloride, sodium sulfate, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate,

magnesium sulfate, magnesium chloride, aluminum chloride, and calcium chloride, and a neutral substance selected from maltodextrin, mannitol, sorbitol, PEG 200 to PEG 20000, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, glyceryl monostearate, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof, Poloxamer (polyethylene-propylene glycol copolymer or polyoxvethylene-polyoxypropylene copolymer), and docusate sodium, or a combination thereof, and a water insoluble substance selected from liquid paraffin, wax, petrolatum and lanolin. Preferably, the ointment composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

[078] In some embodiments, the composition is formulated as an anhydrous ointment comprising a water soluble substance selected from citric acid, lactic acid, magnesium sulfate, sodium sulfate, sodium chloride,poloxamer, polysorbate, sorbitol, mannitol, and PEG 200 to 20000, a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or any combination thereof, and a glucocorticoid, wherein the composition comprises about 1% to about 50% of the water soluble substance by weight of the total weight of the composition, and the composition comprises less than about 5% of water by weight of the total weight of the composition. The glucocorticoid may be selected from 0.1% mometasone, 0.1%-1% (e.g., 0.1%-0.5%) hydrocortisone, 0.1%-0.5% triamcinolone, 0.05% dexamethasone, 0.1% betamethasone, 0.05% halometasone, 0.025% fludrocortisone acetate, 0.02% clobetasol, 0.1% amcinonide, 0.05% desonide, 0.1% halcinonide, 0.05% fluticasone, and 0.5% prednisolone.

[079] In some embodiments, the composition is formulated as an anhydrous ointment comprising a water soluble substance selected from sodium sulfate, magnesium sulfate, sodium chloride, a water insoluble substance selected from liquid paraffin, petrolatum, and lanolin, or any combination thereof, and a glucocorticoid, wherein the composition comprises about 0.5 % to about 50% of the water soluble substance by weight of the total weight of the composition, and the composition comprises less than about 5% of water by weight of the total weight of the composition. The glucocorticoid may be selected from 0.1% mometasone, 0.1%-1% (e.g., 0.1%-0.5%) hydrocortisone, 0.1%-0.5% triamcinolone, 0.05% dexamethasone, 0.1% betamethasone, 0.05% halometasone, 0.025% fludrocortisone acetate, 0.02% clobetasol, 0.1% amcinonide, 0.05% desonide, 0.1% halcinonide, 0.05% fluticasone, and 0.5% prednisolone.

[080] In some embodiments, the composition is formulated as an anhydrous ointment comprising a mixture of liquid paraffin, petrolatum, 5% to 25% of sodium sulfate and less than 5% of water by the total weight of the composition.

[081] In some embodiments, the composition is formulated as an anhydrous ointment comprising liquid paraffin, petrolatum, 5% to 40% of dodecyl sulfate and less than 5% of water by the total weight of the composition.

[082] In some embodiments, the composition is formulated as an anhydrous ointment comprising liquid paraffin, petrolatum, 5% to 40% of PEG 6000 to PEG 20000 and less than 5% of water by the total weight of the composition.

[083] In some embodiments, the composition is formulated as an anhydrous ointment comprising liquid paraffin, petrolatum, 5% to 40% of polysorbate of molecular weight Tween 20, Tween 60 to Tween 80 and less than 5% of water by the total weight of the composition.

[084] In some embodiments, the composition is formulated as an anhydrous ointment comprising liquid paraffin, petrolatum, 5% to 20% of docusate sodium and 5% to 20% of glycerin and less than 5% of water by the total weight of the composition.

[085] In some embodiments, the composition is formulated as an anhydrous powder comprising a water soluble substance comprising an organic acid selected from malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, and citric acid, and a water insoluble substance selected from sublimed sulfur, sulfur, calamine, zinc oxide, magnesium stearate, a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, and tapioca starch. Preferably, the powder composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

[086] In some embodiments, the composition is formulated as an anhydrous powder comprising a water soluble substance comprising a metallic salt selected from sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium chloride, sodium sulfate, sodium phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, potassium phosphate, magnesium sulfate, magnesium chloride, aluminum chloride, and calcium chloride, and a water insoluble substance selected from sublimed sulfur, calamine, zinc oxide, calcium carbonate, microcrystalline cellulose, magnesium stearate, and a starch including corn starch, pregelatinized starch, rice starch, sweet potato starch, tapioca starch. Preferably,

the powder composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

[087] In some embodiments, the composition is formulated as an anhydrous powder comprising sodium salt of an acid including sodium chloride, sodium sulfate, sodium ascorbate, calamine, zinc oxide, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[088] In some embodiments, the composition is formulated as an anhydrous powder comprising potassium salt of an acid including potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, potassium phosphate, zinc oxide, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[089] In some embodiments, the composition is formulated as an anhydrous powder comprising magnesium salt of an acid including magnesium sulfate and magnesium chloride, zinc oxide, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[090] In some embodiments, the composition is formulated as an anhydrous powder comprising calcium chloride, zinc oxide, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[091] In some embodiments, the composition is formulated as an anhydrous powder comprising carbohydrate including maltodextrin, mannitol or sorbitol, galactose, fructose, glucose, maltose and sugar, zinc oxide, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[092] In some embodiments, the composition is formulated as an anhydrous powder comprising maltodextrin, PEG 200 to PEG 20000, monosaccharides including glyceryl monostearate, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof, Poloxamer (polyethylene-propylene glycol copolymer or polyoxvethylene-polyoxypropylene copolymer), and docusate sodium, or a combination thereof, and a water insoluble substance selected from liquid paraffin, wax, petrolatum and lanolin. Preferably, the ointment composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total

weight of the composition.

[093] In some embodiments, the composition is formulated as an anhydrous powder comprising potassium salt of an acid including potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, potassium phosphate, calamine, zinc oxide, microcrystalline cellulose, magnesium stearate, and a starch including corn starch; the powder composition comprises less than about 5% by weight of the total weight of the composition.

[094] In some embodiments, the composition is formulated as an anhydrous powder comprising a water soluble substance comprising a neutral substance selected from maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, and docusate sodium, or a combination thereof, and a water insoluble substance selected from sublimed sulfur, sulfur, calamine, zinc oxide, magnesium stearate, and a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, and tapioca starch. Preferably, the powder composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

[095] In some embodiments, the composition is formulated as an anhydrous powder comprising a water soluble substance comprising magnesium sulfate, sodium sulfate, sodium chloride, mannitol, sorbitol, or a combination thereof, and a water insoluble substance selected from sublimed sulfur, sulfur, calamine, zinc oxide, magnesium stearate, and a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, and tapioca starch. Preferably, the powder composition comprises less than about 5%, even more preferably less than about 3% of water by weight of the total weight of the composition.

Methods

[096] The compositions of the invention is particularly useful for the treatment of dermal diseases including severe eczema and psoriasis. Accordingly, in one embodiment, the invention relates to methods of treating a dermal disease by administering the compositions of the invention. In another embodiment, the invention relates to use of the compositions of the invention for the preparation of a medicament intended to be topically applied to the skin of a subject suffering from a dermal disease.

[097] As will be appreciated by one skilled in the art, the compositions of the invention may be used for the treatment of various dermal diseases and conditions including but not limited to eczema and psoriasis. Skin eczema refers to several conditions that share a

pattern of changes in the surface of the skin. Eczema appears as an episode of skin inflammation that may present as itching, scaling and erythema of the skin. When it develops into a long-term condition (chronic eczema), it leads to thickening of the skin, scaling, flaking, dryness and colour changes. There are many types of eczema, depending on the cause, shape and location of the rash. Some are related to allergies or contact with irritating chemicals. Some are associated with or caused by underlying medical conditions that cause fluid retention in the legs.

[098] The terms "eczema" and "dermatitis" are used interchangeably and are meant to define inflammation that affects the epidermis and the superficial dermis and is characterised by featuring red and hot skin. In some instances, dermatitis further features oedema producing intradermal vesicles which causes weeping of fluid onto the surface, crusting, scaling and fissuring.

[099] The term 'dermal disease' as used herein refers to various types of inflammatory skin disease or disorder. Thus, a dermal disease as used herein may include eczema, miliaria, diaper rash, psoriasis and ulcers of diabetes mellitus. The types of eczema include but are not limited to atopic dermatitis, hand eczema, infantile eczema, child hood eczema, adult eczema, keratosis pilaris, ichthyosis vulgaris, hand and foot dermatitis, pompholyx, discoid eczema, nummular eczema, allergic contact dermatitis, irritant contact dermatitis, over-treatment dermatitis, neurodermatitis, asteatotic eczema, stasis dermatitis, lichen simplex chronicus, prurigo nodularis, seborrheic dermatitis, seborrhea and psoriasis.

[0100] Eczemas may be divided into endogenous eczemas and exogenous eczemas. Endogenous eczemas include at least atopic dermatitis including various forms (e.g., infantile eczema, childhood eczema, adult eczema, keratosis pilaris, and ichthyosis vulgaris), pompholyx, discoid eczema and nummular eczema. Exogenous eczemas include at least allergic contact dermatitis, irritant contact dermatitis, and hand eczema. Additionally, the term "eczema" may also encompass stasis dermatitis, asteatotic eczema, lichen simplex chronicus, psoriasis, seborrheic dermatitis and seborrhea.

[0101] In some embodiments, the invention relates to methods of treating a dermal disease (e.g., eczema) in a subject using a topical composition that does not include a therapeutic agent useful for the treatment of a dermal disease.

[0102] In some embodiments, the topical compositions of the invention and known therapeutic agents may be used in a combination therapy. For example, the compositions of the invention and therapeutic agents may be administered in a sequential manner in a regimen that will provide beneficial effects of the drug combination. Alternatively, the compositions of the invention and known therapeutic agents may be coadministered in a

substantially simultaneous manner such as in a single formulation (i.e., in the same composition) having a fixed ratio or in multiple, separate formulations of each agent. In some embodiments, the combination therapy has a synergistic effect, particularly for severe eczema, where a beneficial effect is observed to be greater than the effect produced by each compound administered individually.

[0103] In some embodiments, methods of treating a dermal disease (e.g., eczema) in a subject comprise the steps of a) administering to the subject a topical therapeutic agent (e.g., a glucocorticoid or a salt thereof, an antihistamine, or a JAK1/JAK2 inhibitor); and b) administering to the subject an effective amount of a topical composition of the invention. Preferably, the topical composition is formulated as a powder. For example, methods of treating eczema may comprise applying a therapeutic cream comprising a glucocorticoid (e.g., hydrocortisone) to a dermal lesion then applying a powder composition of the invention by dusting the powder composition to the same dermal lesion covering the therapeutic cream. Preferably, the eczema is severe eczema. Thus, the invention also relates to a kit when used for the treatment of a dermal disease comprising a) a topical therapeutic agent (e.g., a cream of a glucocorticoid or a salt thereof, an antihistamine, or a JAK1/JAK2 inhibitor); and b) a topical powder composition of the invention.

[0104] An effective amount of the topical compositions that are administered and the dosage regimen for treating a dermal disease such as eczema, miliaria, diaper rash, psoriasis and ulcers of diabetes mellitus depend on a variety of factors, including the age, weight, sex, and medical condition of the subject, the area of the inflammation of the skin, the severity of the disease, the route and frequency of administration, and whether a further therapeutic agent is administered, and therefore may vary widely. Such treatments may be administered as often as necessary and for the period of time judged necessary by the treating physician. One of skill in the art will appreciate that the dosage regime or therapeutically effective amount of the topical composition to be administrated may need to be optimized.

[0105] Topical compositions of the invention may be administered to a subject multiple times per day (e.g., two, three ,four or six times per day), daily, every two days, every three days, every four days, or every 5 days, once weekly, or as required. Preferably, the topical compositions are applied once to three times daily.

[0106] It will be appreciated by one of skill in the art that dosage will depend on the particular composition, the proportion or percentage of the water soluble substance in the composition, its potency, and whether or not a further therapeutic agent is administered. The dosage of the topical composition is understood to be large enough to produce the

desired effect in which the dermal disease such as eczema and the symptoms associated therewith are ameliorated or reversed, but not be so large as to cause unmanageable side effects. It will be understood, however, that the specific dosage for a subject will depend on a variety of factors including the body weight, general health, sex and diet of the individual being treated, other drugs or therapy which have previously been administered, and the severity of the disease, as is well understood by the skilled person in the art. The dosage can also be adjusted by the individual physician in the event of any complication.

[0107] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

[0108] Embodiments of the invention will now be discussed in more detail with reference to specific examples which are provided for exemplification only and which should not be considered as limiting the scope of the invention in any way.

Examples

[0109] **General Method of producing a powder composition**

[0110] One or more of a water soluble substance including: an organic acid selected from malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, propanedioic acid and lactic acid, a metallic salt selected from sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium chloride, sodium sulfate, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, potassium lactate, magnesium sulfate, magnesium chloride, calcium chloride, zinc carbonate, calcium carbonate, and aluminum chloride, or a neutral substance selected from maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, docusate sodium, and sodium dodecyl sulfate, or a combination thereof, were added to a mixer. One or more of a water insoluble substance including microcrystalline cellulose, calamine, sulfur, zinc oxide, or a starch were then added to the mixer containing the one or more water soluble substance and mixed using mechanical force to form a powder mixture. The powder was further mixed in a wet granulator or passed through a grinder or pulverizer to produce a fine powder composition. The fine powder was collected, passed through a mesh, and filled into a granular bag or a plastic bottle.

[0111] **General Method of producing an ointment composition**

[0112] One or more of a water soluble substance including: an organic acid selected from malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, propionic acid, malonic acid, citric acid, propanedioic acid and lactic acid, a metallic salt selected from sodium acetate, sodium propionate, sodium malonate, sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium fumarate, sodium chloride, sodium sulfate, sodium phosphate, potassium phosphate, potassium malate, potassium citrate, potassium acetate, potassium propionate, potassium malonate, potassium succinate, potassium lactate, potassium tartrate, potassium maleate, potassium fumarate, potassium chloride, potassium sulfate, potassium lactate, magnesium sulfate, magnesium chloride, calcium chloride, zinc carbonate, calcium carbonate, and aluminum chloride, or a neutral substance selected from maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, docusate sodium, and sodium dodecyl sulfate, or a combination thereof, accounted for 3% to 90% of the total weight of the composition were added to a mixer. One or more of a water insoluble substance including glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil and fatty alcohol were then added to the mixer containing the one or more water soluble substance and mixed with less than 5% of water by weight of the total weight of composition and dissolved in a water bath over 60°C to form a transparent liquid. A high-speed shear machine was used for shearing and dispersing to give a uniform ointment composition. The uniform ointment was collected and filled into a plastic bottle.

[0113] **Example 1: Anhydrous powder composition comprising malic acid**

[0114] 500 g of malic acid, 490 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and 50 g of the powder mixture was collected and filled into a bottle.

[0115] **Example 2: Anhydrous powder composition comprising magnesium sulfate**

[0116] 120 g of magnesium sulfate, 60 g of maltodextrin, 60 g of mannitol, 60 g of PEG 6000, 60 g of calamine, 60 g of zinc oxide, 280 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and 50 g of the powder mixture was collected and filled into a bottle.

[0117] **Example 3: Anhydrous powder composition comprising maltodextrin**

[0118] 200 g of maltodextrin, 120 g of magnesium sulfate, 670 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant

powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0119] **Example 4: Anhydrous powder composition comprising PEG 6000 and malic acid**

[0120] 100 g of PEG 6000, 200 g of malic acid, 690 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0121] **Example 5: Anhydrous powder composition comprising mannitol**

[0122] 200 g of mannitol, 790 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0123] **Example 6: Anhydrous powder composition comprising maltodextrin, magnesium sulfate, and malic acid**

[0124] 100 g of magnesium sulfate,100 g of maltodextrin, 200 g of malic acid, 590 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a grinder. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0125] **Example 7: Anhydrous powder composition comprising sodium sulfate**

[0126] 400 g of sodium sulfate, 590 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0127] **Example 8: Anhydrous powder composition comprising magnesium sulfate**

[0128] 400 g of magnesium sulfate, 590 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a pulverizer. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0129] **Example 9: Ointment composition comprising hydrocortisone butyrate, white petroleum, liquid paraffin and butyric acid**

[0130] 18.18 g of liquid paraffin and 162.28 g of white petroleum were placed in a beaker and heated in a water bath at 75°C until they were at liquid state. After the liquid paraffin and petroleum were completely dissolved into a transparent solution, 200 mg of hydrocortisone butyrate and 19.96 g of butyric acid were added to the beaker. The content was mixed with a high-speed mixer. The resulting solution was uniform and filled into a

bottle. The acidic smell was very strong and unpleasant for butyric acid (so as propionic acid and acetic acid)

[0131] **Example 10: Dexamethasone acetate ointment comprising malic acid (10g: 5mg)**

[0132] 200 g of liquid paraffin and 600 g of white petrolatum were placed in a beaker and heated in a water bath at 70°C until liquid state was reached. 500 mg of dexamethasone acetate was added to the beaker. 200 g of malic acid was then added to the same beaker and stirred evenly. 50 g of the ointment was filled into bottles. A homogeneous, slightly milky white ointment was formed, and no particles or clumps could be seen or detected by hand after cooling.

[0133] **Example 11: Dexamethasone acetate ointment comprising sodium malate (10g:5mg)**

[0134] 200 g of liquid paraffin and 600 g of white petrolatum were placed in a beaker and heated in a water bath at 70°C until liquid state was reached. 500 mg of dexamethasone acetate was placed in the beaker. 200 g of sodium malate was then placed in the same beaker and stirred evenly. 50 g of the ointment was filled into the bottles. A homogeneous, slight milky white ointment was formed.

[0135] **Example 12: Body powder comprising sodium lactate and maltodextrin**

[0136] 100 g of sodium lactate, 300 g of maltodextrin, 590 g of corn starch, and 10 g of magnesium stearate were mixed and grounded together by a grinder. The resultant powder was passed through 120 mesh and the powder mixture was collected and filled into a bottle.

[0137] **Example 13: Ointment comprising petrolatum, liquid paraffin and sodium ascorbate**

[0138] 30 g of liquid paraffin and 120 g of white petrolatum was placed in a beaker which was heated to a liquid state in a water bath at 60°C, then 15 g of sodium ascorbate was added to the beaker. The contents were mixed with a high speed mixer until uniform state was obtained. The ointment was filled into an aluminium tube and then sealed.

[0139] **Example 14: Ointment comprising petrolatum, liquid paraffin and malic acid**

[0140] 18 g of liquid paraffin and 162 g of white petrolatum were placed into a beaker which was heated to a liquid state in a water bath at 75-80°C, then 20 g of malic acid was added to the beaker. The contents were mixed with a high-speed mixer until uniform state was obtained. The ointment was filled into an aluminum tube and then sealed.

[0141] **Example 15: Ointment comprising petrolatum, liquid paraffin and tartaric acid**

[0142] 18 g of liquid paraffin and 162 g of petrolatum were placed into a beaker which was heated to a liquid state in a water bath at 75-80°C, then 20 g of tartaric acid was added into the beaker. The contents were mixed with a high-speed mixer until uniform state was obtained. The ointment was filled into an aluminum tube and then sealed.

[0143] **Example 16: Ointment comprising petrolatum, liquid paraffin and sodium lactate**

[0144] 40 g liquid paraffin and 120 g petrolatum were placed into a beaker which was heated to a liquid state in a water bath at 75-80°C, then 40 g of sodium lactate was added into the beaker. The contents were mixed with a high-speed mixer until uniform state was obtained. The ointment was filled into an aluminum tube and then sealed.

[0145] **Example 17: Ointment comprising petrolatum, liquid paraffin and docusate sodium**

[0146] 100 g of liquid paraffin and 325 g of petrolatum were placed in a beaker and heated to a liquid state in a water bath at 80°C, then 75 g of docusate sodium was added into the beaker. The contents were mixed with a high-speed mixer until uniform liquid was obtained. The ointment was filled into an aluminum tube and then sealed.

[0147] **Example 18: Ointment comprising petrolatum, liquid paraffin and 3% sodium dodecyl sulfate (SDS)**

[0148] 120 g of liquid paraffin and 171 g of petrolatum were placed in a beaker and heated to a liquid state in a water bath at 80°C, then 9 g of sodium dodecyl sulfate was added into the beaker. The contents were mixed with a high-speed mixer until uniform liquid was obtained. The ointment was filled into an aluminum tube and then sealed.

[0149] **Example 19: Ointment comprising petrolatum, liquid paraffin and 15% SDS**

[0150] 40 g of liquid paraffin and 130 g of petrolatum were placed into a beaker and heated to a liquid state in a water bath at 80°C, then 30 g of sodium dodecyl sulfate was added into the beaker. The contents were mixed with a high-speed mixer until uniform liquid was obtained. The ointment was filled into an aluminum tube and then sealed.

[0151] **Example 20: Ointment comprising petrolatum, liquid paraffin, 9% SDS and 0.1% Triamcinolone acetonide**

[0152] 122.7 g of liquid paraffin and 150 g of petrolatum were placed into a beaker, heated in a water bath at 80°C to the liquid state, then 0.3 g of triamcinolone acetonide and 27 g of sodium dodecyl sulfate were added to the beaker. The contents were mixed with a high-

speed mixer until a uniform liquid was obtained. The ointment was filled into an aluminum tube and then sealed.

[0153] **Example 21: Ointment comprising petrolatum, liquid paraffin and 10% PEG 6000**

[0154] 70 g of liquid paraffin and 110 g of petrolatum were placed into a beaker and heated to liquid state in a water bath at 75°C, then 20 g of PEG 6000 was added into the beaker. The contents were mixed with a high-speed mixer until uniform liquid state was obtained. The ointment was filled into an aluminum tube and then sealed.

[0155] **Example 22: A body powder comprising sodium sulfate, sodium chloride, sodium dodecyl sulfate, magnesium sulfate, magnesium chloride, and microcrystalline cellulose**

[0156] 400 g of sodium sulfate, 400 g of sodium chloride, 400 g of sodium dodecyl sulfate, 400 g of magnesium sulfate, 400 g of magnesium chloride, 400 g of ascorbic acid and 3600 g of microcrystalline cellulose were mixed in a mixer, and the resulting powder was passed through a 120 mesh crusher. 100 g of magnesium stearate was added to the mixer containing the fine powder and the powder was mixed for 20 minutes. 60 g of the powder was filled into a plastic bottle and then sealed.

[0157] **Example 23: A body powder comprising maltodextrin, mannitol, PEG and docusate sodium**

[0158] 500 g of maltodextrin, 500 g of mannitol, 500 g of PEG 6000, 500 g of docusate sodium, 500 g of sodium dodecyl sulfate, and 3500 g of microcrystalline cellulose were mixed in a mixer, and the resulting powder was passed through a 120 mesh crusher. 100 g of magnesium stearate was added to the mixer containing the fine powder and the powder was mixed for 20 minutes. 60 g of the powder was filled into a plastic bottle and then sealed.

[0159] **Example 24: Composition comprising 65% white petrolatum, 20% liquid paraffin and 15% poloxamer**

[0160] 100 g of liquid paraffin and 325 g of white petrolatum were placed into a beaker and heated in water bath to 80°C until completely dissolved into a transparent liquid and well mixed. 75 g poloxamer was then added into the beaker and stirred for 15 minutes until the poloxamer was melted using a high-speed shearer to form a uniform colour liquid. The mixture was filled into an aluminium tube then sealed.

[0161] **Case study 1**

[0162] A human patient with skin eczema was treated with a hydrocortisone butyrate cream

followed by a topical composition formulated in powder form (the components of the power composition is listed in Table 1).

[0163] The hydrocortisone butyrate cream was applied to the dermal lesion and the powder composition was applied on top of the cream. The patient was treated twice daily for two days. Following two days of treatment with the above combination, itching had resolved, and signs of eczema further decreased compared to when the patient was treated with the hydrocortisone butyrate cream alone one or more times daily for two weeks.

Table 1. Body powder comprising sodium tartrate

Substance	**Amount (g)**
sodium tartrate	200 g
croscarmellose sodium	300 g
calcium carbonate	200 g
pregelatinized starch	300 g
menthol	5 g
magnesium stearate	20 g

[0164] **Case study 2**

[0165] An 80 year old patient with skin eczema was treated with a powder comprising sodium sulfate, magnesium sulfate, 55% starch, microcrystalline cellulose, calamine, zinc oxide, and ascorbic acid. The patient suffered from skin abrasions with bleeding and itchiness. The powder was directly applied onto the patient's skin. After application of the powder, the itchiness stopped within 60 minutes. The powder was used three to four times a day when the patient felt itchiness. Following about 15 days of treatment with the above powder, itching and swelling were resolved and signs of eczema disappeared.

Table 2. Powder composition

Substance (g)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
malic acid	500	600	/	/	/	/	/	/	/	/	/	/	/	/	200	/	/
sodium ascorbate	/	/	600	/	/	/	/	/	/	/	/	/	/	/	/	/	/
ascorbic acid	/	/	/	600	/	/	/	/	/	/	/	/	/	/	/	/	/
PEG 6000	/	/	/	/	100	200	/	/	/	/	/	/	/	/	/	/	/
mannitol	/	/	/	/	/	/	200	/	/	/	/	/	/	/	/	/	/
maltodextrin	/	/	/	/	/	/	/	200	/	/	/	/	/	/	100	/	/
poloxamer	/	/	/	/	/	/	/	/	100	/	/	/	/	/	100	/	/
$NaHCO_3$	/	/	/	/	/	/	/	/	/	200	/	/	/	/	/	/	/
sodium chloride	/	/	/	/	/	/	/	/	/	/	200	400	/	/	/	/	/
sodium citrate	/	/	/	/	/	/	/	/	/	/	/	/	400	/	/	/	/
calcium chloride	/	/	/	/	/	/	/	/	/	/	/	/	/	400	/	/	/
sodium sulfate	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	400	/
magnesium sulfate	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	400
corn starch	490	390	390	390	890	790	790	790	890	790	790	590	590	590	590	590	590
magnesium stearate	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

[0157] Table 2 shows 17 examples of powder compositions and their individual components in grams. A grinder was used to grind the components together into powder form. The resultant powder was passed through a 120 mesh and the powder mixture was collected and filled into a bottle.

Claims:

1. A topical composition comprising:
a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and a water insoluble substance.

2. The composition of claim 1, further comprising a therapeutic agent for the treatment of a dermal disease.

3. The composition of claim 1 or 2, wherein the organic acid is selected from the group comprising malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, and propanedioic acid.

4. The composition of any one of claims 1 to 3, wherein the metallic salt is selected from the group comprising sodium, potassium, magnesium, calcium and aluminum salt of an acid.

5. The composition of claim 4, wherein the acid is selected from a mineral acid including sulfuric acid, hydrochloric acid, phosphoric acid and organic acid including acetic acid, propionic acid, malonic acid, malic acid, succinic acid, maleic acid, citric acid, tartaric acid, lactic acid, ascorbic acid and fumaric acid.

6. The composition of claim 4, wherein the sodium salt is selected from the group comprising of sodium acetate, sodium propionate, sodium malonate, sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium sulfate, sodium chloride, sodium fumarate, sodium phosphate and sodium dodecyl sulfate.

7. The composition of claim 4, wherein the potassium salt is selected from the group comprising of potassium acetate, potassium propionate, potassium malonate,potassium phosphate, potassium malate, potassium citrate, potassium succinate , potassium lactate, potassium tartrate, potassium maleate, potassium sulfate, potassium chloride, potassium fumarate, and potassium dodecyl sulfate.

8. The composition of claim 4, wherein the magnesium salt is magnesium sulfate or magnesium chloride.

9. The composition of claim 4, wherein the metallic salt is calcium chloride or aluminum chloride.

10. The composition of claim 4, wherein the metallic salt is calcium chloride.

11. The composition of any one of claims 1 to 10, wherein the neutral substance is selected from the group comprising of maltodextrin, mannitol, sorbitol, monosaccharides, disaccharides,

PEG 200 to PEG 20000, polyethylene-propylene glycol copolymer, docusate sodium, polysorbate, poloxamer, and sodium dodecyl sulfate.

12. The composition of any one of claims 1 to 11, wherein the composition is an anhydrous powder comprising a water soluble substance and a non-water soluble substance and less than 5% of water.

13. The composition of any one of claims 1 to 11, wherein the amount of water soluble substance is 2 to 99% of the total weight of the composition.

14. The composition of any one of claims 1 to 11, wherein the composition is an anhydrous ointment comprising more than 3% of water soluble substance and a non-water soluble ointment base and less than 5% of water.

15. The composition of any one of claims 1 to 11, wherein the composition is an anhydrous ointment comprising 3 to 90 % of water soluble substance of the total weight of the composition and a non-water soluble ointment base and less than 5% of water.

16. The composition of claim 1, wherein the composition is a powder comprising sodium sulfate, sodium chloride, sodium dodecyl sulfate, magnesium sulfate, ascorbic acid, microcrystalline cellulose, and less than 5% of water of the total weight of the composition.

17. The composition of any one of claims 1 to 11, wherein the composition is formulated as an ointment, and wherein the water insoluble substance is selected from the group consisting of glyceryl monostearate, stearic acid, petrolatum, liquid paraffin, glycerin, wax, lanolin, mineral oil and fatty alcohol.

18. The composition of any one of claims 1 to 11, wherein the composition is formulated as a powder, and wherein the water insoluble substance is selected from the group comprising of talc, sublimed sulfur, sulfur, calamine, zinc oxide, a starch including pregelatinized starch, corn starch, rice starch, sweet potato starch, tapioca starch and magnesium stearate.

19. The composition of any one of claims 1 to 18, further comprising a therapeutic agent selected from the group consisting of a glucocorticoid including amcinonide, beclometasone, betamethasone, clobetasol, ciclesonide, desonide, dexamethasone, fludrocortisone acetate, fluocinolone acetonide, fluocinonide, flunisolide, fluocortolone, fluticasone, halcinonide, halometasone, hydrocortisone, mometasone, prednisolone, tixocortol pivalate, and triamcinolone acetonide or a salt thereof, tacrolimus, pimecrolimus, and crisaborole, an antihistamine including doxepin hydrochloride, diphenhydramine, and loratadine, and a JAK1/JAK2 inhibitor including dalbitux, upadatinib, and ruxolitinib.

20. The composition of any one of claims 1 to 19, wherein the composition is substantially anhydrous and comprises less than about 5% of water by weight of the total weight of the composition.

21. The composition of any one of claims 1 to 20, wherein the composition comprises about 2% to about 90% of a water soluble substance by weight of the total weight of the composition.

22. The composition of any one of claims 1 to 13, 16, or 18-21, wherein the composition is formulated as a powder, and wherein the composition comprises about 3% to about 99% of a water soluble substance selected from an organic acid, a metallic salt and a neutral substance or a combination thereof, by weight of the total weight of the composition.

23. The composition of claim 1, wherein the water soluble substance of the composition comprises:

a. a metallic salt selected from the group consisting of sodium acetate, sodium propionate, sodium malonate, sodium malate, sodium citrate, sodium succinate, sodium lactate, sodium tartrate, sodium maleate, sodium sulfate, sodium chloride, sodium fumarate, sodium phosphate, potassium acetate, potassium propionate, potassium malonate,potassium phosphate, potassium malate, potassium citrate, potassium succinate , potassium lactate, potassium tartrate, potassium maleate, potassium sulfate, potassium chloride, potassium fumarate, magnesium sulfate, magnesium chloride, calcium chloride, and aluminum chloride; or

b. an organic acid selected from the group consisting of malic acid, succinic acid, maleic acid, ascorbic acid, tartaric acid, citric acid, and propanedioic acid; or

c. a neutral substance selected from the group consisting of maltodextrin, mannitol, sorbitol, PEG 1000 to PEG 20000, monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, glycerin, polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80 and sodium dodecyl sulfate or a combination thereof, Poloxamer, and docusate sodium, or a combination thereof; and

a water insoluble substance selected from the group consisting of sublimed sulfur, sulfur, calamine, zinc oxide, a starch, or a combination thereof,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as a powder.

24. The composition of any one of claims 1 to 23, wherein the water soluble substance is a neutral substance selected from the group consisting of monosaccharides including galactose, fructose and glucose, disaccharides including maltose and sugar, maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, docusate sodium, glycerin,polysorbate including Tween 20, Tween 40, Tween 60 and Tween 80, Poloxamer, and sodium dodecyl sulfate or a combination thereof.

25. The composition of claim 1 or 2, wherein the composition is formulated as an ointment, wherein the composition comprises:

a water soluble substance selected from the group consisting of a metallic salt, an organic acid and a neutral substance; and

a water insoluble substance selected from the group consisting of petrolatum, liquid paraffin, glycerin,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

26. The composition of claim 1 or 2, wherein the composition comprises magnesium sulfate, sodium chloride, sodium sulfate, maltodextrin, mannitol, sorbitol, PEG 1200 to PEG 20000, docusate sodium, or a combination thereof, and less than 5% of the water by weight of the total weight of the composition.

27. A topical composition of claim 1 or 2, comprising:

a water soluble substance selected from the group consisting of magnesium sulfate, sodium sulfate, sodium chloride, potassium chloride, potassium sulfate, polyethylene-propylene glycol copolymer, and PEG 200 to PEG 20000, sodium dodecyl sulfate or a combination thereof;

a water insoluble substance selected from the group consisting of liquid paraffin, petrolatum, and lanolin, or a combination thereof; and

a glucocorticoid or its salt thereof,

wherein the water soluble substance is about 3% to about 60% by weight of the total weight of the composition,

wherein the composition comprises less than about 5% of water by weight of the total weight of the composition, and

wherein the composition is formulated as an ointment.

28. The topical composition of claim 27, wherein the glucocorticoid is selected from the group consisting of about 0.1% mometasone, 0.1%-0.5% hydrocortisone, 0.1%-0.5% triamcinolone, 0.05% dexamethasone, 0.1% betamethasone, 0.05% halometasone, 0.025% fludrocortisone acetate, 0.02% clobetasol, 0.1% amcinonide, 0.05% desonide, 0.1% halcinonide, 0.05% fluticasone, and 0.5% prednisolone.

29. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, 3% to about 60% of soluble substance comprising sodium sulfate, magnesium sulfate, sodium dodecyl sulfate (SDS), PEG 400 to PEG 20000, polysorbate Tween 20, Tween 40, Tween 60 or Tween 80 by weight of the total weight of the composition, and wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

30. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, and 5% to about 15% of sodium chloride by weight of the total weight of the composition, and wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

31. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, and 3% to about 60% of sodium dodecyl sulfate by weight of the total weight of the composition, wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

32. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, and 3% to about 60% of PEG 1000 to PEG 10000 by weight of the total weight of the composition, wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

33. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, and 3% to about 60% of polysorbate Tween 20, Tween 40, Tween 60, or Tween 80 by weight of the total weight of the composition, and wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

34. The topical composition of claim 1, wherein the composition is an ointment comprising a liquid paraffin, a petrolatum, and 3% to about 60% of docusate sodium by weight of the total weight of the composition, and wherein the composition comprises less than about 5% of water by weight of the total weight of the composition.

35. A method of treating a dermal disease in a subject comprising administering to the subject an effective amount of the topical composition of any one of claims 1 to 34, wherein

the topical composition is formulated as a powder or ointment.

36. The method of claim 35, wherein the dermal disease is selected from the group consisting of eczema, atopic eczema, neurodermatitis, contact dermatitis, chronic eczema, infant eczema, miliaria, diaper rash, psoriasis and ulcer of diabetes mellitus.

37. Use of a composition comprising a water soluble substance selected from an organic acid, a metallic salt of an acid, and a neutral substance, or a combination thereof, and a water insoluble substance, in the manufacture of a topical medicament for the treatment of a dermal disease, wherein the medicament is substantially anhydrous.

38. Use of a composition of any one of claims 1 to 34 in the manufacture of a topical medicament for the treatment of a dermal disease, wherein the medicament is substantially anhydrous.