FOAMABLE COMPOSITION COMBINING A POLAR SOLVENT AND A HYDROPHOBIC CARRIER

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ABSTRACT

The present invention relates to a foamable vehicle or cosmetic or pharmaceutical composition, comprising: (1) an organic carrier, at a concentration of 10% to 70% by weight, wherein said organic carrier concurrently comprises: (i) at least one hydrophobic organic carrier, and (ii) at least one polar solvent; (2) at least one surface-active agent; (3) water; and (4) at least one liquefied or compressed gas propellant at a concentration of 3% to 25% by weight of the total composition.

The present invention further provides a method of treating, alleviating or preventing a disorder of mammalian subject, comprising administering the above-mentioned compositions to an afflicted target site.
FOAMABLE COMPOSITION COMBINING A POLAR SOLVENT AND A HYDROPHOBIC CARRIER

CROSS REFERENCE TO RELATED APPLICATIONS


BACKGROUND OF THE INVENTION

[0006] This invention relates to foamable pharmaceutical and cosmetic compositions.

[0007] Foams and, in particular, foam emulsions are complicated systems which do not form under all circumstances. Changes in foam emulsion composition, such as by the addition of active ingredients may destabilize the foam. There is therefore a need for a foam composition which provides desirable properties to the skin and can remain stable whilst accommodating a variety of active ingredients.

[0008] U.S. Pat. No. 6,126,920 (“the ‘920 Patent”) discloses treatment of various skin diseases, and in particular, scalp psoriasis, using a foamable pharmaceutical composition containing a corticosteroid active substance, an aliphatic alcohol, water, a fatty alcohol, a surface-active agent, a propellant and a buffering agent. The foamable composition contains 40-90% w/w composition of an aliphatic alcohol. The ‘920 Patent is typical of many compositions that use aliphatic alcohols in the foam composition. The alcohol promotes fast drying and thereby addresses the sticky feeling left by many topical formulations after application; however, alcohols, and in particular the methyl, ethyl and isopropyl alcohols preferred in the ‘920 Patent, are dehydrating agents and may cause skin to become dry and cracked. U.S. Pat. Application Pub. No. US2004/0151671 provides pharmaceutical compositions in a pressurized container, comprising a quick breaking alcoholic foaming agent. U.S. Pat. No. 5,783,202 provides a pediculicidal mousse composition containing a pediculicidal agent containing (a) from about 0.1 to about 10% w/w of a pediculicidal agent (b) about 70 to about 97% w/w, a foaming agent, which is preferably a quick breaking alcoholic foaming agent; and (c) from about 3 to about 20% w/w of an aerosol propellant. U.S. Pat. No. 6,730,288 teaches a pharmaceutical foam composition including (a) active ingredient; (b) an occlusive agent; (c) an aqueous solvent; and (d) a non-solvent wherein the active ingredient is insoluble in water and insoluble in both water and the occlusive agent; and wherein there is enough occlusive agent to form an occlusive layer on the skin.

[0009] A few dermatological foam products are available on the market.

[0010] OluIx™ Foam, produced by Connetics, Inc., contains clobetasol propionate. Each gram of OluIx™ Foam contains 0.5 mg clobetasol propionate, USP, in a thermobable foam, which consists of ethanol (60%), purified water, propylene glycol, cetyl alcohol, stearyl alcohol, polysorbate 60, citric acid, and potassium citrate. It is dispensed from an aluminum can pressurized with a hydrocarbon propellant (propane/butane). LuxiQ™ corticosteroid foam medication contains 1.2 mg betamethasone valerate per gram, in a vehicle, comprising ethanol (60.4%), purified water, propylene glycol, cetyl alcohol, stearyl alcohol, polysorbate 60, citric acid, and potassium citrate, and pressurized with a hydrocarbon propellant. Alcohol is known to impair the integrity of the skin barrier, dry the skin and cause skin irritation. The incidence skin irritation (burning, itching and stinging) as detailed the package inserts of the above mentioned products is very high (54%), probably due to the high alcohol content. Moreover, the respective incidence of skin irritation caused by the vehicle of these forms is 75%.

[0011] Thus, while alcohol is useful in solubilizing an active agent and enabling effective dermal penetration of an active agent is desirable, the development of a safe foam vehicle, which will overcome the evident skin drying and irritation caused by alcohol, is warranted.

[0012] Furthermore, foam compositions that possess a lesser degree of thermal sensitivity, thus being more useful for the treatment of large skin areas are desired.

SUMMARY OF THE INVENTION

[0013] The present invention relates to a foamable vehicle or cosmetic or pharmaceutical composition comprising:

1) an organic carrier, at a concentration of about 10% to about 70% by weight, wherein said organic carrier concurrently comprises:
In one or more embodiments a foamable cosmetic or pharmaceutical vehicle is provided wherein the ratio of the hydrophobic organic carrier and the polar solvent are selected to provide a selected pharmacological or safety property.

In one or more embodiments a foamable cosmetic or pharmaceutical vehicle is provided also incorporating a polymeric agent.

In one or more embodiments the polymeric agent is selected from a biodegradable agent, a gelling agent, a film forming agent and a phase change agent and can be from about 0.01% to about 5% by weight.

In one or more embodiments, a pharmaceutical or cosmetic foamable product is provided, wherein a pharmaceutical or a cosmetic active agent is incorporated in a foamable vehicle, which contains a polar solvent and a hydrophobic organic carrier.

Thus, in one or more embodiments, the pharmaceutical or cosmetic foamable product comprises:

1. an effective concentration of at least one pharmaceutical or cosmetic active agent;
2. an organic carrier, at a concentration of about 10% to about 70% by weight, wherein said organic carrier concurrently comprises
3. (i) at least one hydrophobic organic carrier and
4. (ii) at least one polar solvent
5. (2) at least one surface-active agent;
6. (3) water; and
7. (4) at least one liquefied or compressed gas propellant at a concentration of about 3% to about 25% by weight of the total composition.

In one or more embodiments a foamable cosmetic or pharmaceutical vehicle comprises:

1. an organic carrier, at a concentration of about 10% to about 70% by weight, wherein said organic carrier concurrently comprises
2. (i) at least one hydrophobic organic carrier and
3. (ii) at least one polar solvent
4. (2) at least one surface-active agent;
5. (3) water; and
6. (4) at least one liquefied or compressed gas propellant at a concentration of about 3% to about 25% by weight of the total composition.

In one or more embodiments the foamable cosmetic or pharmaceutical vehicle comprises:

1. an organic carrier, at a concentration of about 10% to about 70% by weight, wherein said organic carrier concurrently comprises
2. (i) at least one hydrophobic organic carrier and
3. (ii) at least one polar solvent
4. (2) at least one surface-active agent;
5. (3) water; and
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2. (i) at least one hydrophobic organic carrier and
3. (ii) at least one polar solvent
4. (2) at least one surface-active agent;
5. (3) water; and
6. (4) at least one liquefied or compressed gas propellant at a concentration of about 3% to about 25% by weight of the total composition.

Polar Solvent

A “polar solvent” is an organic solvent, typically soluble in both water and oil. Certain polar solvents possess the beneficial property of a humectant, being a substance, which helps retain moisture, for example propylene glycol and glycerin.

In one or more embodiments, the polar solvent is a humectant.

According to one or more embodiments, the polar solvent comprises a short chain alcohol. Short chain alcohols, having up to 5 carbon atoms in their carbon chain skeleton and one hydroxyl group, such as ethanol, propanol, isopropanol, butanol, iso-butanol, t-butanol and pentanol. In one or more embodiments the concentration of the short chain alcohols is from about 5% to about 70%, preferably from about 10% to about 60%.

In one or more embodiments, the polar solvent is a polyol. Polyols are organic substances that contain at least two hydroxy groups in their molecular structure.

In one or more embodiments, the polar solvent contains an diol (a compound that contains two hydroxy groups in its molecular structure), such as propylene glycol (e.g., 1,2-propylene glycol and 1,3-propylene glycol), butanediol (e.g., 1,4-butanediol), butanediol (e.g., 1,3-butanediol and 1,4-butanediol), butanediol, pentanediol (e.g., 1,5-pentanediol), hexanediol (e.g., 1,6-hexanediol), octanediol (e.g., 1,8-octanediol), neopentyl glycol, 2-methyl-1,3-
propanediol, diethylene glycol, triethylene glycol, tetraethylene glycol, dipropylene glycol and dibutylene glycol.

In one or more embodiments, the polar solvent contains a triol (a compound that contains three hydroxyl groups in its molecular structure), such as glycerin and 1,2,6-Hexanetriol.

Other non-limiting examples of polar solvents include pyrrolidones, (such as N-methyl-2-pyrrolidone and 1-methyl-2-pyrrolidinone), dimethyl isosorbide, 1,2,6-hexanetriol, dimethyl sulfoxide (DMSO), ethyl propanol, dimethylacetamide (DMAC) and alpha hydroxy acids, such as lactic acid and glycolic acid.

According to still other embodiments, the polar solvent is a polyethylene glycol (PEG) or PEG derivative that is liquid at ambient temperature, including PEG2000 (MW (molar weight) about 190-210 kD), PEG300 (MW about 285-315 kD), PEG4000 (MW about 380-420 kD), PEG600 (MW about 570-630 kD) and higher MW PEGs such as PEG 4000, PEG 6000 and PEG 10000 and mixtures thereof.

Polar solvents are known to enhance the penetration of active ingredient into the skin and through the skin, and therefore, their inclusion in the composition of the present invention is desirable, despite their undesirable skin drying and irritation potential. There is at one level a commonality between the different polar solvents and their penetration enhancement properties. However, lower molecular weight alcohols can sometimes be more potent as a solvent, for example by extracting lipids from the skin layers more effectively, which characteristic can adversely affect the skin structure and cause dryness and irritation. Therefore the selection of the hydrophobic carrier to counteract these negative effects may be of more importance when using the lower molecular weight alcohols.

Hydrophobic Solvent

A “hydrophobic organic carrier” as used herein refers to a material having solubility in distilled water at ambient temperature of less than about 0.1 gm per 100 ml., more preferable less than about 0.5 gm per 100 ml., and most preferably less than about 0.1 gm per 100 ml.

The identification of a hydrophobic organic carrier or “hydrophobic solvent”, as used throughout this specification synonymously, is not intended to characterize the solubilization capabilities of the solvent for any specific active agent or any other component of the foaming composition. Rather, such information is provided to aid in the identification of materials suitable for use as a hydrophobic carrier in the foaming compositions described herein.

In one or more embodiments, the hydrophobic organic carrier is a high-melting point hydrocarbon, such as, petrolatum.

In one or more other embodiments the use of high melting point hydrocarbons, such as petrolatum in concentrations of more than 10%, are not desirable since they have a waxy feeling when applied to the skin; and, in certain additional embodiments, when an extensive refattening effect is required, then petrolatum in concentrations of more than 10%, for example between about 10% and about 50% is included in the composition of the present invention.

According to one or more embodiments, hydrophobic solvents are liquid oils originating from vegetable, marine or animal sources. Suitable liquid oil includes saturated, unsaturated or polyunsaturated oils. By way of example, the unsaturated oil may be olive oil, corn oil, soybean oil, canola oil, cottonseed oil, coconut oil, sesame oil, sunflower oil, borage seed oil, syzygium aromaticum oil, hempseed oil, herring oil, cod-liver oil, salmon oil, flaxseed oil, wheat germ oil, evening primrose oils or mixtures thereof, in any proportion.

Suitable hydrophobic solvents also include polyunsaturated oils containing polyunsaturated fatty acids. In one or more embodiments, the unsaturated fatty acids are selected from the group of omega-3 and omega-6 fatty acids. Examples of such polyunsaturated fatty acids are linoleic and linolenic acid, gamma-linoleic acid (GLA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Since unsaturated fatty acids are known for their skin-conditioning effect, which contribute to the therapeutic benefit of the present foamy composition. Thus, the hydrophobic solvent can include at least 6% of an oil selected from omega-3 oil, omega-6 oil, and mixtures thereof.

In the context of the present invention, oils that possess therapeutically beneficial properties are termed as “therapeutically active oil.”

Another class of hydrophobic solvents is the essential oils, which are also considered therapeutically active oils, and which contain active biologically occurring molecules and, upon topical application, exert a therapeutic effect. Non-limiting examples of essential oils include rosehip oil, which contain retinoids and is known to reduce acne and post-acne scars, and tea tree oil, which possess antibacterial, antifungal and antiviral properties. Other examples of essential oils are oils of anise, basil, bergamont, camphor, cardamom, carrot, canola, cassia, catnip, cedarwood, citronella, clove, cypress, eucalyptus, frankincense, garlic, ginger, grapefruit, hyssop, jasmine, jojoba, lavender, lavandin, lemon, lime, mandarin, marjoram, myrrh, neroli, nutmeg, orange, peppermint, petitgrain, rosemary, sage, spearmint, star anise, tangerine, thyme, vanilla, verbena and white clover.

Another class of therapeutically active oils includes liquid hydrophobic plant-derived oils, which are known to possess therapeutic benefits when applied topically.

Silicone oils also may be used and are desirable due to their known skin protective and occlusive properties. Suitable silicone oils include non-volatile silicones, such as polyalkyl siloxanes, polyaryl siloxanes, polyalkylaryl siloxanes and polyether siloxane copolymers, poly(dimethyl)siloxanes (dimethicones) and poly(dimethylsiloxane)-(diphenylsiloxane) copolymers. Silicone oils are also considered therapeutically active oil, due to their barrier retaining and protective properties.

A further class of hydrophobic carriers includes hydrophobic liquids, selected from the family of organic liquids described as “emollients.” Emollients possess a softening or soothing effect, especially when applied to body areas, such as the skin and mucosal surfaces. Examples of suitable emollients include isopropyl myristate, isopropyl palmitate, isopropyl stearate, diisopropyl adipate, disopropyl dimerate, maleated soybean oil, octyl palmitate, cetyl lactate, cetyl ricinoleate, tocopheryl acetate, cetyl acetate, tocopheryl linoleate, wheat germ glycerides, arachidyl propionate, myristyl lactate, decyl oleate, propylene glycol ricinoleate, isopropyl lanolate, pentaerythritol tetraesterate, neopentylglycol dicaprylate/dicaprate, isononyl isononano-
ate, isostearyl isononanoate, myristyl myristate, octyl dodecanol, sucrose esters of fatty acids and octyl hydroxystearate.

[0059] The foamable composition of the present invention can be an emulsion, or microemulsion, including an aqueous phase and an organic carrier phase.

[0060] One non-limiting benefit of combining a polar solvent and a hydrophobic carrier is apparent in the resulting conservation of skin barrier properties.

[0061] Another non-limiting benefit of combining a polar solvent and a hydrophobic carrier is further apparent in the reduction of skin irritation.

[0062] Another non-limiting benefit of the vehicle or composition of the present invention is to provide increased penetration of the active or beneficial agent whilst replenishing the skin for example by moisturizing or adding fats or oils.

[0063] The ratio between the polar solvent and the hydrophobic carrier is determined according to the desirable pharmacologic and safety properties of the product. Typically, the polar solvent to hydrophobic carrier ranges between about 1:4 and about 4:1. For example, about 1:4, about 1:2, about 3:4, about 1:1, about 5:4, about 4:2, about 2:1, about 3:1 and about 4:1. When high solubilization and/or enhanced dermal or transdermal delivery of a drug is desirable, the polar solvent to hydrophobic carrier is selected within the range of about 1:1 and about 4:1, for example, about 1:1, about 5:4, about 6:4, about 7:4, about 2:1, about 3:1 and about 4:1. Yet, in other cases, when the need of enhanced skin protection and skin barrier build-up is more pronounced, the polar solvent to hydrophobic carrier is selected within the range of about 2:8 and about 1:1, for example, about 1:4, about 1:2, about 3:4 and about 1:1.

[0064] The following table, Table 1 exemplifies, in a non-limiting manner, pairs of polar solvent and the hydrophobic carrier, as provided in the present invention. The examples of the previous paragraph are incorporated herein by reference.

<table>
<thead>
<tr>
<th>Exemplary Polar Solvent</th>
<th>Exemplary Hydrophobic Carrier</th>
<th>Polar Solvent/ Hydrophobic Carrier Ratio</th>
<th>Comment</th>
</tr>
</thead>
</table>
| A short chain alcohol, selected from ethanol, propanol, isopropanol, butanol | A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride and silicone oil | Between about 1:4 and about 4:1 | To provide enhanced delivery of an active agent, while conserving skin barrier.
| A short chain alcohol, selected from ethanol, propanol, isopropanol, butanol | Ester of fatty acid | Between about 1:4 and about 4:1 | To provide enhanced delivery of an active agent, while conserving skin barrier.
| A short chain alcohol, selected from ethanol, propanol, isopropanol, butanol | Combination of at least one triglyceride and at least one ester of a fatty acid | Between about 1:4 and about 4:1 | To provide enhanced delivery of an active agent, while conserving skin barrier.
| A polyethylene glycol PEG | A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride and silicone oil | Between about 1:1 and about 4:1 | To provide enhanced delivery of an active agent, while conserving skin barrier.
| Dimethyl isosorbide | A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride and silicone oil | Between about 1:1 and about 4:1 | To provide enhanced delivery of an active agent, while conserving skin barrier.
| Dimethyl isosorbide | A triglyceride | Between about 4:1 and about 1:4 | To provide increased solubility of a drug, enhanced delivery and skin barrier build-up.
<table>
<thead>
<tr>
<th>Exemplary Polar Solvent</th>
<th>Exemplary Hydrophobic Carrier</th>
<th>Polar Solvent/Hydrophobic Carrier Ratio</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethyl isosorbide</td>
<td>Capric-caprylic triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide increased solubility of a drug, enhanced delivery and skin barrier build-up</td>
</tr>
<tr>
<td>Dimethyl isosorbide</td>
<td>Ester of fatty acid</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide increased solubility of a drug, enhanced delivery and skin barrier build-up</td>
</tr>
<tr>
<td>Dimethyl isosorbide</td>
<td>Combination of at least one triglyceride and at least one ester of a fatty acid</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide increased solubility of a drug, enhanced delivery and skin barrier build-up</td>
</tr>
<tr>
<td>A diol selected from the group of propylene glycol, butanediol, hexanediol, octanediol, propanediol, diethylene glycol, triethylene glycol, tetraethylene glycol, dipropylene glycol and dibutylene glycol.</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride and silicone oil</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced skin barrier build-up</td>
</tr>
<tr>
<td>A triol (a compound that contains three hydroxy groups in its molecular structure), such as glycerin and 1,2,6-Hexanetriol.</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced skin barrier build-up</td>
</tr>
<tr>
<td>An alpha hydroxy acids, such as lactic acid and glycolic acid</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced skin barrier build-up</td>
</tr>
<tr>
<td>DMSO</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced skin barrier build-up</td>
</tr>
<tr>
<td>A pyrrolidone, such as N-methyl-2-pyrrolidone and 1-methyl-2-pyrrolidinone</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced delivery of an active agent, while conserving skin barrier</td>
</tr>
<tr>
<td>A combination of at least two polar solvents</td>
<td>A hydrophobic carrier, selected from mineral oil, petrolatum, isopropyl myristate, isopropyl palmitate, a triglyceride</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide enhanced skin barrier build-up, which facilitates the recovery of damaged skin.</td>
</tr>
<tr>
<td>A combination of at least two polar solvents</td>
<td>Ester of fatty acid</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide increased solubility of a drug, enhanced delivery and skin barrier build-up</td>
</tr>
<tr>
<td>A combination of at least two polar solvents</td>
<td>Combination of at least one triglyceride and at least one ester of a fatty acid</td>
<td>Between about 1:4 and about 1:1</td>
<td>To provide increased solubility of a drug, enhanced delivery and skin barrier build-up</td>
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</tbody>
</table>
In one or more embodiments, the polar solvent consists of a single polar solvent. Yet, in additional embodiments, the polar solvent consists of a combination of two or more polar solvents.

In one or more embodiments, the hydrophobic carrier consists of a single polar solvent. Yet, in additional embodiments, the hydrophobic carrier consists of a combination of two or more hydrophobic carriers.

In order to derive a composition which is readily formable upon release from a pressurized container, additional components are required, as provided hereinbelow.

Surface Active Agent

Surface-active agents (also termed “surfactants”) include any agent linking oil and water in the composition, in the form of emulsion. A surfactant’s hydrophilic-lipophilic balance (HLB) describes the emulsifier’s affinity toward water or oil. The HLB scale ranges from 1 (totally lipophilic) to 20 (totally hydrophilic), with 10 representing an equal balance of both characteristics. Lipophilic emulsifiers form water-in-oil (w/o) emulsions; hydrophilic surfactants form oil-in-water (o/w) emulsions. The HLB of a blend of two emulsifiers equals the weight fraction of emulsifier A times its HLB value plus the weight fraction of emulsifier B times its HLB value (weighted average). The surface-active agent according to the present invention has an HLB value, suitable for stabilizing an emulsion comprising the aqueous phase and the organic carrier of the composition.

According to one or more embodiments of the present invention, the surface-active agent has a hydrophilic lipophilic balance (HLB) between about 9 and about 14, which is the required HLB of the HLB required to stabilize an O/W emulsion of a given oil of most oils and hydrophobic solvents. Thus, in one or more embodiments, the composition contains a single surface active agent having an HLB value between about 9 and about 14 (e.g., about 9, about 10, about 11, about 12, about 13 and about 14), and in one or more embodiments, the composition contains more than one surface active agent and the weighted average of their HLB values is between about 9 and about 14 (e.g., about 9, about 10, about 11, about 12, about 13 and about 14). Yet, in other embodiments, when a water-in-oil emulsion is desirable, the composition contains one or more surface-active agents, having an HLB value between about 2 and about 9 (e.g., about 2, about 3, about 4, about 5, about 6, about 7, about 8 and about 9).

The surface-active agent is selected from anionic, cationic, nonionic, zwitterionic, ampholytic and amphoteric surfactants, as well as mixtures of these surfactants. Such surfactants are well known to those skilled in the therapeutic and cosmetic formulation art. Non-limiting examples of possible surfactants include polysorbates, such as polyoxyethylene (20) sorbitan monostearate (‘Tween 60) and poly (oxyethylene) (20) sorbitan monooleate (‘Tween 80); poly (oxyethylene) (POE) fatty acid esters, such as Myrj 45, Myrj 49, Myrj 52 and Myrj 59; poly(oxyethylene) alkyl ethers, such as poly(oxyethylene) cetyl ether, poly(oxyethylene) palmitol ether, polyethylene oxide hexadecyl ether, polyethylene glycol cetyl ether, brij 38, brij 52, brij 56 and brij W1; sucrose esters, partial esters of sorbitol and its anhydrides, such as sorbitan monolaurate and sorbitan monolaurate; mono or diglycerides, isoceteth-20, sodium methyl cocoyl taurate, sodium methyl oleoyl taurate, sodium lauryl sulfate, triethanolamine lauryl sulfate and betaines.

In one or more embodiments of the present invention, the surface-active agent includes a non-ionic surfactant. Non-ionic surfactants are known to be irritants. Therefore, non-ionic surfactants are preferred in applications including sensitive tissue such as found in most mucosal tissues, especially when they are infected or inflamed. We have surprisingly found that non-ionic surfactants alone provide foams of excellent quality, i.e. a score of “E” according to the grading scale discussed herein below.

In one or more embodiments, the surface-active agent includes a mixture of a non-ionic surfactant and an ionic surfactant in a ratio in the range of about 100:1 to about 6:1. In one or more embodiments, the non-ionic to ionic surfactant ratio is greater than about 6:1, or greater than about 8:1; or greater than about 14:1, or greater than about 16:1, or greater than about 20:1.

In one or more embodiments of the present invention, a combination of a non-ionic surfactant and an ionic surfactant (such as sodium lauryl sulphate and cocamidopropylbetaine) is employed, at a ratio of between 1:1 and 20:1, for example, about 1:1, about 4:1, about 8:1, about 12:1, about 16:1 and about 20:1, or at a ratio of 4:1 to 10:1, for example, about 4:1, about 6:1, about 8:1 and about 10:1. The resultant foam has a low specific gravity, e.g., less than 0.1 g/ml.

Thus, in an exemplary embodiment, a combination of an non-ionic surfactant having HLB of less than about 9 and a non-ionic surfactant having HLB of equal or more than about 9 is employed, at a ratio of between about 1:8 and about 8:1, or at a ratio of about 4:1 to about 1:4, wherein the HLB of the combination of emulsifiers is between 9 and about 14.

In one or more embodiments of the present invention, the surface-active agent includes mono-, di- and triesters of sucrose with fatty acids (sucrose esters), prepared from sucrose and esters of fatty acids or by extraction from sucro-glycerides. Suitable sucrose esters include those having high monoester content, which have higher HLB values.

The total surface-active agent is in the range of about 0.1 to about 5% of the composition, and is occasionally less than about 2% or less than about 1%.

Polymeric Agent

In one or more embodiments, the foamy composition contains a polymeric agent. The polymeric agent serves to stabilize the foam composition and to control drug residence in the target organ. Exemplary polymeric agents are classified below in a non-limiting manner. In certain cases, a given polymer can belong to more than one of the classes provided below.

In one or more embodiments, the composition of the present invention includes a gelling agent. A gelling agent controls the residence of a therapeutic composition in the target site of treatment by increasing the viscosity of the composition, thereby limiting the rate of its clearance from the site. Many gelling agents are known in the art to possess mucoadhesive properties.

The gelling agent can be a natural gelling agent, a synthetic gelling agent and an inorganic gelling agent. Exemplary gelling agents that can be used in accordance with one or more embodiments of the present invention include, for example, naturally-occurring polymeric materials, such as locust bean gum, sodium alginate, sodium carrageean, egg albumin, gelatin agar, carrageean gum,
sodium alginate, xanthan gum, quince seed extract, tragacanth gum, guar gum, starch, chemically modified starches and the like, semi-synthetic polymeric materials as cellulose ethers (e.g., hydroxyethyl cellulose, hydroxypropyl cellulose, methyl cellulose, carboxymethyl cellulose, methylhydroxyethylcellulose, methylhydroxypropylcellulose, hydroxypropylmethyl cellulose, hydroxyethylcellulose and carboxymethylhydroxyethylcellulose), guar gum, hydroxypropyl guar gum, soluble starch, cationic celluloses, cationic gums, and the like, and synthetic polymeric materials, such as carboxyvinyl polymers, polyvinylpyrrolidone, polyvinyl alcohol, polyacrylic acid polymers, polyethacrylate acid polymers, polyvinyl acetate polymers, polyvinyl chloride polymers, polyvinylidene chloride polymers and the like. Mixtures of the above compounds are also contemplated.

Further exemplary gelling agents include the acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers. Non-limiting examples include Carbopol® 934, Carbopol® 940, Carbopol® 950, Carbopol® 980, Carbopol® 951 and Carbopol® 981.

Yet, in other embodiments, the gelling agent includes inorganic gelling agents, such as silicone dioxide (fumed silica).

Mucoadhesive/bioadhesive has been defined as the attachment of synthetic or biological macromolecules to a biological tissue. Mucoadhesive agents are a class of polymeric biomaterials that exhibit the basic characteristic of a hydrogel, i.e., swell by absorbing water and interacting by means of adhesion with the mucous that covers epithelia. Compositions of the present invention may contain a mucoadhesive macromolecule or polymer in an amount sufficient to confer bioadhesive properties. The bioadhesive macromolecule enhances the delivery of biologically active agents on or through the target surface. The mucoadhesive macromolecule may be selected from acrylic, hydroxypropyl methylcellulose; basic amine-bearing polymers such as chitosan; acidic polymers obtainable from natural sources, such as alginic acid, hyaluronic acid, pectin, gumartracanthum, and caraya gum; and neutral synthetic polymers, such as carboxymethylcellulose (CMC); neutral synthetically modified natural polymers, such as (hydroxypropyl)methylcellulose; basic amine-bearing polymers such as chitosan; acidic polymers obtainable from natural sources, such as alginic acid, hyaluronic acid, pectin, gumartracanthum, and caraya gum; and neutral synthetic polymers, such as polyvinyl alcohol or their mixtures. An additional group of mucoadhesive polymers includes natural and chemically modified cyclodextrin, especially hydroxypropyl-β-cyclodextrin. Such polymers may be present as free acids, bases, or salts, usually in a final concentration of about 0.01% to about 0.5% by weight. Many mucoadhesive agents are known in the art to also possess gelling properties.

In one or more embodiments, the polymeric agent contains a film-forming component. The film-forming component may include a water-insoluble alkyl cellulose or hydroxyalkyl cellulose. Exemplary alkyl cellulose or hydroxyalkyl cellulose polymers include ethyl cellulose, propyl cellulose, butyl cellulose, cellulose acetate, hydroxypropyl cellulose, hydroxybutyl cellulose, and ethylhydroxyethyl cellulose, alone or in combination. In addition, a plasticizer or a cross-linking agent may be used to modify the polymer’s characteristics. For example, esters such as dibutyl or diethyl phthalate, amides such as diethylidiphenyl urea, vegetable oils, fatty acids and alcohols such as oleic and myristic acid may be used in combination with the cellulose derivative.

In one or more embodiments, the polymeric agent includes a phase change polymer, which allows the composition behavior from fluid-like prior to administration to semi-solid-like upon contact with the target mucosal surface. Such phase change results from external stimuli, such as changes in temperature or pH and exposure to specific ions (e.g., Ca²⁺). Non-limiting examples of phase change polymers include poly(N-isopropylamide) and Poloxamer 407®.

The polymeric agent is present in an amount in the range of about 0.01% to about 5.0% by weight of the foam composition. In one or more embodiments, it is typically less than about 1 wt % of the foamable composition.

Preferably, a therapeutically effective foam adjuvant is included in the foamable compositions of the present invention to increase the foaming capacity of surfactants and/or to stabilize the foam. In one or more embodiments of the present invention, the foam adjuvant includes fatty alcohols having 15 or more carbons in their carbon chain, such as cetyl alcohol and stearyl alcohol (or mixtures thereof). Other examples of fatty alcohols are arachidyl alcohol (C20), behenyl alcohol (C22), 1-triacontanol (C30), as well as alcohols with longer carbon chains (up to C50). Fatty alcohols, derived from beeswax and including a mixture of alcohols, a majority of which has at least 20 carbon atoms in their carbon chain, are especially well suited as foam adjuvant agents. The amount of the fatty alcohol required to support the foam system is inversely related to the length of its carbon chains. Foam adjuvants, as defined herein are also useful in facilitating improved spreadability and absorption of the composition.

In one or more embodiments of the present invention, the foam adjuvant includes fatty acids having 16 or more carbons in their carbon chain, such as hexadecanoic acid (C16) stearic acid (C18), arachidic acid (C20), behenic acid (C22), octacosanoic acid (C28), as well as fatty acids with longer carbon chains (up to C50), or mixtures thereof. As for fatty alcohols, the amount of fatty acids required to support the foam system is inversely related to the length of its carbon chain.

In one or more embodiments, a combination of a fatty acid and a fatty ester is employed.

Optionally, the carbon atom chain of the fatty alcohol or the fatty acid may have a double bond. A further class of foam adjuvant agent includes a branched fatty alcohol or fatty acid. The carbon chain of the fatty acid or fatty alcohol also can be substituted with a hydroxyl group, such as 12-hydroxy stearic acid.

A property of the fatty alcohols and fatty acids used in context of the composition of the present invention is related to their therapeutic properties per se. Long chain saturated and mono unsaturated fatty alcohols, e.g., stearyl alcohol, erucyl alcohol, arachidyl alcohol and behenyl alcohol (docosanol) have been reported to possess anti-viral, antifungal, antiproliferative and anti-inflammatory properties (see, U.S. Pat. No. 4,874,794). Longer chain fatty alcohols, e.g., tetracosanol, hexacosanol, heptacosanol, octacosanol, triacontanol, etc., are also known for their metabolism modifying properties and tissue energizing properties. Long chain fatty acids have also been reported to possess anti-infective characteristics.
[0091] In one or more embodiments, the active agent is encapsulated in particles, microparticles, nanoparticles, microcapsules, spheres, microspheres, nanocapsules, nanoparticles, liposomes, micosomes, polymer matrix, nanocrystals or microsponges.

[0092] The composition of the present invention may further optionally include a variety of formulation excipients, which are added in order to fine-tune the consistency of the formulation, protect the formulation components from degradation and oxidation and modify their consistency. Such excipients may be selected, for example, from stabilizing agents, antioxidants, humectants, preservatives, colorant and odorant agents and other formulation components, used in the art of formulation.

[0093] Aerosol propellants are used to generate and administer the foamy composition as a foam. The total composition including propellant, foamy compositions and optional ingredients is referred to as the foamy carrier. The propellant makes up about 3% to about 25% (w/w) of the foamy carrier or composition. Examples of suitable propellants include volatile hydrocarbons such as butane, propane, isobutane or mixtures thereof, and fluorocarbon gases.

Non-Flammable Stable Foam Compositions

[0094] Alcohol and organic solvents render foams inflammable. It has been surprisingly discovered that fluorohydrocarbon propellants, other than chloro-fluoro carbons (CFCs), which are non-ozone-depleting propellants, are particularly useful in the production of a non-flammable foamy composition. A test according to European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test" revealed that compositions containing an organic carrier that contains a hydrophobic organic carrier and/or a polar solvent, which are detected as inflammable when a hydrocarbon propellant is used, become non-flammable, while the propellant is an HFC propellant.

[0095] Such propellants include, but are not limited to, hydrofluorocarbon (HFC) propellants, which contain no chlorine atoms, and as such, fall completely outside concern about stratospheric ozone destruction by chlorofluorocarbons or other chlorinated hydrocarbons. Exemplary non-flammable propellants according to this aspect of the invention include propellants made by DuPont under the registered trademark Dymel, such as 1,1,2,2-tetrafluoroethane (Dymel 134), and 1,1,2,3,3 heptafluoropropane (Dymel 227). HFCs possess Ozone Depletion Potential of 0.00 and thus, they are allowed for use as propellant in aerosol products.

[0096] Notably, the stability of foamable emulsions including HFC as the propellant is improved in comparison with the same composition made with a hydrocarbon propellant.

Active Agents

[0097] It is to be understood that the active agents useful herein can in some instances provide more than one benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit the active agent to that particular application or applications listed.

[0098] The composition of the present invention comprises an active agent that provides therapeutic or cosmetic activity.

[0099] Non-limiting examples of active agents include an anti-aging, an antibiotic, an antibacterial agent, an antifungal agent, an antivirus agent, a steroidal anti-inflammatory agent, a nonsteroidal anti-inflammatory agent, an immunosuppressive agent, an immunomodulator, an immunoregulating agent, a hormonal agent, a steroid, a vasoactive agent, a vasoconstrictor, a vasodilator, vitamin A, a vitamin A derivative, a retinoid, vitamin B, a vitamin B derivative, vitamin C, a vitamin C derivative, vitamin D, a vitamin D derivative, vitamin E, a vitamin E derivative, vitamin F, a vitamin F derivative, vitamin K, a vitamin K derivative, a wound healing agent, a burning agent, a disinfectant, an anesthetic, an antiallergic agent, an alpha hydroxyl acid, lactic acid, glycolic acid, a beta-hydroxy acid, a protein, a peptide, a neuropeptide, an allergen, an immunogenic substance, a haptene, an oxidizing agent, an antioxidant, a dicarboxylic acid, azelaic acid, sebacic acid, adipic acid, fumaric acid, an insecticide, an antiproliferative agent, an anticancer agent, a photodynamic therapy agent, an anti-aging agent, a radical scavenger, a metal oxide (e.g., titanium dioxide, zinc oxide, zirconium oxide, iron oxide), silicone oxide, talc, an anti-scene agent, a skin whitening agent, a self tanning agent, an anti-cellulite agent, a skin protective agent, a masking agent, an anti-wart agent, a retarding agent, a lubricating agent and mixtures thereof at any proportion. The concentration of the active agent can be adapted to exert a therapeutic effect on a disease when applied to an afflicted area. Various different therapeutic effects of the herbs and their extracts are, for example, illustrated in the above-mentioned references.

[0100] In one or more embodiments the active agent may be an extract or tincture of one or more beneficial agents that have beneficial properties, for example, when applied to the skin, a body surface, a body cavity or a mucosal surface. The extract can be, for example, alcoholic, hydroalcoholic, propylene glycol, glycerine, dry, press, cold, hot, liquid carbon dioxide, oil or other process known in the art. The extract or tincture may comprise of substances of animal, plant, (such as herb, fruit, vegetable) mineral or other origin. Nonlimiting examples are proteins, polypeptides, sugars, hyaluronic acid, and coal tar. Herbal extracts may be from any known therapeutic herb, as listed for example in Herbal Medicines, London: Pharmaceutical Press Electronic Version 2006 or in the American Herbal Association electronic publication Herbal gram or in German Compendium herbs, such as, angelica, calendula, celery, coltsfoot, comfrey, dandelion, jamaica dogwood, kava, marshmallow, prickly ash, northern prickly ash, southern senna, valerian, agrimony, aloe vera, allafla, artichoke, avens, bayberry, bloodroot, blue flag, bogbean, boldo, boneset, broom, buchu, burdock, burnet, calamus, calendula, cascarra, centaury, cereus, chamomile, german chamomile, roman chamomile, cinnamon, clivers, clover, cloths, croton, cola, coriander, couchgrass, cowslip, damiana, devil’s claw, drosera, echinacea, elder, elecampane, euphorbia, eyebright, figwort, frangula, fucus, fumitory, garlic, golden seal, gravel root, ground ivy, guaiacum, hawthorn, holy thistle, hops, horehound black, horehound white, horse chestnut hrendaee, ispaghula, juniper, lady’s lipper, life root, lime flower, liquorice, lobelia, mate, meadowsweet, mistletoe, motherwort, myrrh, nettle, parsley, parley, pier, passionflower, pennyroyal, pilewort, ...
plantain, pleurisy root, pokerooot, pulsatilla, queen’s delight, raspberry, red clover, rosemary, sage, sarsaparilla, sassafras, scullcap, senega, shepherd’s purse, skunk cabbage, slippery elm, squill, St. John’s wort, stone root, tansy, thyme, uva-ursi, vervain, wild carrot, wild lettuce, willow, witch hazel, yarrow and yellow dock.

[0101] When the extract is dissolved in a polar solvent, such as a short chain alcohol (e.g., ethanol and isopropyl alcohol), propylene glycol and glycerin, then the polar solvent of the extract can also comprise part or all of the “polar solvent” component of the foamy composition, as specified throughout this specification and likewise the polar solvent of the foamy composition can also comprise as part or all of the “polar solvent” component of the extract.

[0102] In one or more embodiments, the active agent is an anti-inflammatory agent, an antibiotic agent, an anti-fungal agent, an anti-viral agent and an anti-parasite agent.

[0103] The antibacterial drug can be active against gram positive and gram-negative bacteria, protozoa, aerobic bacteria and anaerobic ones.

[0104] In one or more embodiments, the antibiotic agent is selected from the classes consisting of beta-lactam antibiotics, synthetic and semi-synthetic penicillins, aminoglycosides, ansa-type antibiotics, anaquinones, antibiotic azoles, antibiotic glycopeptides, macrolides, antibiotic nucleosides, antibiotic peptides, antibiotic polycycles, quinolones, fluoroquinolones, antibiotic steroids, cyclosporines, sulfonamides, tetracycline, chloramphenicol, dicarboxylic acids, such as asazolic acid, salicylates, antibiotic metals, oxidizing agents, substances that release free radicals and/or active oxygen, cationic antimicrobial agents, quaternary ammonium compounds, biguanides, triganids, bisbiguanides and polymers thereof and naturally occurring antibiotic compounds.

[0105] Additional antibacterial agents, which are non-specific, include strong oxidants and free radical liberating compounds, such as hydrogen peroxide, bleaching agents (e.g., sodium, calcium or magnesium hypochloride and the like), iodine, chlorohexidine and benzoyl peroxide.

[0106] The anti-fungal agent can be an azole compound. Exemplary azole compounds include azoles selected from the group consisting of ketoconazole, fluconazole, triazoles, mena-zole, ketoconazole, clotrimazole, econazole, mephazol, bifonazole, butoconazole, fenticonazole, isoconazole, oxiconazole, sertaconazole, sulconazole, thiabendazole, ticoconazole, fluconazole, itraconazole, rancouzoaze and posaconazole.

[0107] Additional exemplary anti-fungal agents include griseofulvin, ciclopirox, amorolfine, terbinafine, Amphotericin B, potassium iodide, flucytosine (5FC) and any combination thereof at a therapeutically effective concentration.

[0108] In one or more embodiments, the active agent is an anti-viral agent. Any known antiviral agent, in a therapeutically effective concentration, can be incorporated in the foam composition of the present invention. Exemplary anti-viral agents include, but not limited to, acyclovir, famiclovir, gancyclovir, valganclovir and abacavir.

[0109] In another embodiment according to the present invention, the active agent is an anti-inflammatory or anti-allergic agent. Anti-inflammatory agents can be selected from the group of corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), antihistamines, immunosuppressants, immunomodulators; and any combination thereof at a therapeutically effective concentration.

[0110] Non-limiting examples of corticosteroids include hydrocortisone, hydrocortisone acetate, desonide, betamethasone valerate, clobetasone-17-butyrate, fluconidi, flucinolone acetonide, alconetasone dipropionate, mometasone furoate, prednicarbate, trimcinolone acetonide, betamethasone-17-benzoate, methylprednisolone aceponate, betamethasone dipropionate, halcinonide, triamcinolone acetonide, halobetasol and clobetasol-17-propionate.

[0111] A second class of anti-inflammatory agents, which is useful in the foam of the present invention, includes the non-steroidal anti-inflammatory agents (NSAIDs). The variety of compounds encompassed by this group is well known to those skilled in the art. Specific non-steroidal anti-inflammatory agents useful in the composition invention include, but are not limited to, oxicam, isoxicam, tenoxicam, salsalate, salicylates, such as salicylic acid, ethyl salicylate, methyl salicylate, aspirin, disalcid, benorylate, trilisate, saufpryn, sulpirin, diflunisal, and fendosal; septic acid derivatives, such as diclofenac, fenclofenac, indometacin, tolmetin, isoexepic, ifurofenac, tiopine, zidometacin, acetamin, fentiazac, zomepirac, clindane, oexipenic, felbinac, and ketorolac; fenamates, such as mefenamic, meclofenamic, flufenamic, nilfumic, and tolofamic acids; propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, lenbuten, indoprofen, parprofen, ciproprofen, o xoaprofen, prunoprofen, miroprofen, tioxaprofen, suprofen, alinaprofen, and tiaprogen; and pyrazoles, such as phenybutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

[0112] Any further steroidal and non-steroidal compounds, having the capacity to prevent, alleviate the symptoms of, treat or cure inflammation processes, are generally included, as possible anti-inflammatory agents, according to the present invention.

[0113] Antiallergic active agents include antihistamine compounds, including, in a non limiting manner, thylenediamines, such as pyrilamine (mepryamine), antazoline and methapyrilene; tripeleamine phenotheniazines, such as promethazine, methilazine and tripeprazine; ethanolamines, such as diphenhydramine, bromodiphenhydramine, carbinoxamine, clemastine, dimehydriate, diphenylpyraline, doxylamine and phenyltoloxamine; piperasines, such as cyclizine, busclizine, choroxyzylizine, hydroxyzine, mocylixine and thiethylperazina; alkyamines, such as brompheniramine, pyrrobartuin, desbrompheniramine, tripolidine, dexchlorpheniramine, chlorpheniramine; dimethindene and pheniramine; and piperidines, such as cypromethadine and azatadine. These active agents, as well as additional antihistamines can also be incorporated in the composition of the present invention.

[0114] The composition of the present invention may also comprise an anti-inflammatory or antiallergic agent, wherein said agent reduces the occurrence of pro-inflammatory cytokines or inhibits the effect of pro-inflammatory cytokines.

[0115] Immunosuppressant agents, immunoregulating agents and immunomodulators are chemically or biologically derived agents that modify the immune response or the functioning of the immune system (as by the stimulation of antibody formation or the inhibition of white blood cell activity). Immunosuppressant agents and immunomodula-
tors include, among other options, cyclic peptides, such as cyclosporine, tacrolimus, tre sperimus, pimecrolimus, sirolimus (rapamycin), verolimus, laftunimod, Laxuminod and imiquimod.

[0116] In one or more embodiments, the active agent is a topical anesthetic. Examples of topical anesthetic drugs include, but not limited to, benzocaine, lidocaine, bupivacaine, chloroprocaine, dibucaine, etidocaine, mepracaine, tetracaine, dyclonine, hexylcaine, procaine, cocaine, ketamine, propanoic, and phenol. Mixtures of such anesthetic agents may be synergistically beneficial.

[0117] In one or more embodiments, the active agent is a "keratolytically active agent." The term "keratolytically active agent" refers herein to a compound which loosens and removes the stratum corneum of the skin, or alters the structure of the keratin layers of the skin.

[0118] Suitable keratolytically active agents include phenol and substituted phenolic compounds. Such compounds are known to dissolve and loosen the intracellular matrix of the hyperkeratinized tissue. Dihydroxy benzene and derivatives thereof have been recognized as potent keratolytic agents. Resorcinol (m-dihydroxybenzene) and derivatives thereof are used in anti-acne preparations. Hydroquinone (p-dihydroxybenzene), besides its anti-pigmentation properties, is also keratolytic.

[0119] Vitamin A and its derivatives, such as retinoic acid, isoretinoic acid, retinol and retinal are another preferred class of keratolytically active agents.

[0120] Another group of keratolytically active agents include alpha-hydroxy acids, such as lactic acid and glycolic acid and their respective salts and derivatives; and beta-hydroxy acids, such as Salicylic acid (o-hydroxybenzoic acid) and its salts and pharmacologically acceptable derivatives, which typically possess anti-inflammatory, as well as keratolytic, activity. Yet, another class of preferred keratolytically active agents includes urea and its derivatives.

[0121] In one or more embodiments, the active agent is a retinoid. Retinoids include, for example, retinol, retinal, all-trans retinoic acid and derivatives, isomers and analogs thereof. Eretinate, actretin, isoretinoin, adapalene and tazarotene are further examples of such retinoid isomers and analogs.

[0122] In one or more embodiments, the active agent is an insecticide or an insect repellent agent.

[0123] In one or more embodiments, the active agent is an anti cancer agent.

[0124] In one or more embodiments, the active agent is a photodynamic therapy (PDT) agent. By way of example, such PDT agents can be modified porphyrins, chlorins, bacteriochlorins, phthalocyanines, naphthalocyanines, phorphorides, purpurins, m-THPC, mono-L-aspartyl chlorin e6, bacteriochlorins, phthalocyanines, benzoporphyrin derivatives, as well as photosensitizer precursors, such as aminolevulinic acid (ALA).

[0125] In one or more embodiments, the active agent is an agent useful in the treatment of burns, wounds, cuts and ulcers. The foam compositions of the present invention may comprise a combination of anti-infective agents (against bacteria, fungi and/or viruses), anti-inflammatory agents (steroidal and/or NSAIDs) and pain relieving components.

[0126] The foam compositions of the present invention, with or without further active ingredients, are suitable for the further application as "cosmeceutical" preparation (cosmetic products with therapeutic benefit) to treat "cosmetic" skin disorders, such as aging skin, wrinkles, hyperpigmentation (melasma, chloasma, freckles, etc.), scaly skin and other skin undesirable properties.

[0127] Any cosmetically active agent is considered an active agent in the context of the present invention. The CTEA Cosmetic Ingredient Handbook describes a wide variety of non-limiting cosmetic and pharmaceutical ingredients commonly used in the skin care industry, which are suitable for use in the compositions of the present invention. Examples of these ingredient classes include: abrasives, absorbents, aesthetic components such as fragrances, pigments, colorings/colorants, essential oils, astringents, etc. (e.g., clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate), anti-acne agents, anti-aging agents, anti-fouling agents, anti-microbial agents (e.g., iodopropyl butylcarbamate), antioxidents, binders, biological additives, buffering agents, bulking agents, chelating agents, chemical additives, colorants, cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers or materials, e.g., polymers, for aiding the film-forming properties and substantivity of the composition (e.g., copolymer of ecosene and vinyl pyrrolidone), opacifying agents, pH adjusters, propellants, reducing agents, sequestrants, skin bleaching and lightening agents (e.g., hydroquinone, kojic acid, ascorbic acid, magnesium ascorbyl phosphate, ascorbyl glucosamine), skin-conditioning agents (e.g., humectants, including miscellaneous and occlusive), skin soothing and/or healing agents (e.g., panthenol and derivatives (e.g., ethyl panthenol), aloe vera, pantothenic acid and its derivatives, allantoin, bisabolol, and dipotassium glycyrhrizinate), skin treating agents, and vitamins and derivatives thereof.

[0128] In one or more embodiments, the active agent is an agent useful in the treatment of acne, wrinkles and sears. Examples of useful anti-acne actives include resorcinol, sulfur, salicylic acid and salicylates, alpha-hydroxy acids, nonsteroidal anti-inflammatory agents, benzoyl peroxide, retinoic acid, isoretinoic acid and other retinoid compounds, adapalene, tazarotene, azelaic acid and azelauric acid derivatives, antibiotic agents, such as erythromycin and clindamycin, zinc salts and complexes, and combinations thereof, in a therapeutically effective concentration. Exemplary anti-wrinkle/anti-atrophy active agents suitable for use in the compositions of the present invention include sulfur-containing D and L amino acids and their derivatives and salts, particularly the N-acetyl derivatives; thiol, hydrox acids (e.g., alpha-hydroxy acids such as lactic acid and glycolic acid and their derivatives and salts; or beta-hydroxy acids such as salicylic acid and salicylic acid salts and derivatives), urea, hyaluronic acid, phytic acid, lipoic acid; lysophosphatic acid, skin peel agents (e.g., phenol, resorcinol and the like), vitamin B3 compounds (e.g., niacinamide, nicotinic acid and nicotinic acid salts and esters, including non-vasodilating esters of nicotinic acid (such as tocopheryl nicotinate), nicotinyl amino acids, nicotin alcohol esters of carboxylic acids, nicotinic acid N-oxide and niacinamide N-oxide), vitamin B5 and retinoids (e.g., retinol, retinal, retinoic acid, retinyl acetate, retinyl palmitate, retinyl ascorbate). In the case of dry, scaly skin (xerosis) and ichthyosis such agents can alleviate the symptoms by temporary relief of itching associated with these conditions.

[0129] In one or more embodiments, the active agent is an anti-oxidant or a radical scavenger. Anti-oxidants/radical scavengers such as ascorbic acid (vitamin C) and its salts,
ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate, sodium ascorbyl phosphate, ascorbyl sorbate), tocopherol (vitamin E), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxybenzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, gallie acid and its alkyl esters, especially propyl gallate, uric acid and its salts and alkyl esters, sorbic acid and its salts, lipic acid, amines (e.g., N,N-diethyldihydroxyamine, amino-quinoline), sulfhydryl compounds (e.g., glutathione), dihydroxy furanic acid and its salts, lycine pidolate, arginine pidolate, nordihydroguaiaretic acid, biolavonoids, curcumin, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape skin/seed extracts, melainin, and rosemary extracts may be used.

[0130] It is further pointed out that polyunsaturated fatty acids, containing omega-3 and omega-6 fatty acids (e.g., linoleic and linolenic acid, gamma-linoleic acid (GLA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) are beneficial in the treatment of psoriasis and other skin inflammation conditions. Likewise, emollients and silicone oils exert moisture-retaining and skin protective effects on the skin. Thus, in a preferred embodiment, a skin protective foam is provided, wherein the hydrophobic carrier comprises in full or in part, an organic liquid selected from the group consisting of emollients, silicone oil and oils rich in unsaturated fatty acids.

[0131] In one or more embodiments, the active agent is a self-tanning active Agent, such as dihydroxyacetone.

[0132] According to another embodiment, the active agent comprises solid matter or particulate matter, i.e., material that is not soluble in the liquid carrier composition of the foamable composition. For definition purposes, solid matter shall mean material that is not soluble in the foamable composition more than 10% of the concentration intended to be included in said foamable composition. By way of example, the following classes of solid matter substances are presented: metallic oxides, such as titanium dioxide, zinc oxide, zirconium oxide, iron oxide; silicon containing materials such as silicone oxide and talc; carbon, for example in the form of amorphous carbon or graphite; insoluble oxidizing agents, such as benzoyl peroxide, calcium and magnesium hypochlorite; metallic Silver; cosmetic scrub materials, including, for example meals of strawberry seeds, raspberry seeds, apricot seeds, sweet almond, cranberry seeds; and pigments.

[0133] According to certain embodiments, the active agent is selected from the group of solvent, surface active agent, foam adjuvant and gelling agent, which are, on a case-by-case basis, known to possess a therapeutic benefit.

[0134] In one or more embodiments at least one or at least two active agents are included in the composition.

[0135] Composition and Foam Physical Characteristics and Advantages

[0136] A pharmaceutical or cosmetic composition manufactured using the foamable carrier of the present invention is very easy to use. When applied onto the afflicted body surface of mammals, i.e., humans or animals, it is in a foam state, allowing free application without spillage. Upon further application of a mechanical force, e.g., by rubbing the composition onto the body surface, it freely spreads on the surface and is rapidly absorbed.

[0137] The foamable composition can be in the state of (1) solutions; (2) a readily dispersable suspension; or (3) an emulsion. It is stable, having an acceptable shelf life of a year, or at least two years at ambient temperature, as revealed in accelerated stability tests. Polar solvents, hydrophobic carriers and propellants, which are a mixture of low molecular weight hydrocarbons, tend to impair the stability of emulsions and to interfere with the formation of a stable foam upon release from a pressurized container. It has been observed, however, that the foamable compositions according to the present invention are surprisingly stable. Following accelerated stability studies, they demonstrate desirable texture; they form fine bubble structures that do not break immediately upon contact with a surface, spread easily on the treated area and absorb quickly.

[0138] The composition should also be free flowing, to allow it to flow through the aperture of the container, e.g., and aerosol container, and create an acceptable foam. Compositions containing semi-solid hydrophobic solvents, e.g., white petrolatum, as the main ingredients of the oil phase of the emulsion, exhibit high viscosity and poor flowability and are inappropriate candidates for a foamable composition.

[0139] Foam quality can be graded as follows:

[0140] Grade E (excellent): very rich and creamy in appearance, does not show any bubble structure or shows a very fine (small) bubble structure; does not rapidly become dull; upon spreading on the skin, the foam retains the creaminess property and does not appear watery.

[0141] Grade G (good): rich and creamy in appearance, very small bubble size; “dulls” more rapidly than an excellent foam, retains creaminess upon spreading on the skin, and does not become watery.

[0142] Grade FG (fairly good): a moderate amount of creaminess noticeable, bubble structure is noticeable; upon spreading on the skin the product dulls rapidly and becomes somewhat lower in apparent viscosity.

[0143] Grade F (fair): very little creaminess noticeable, larger bubble structure than a “fairly good” foam, upon spreading on the skin it becomes thin in appearance and watery.

[0144] Grade P (poor): no creaminess noticeable, large bubble structure, and when spread on the skin it becomes very thin and watery in appearance.

[0145] Grade VP (very poor): dry foam, large very dull bubbles, difficult to spread on the skin.

[0146] Topically administrable foams are typically of quality grade E or G, when released from the aerosol container. Smaller bubbles are indicative of more stable foam, which does not collapse spontaneously immediately upon discharge from the container. The finer foam structure looks and feels smoother, thus increasing its usability and appeal.

[0147] As a further aspect of the foam is breakability. The breakable foam is thermally stable, yet breaks under shear force. Sheer-force breakability of the foam is clearly advantageous over thermally induced breakability. Thermally sensitive foams immediately collapse upon exposure to skin temperature and, therefore, cannot be applied on the hand and afterwards delivered to the afflicted area.

[0148] The foam of the present invention has several advantages, when compared with hydroalcoholic foam compositions, such as described in U.S. Pat. Nos. 6,126,920 and 5,783,220.

[0149] (1) Breakability. The foam of the present invention is thermally stable. Unlike hydroalcoholic foam compositions of the prior art, the foam of the present
invention is not “quick breaking”, i.e., it does not readily collapse upon exposure to body temperature environment. Sheer-force breakability of the foam is clearly advantageous over thermally induced breakability, since it allows comfortable application and well directed administration to the target area.

(0150) 2) Skin drying and skin barrier function. Polar solvents known to dry the skin and impair the integrity of the skin barrier. By contrast, combining a polar solvent and a hydrophobic carrier, as described herein, unwanted skin barrier damage is reduced, as demonstrated in tran-epidermal water loss measurements.

(0151) 3) Irritability. Due to the improvement in skin barrier function, skin irritability is corrected.

(0152) In terms of usability, the foamy composition is most advantageous, as revealed by clinical trials:

(0153) (i) Ease of application.

(0154) When foam is released it expands and allows easy spreading on the target area. This advantage is particularly meaningful in regards to the treatment of large skin surfaces.

(0155) Upon application, the foam readily spreads and absorbs into the skin.

(0156) (ii) The Foam is Drip-Free

(0157) The foam is not liquid and therefore does not leak when applied.

(0158) This allows precise application, without the product being spread on clothes or other parts of the body.

(0159) Another property of the foam is specific gravity, as measured upon release from the aerosol can. Typically, foams have specific gravity of less than 0.12 g/mL; or less than 0.08 g/mL, depending on their composition and on the propellant concentration.

(0160) For the purpose of the specification the external limits of the various ranges given are approximate as will be appreciated by those skilled in the art. Therefore, for the purpose of interpreting the outer limits of the range the limits shall be deemed to include up to a 20% leeway outside the range, preferably a 10% leeway.

(0161) Fields of Applications

(0162) According to one or more embodiments of the present invention, the foamy carrier and the foamy pharmaceutical or cosmetic composition of the present invention are intended for administration to an animal or a human subject. In one or more embodiments, the composition is intended to treat the skin, a body surface, a body cavity or a mucosal surface, e.g., the mucosa of the nose, mouth, eye, ear, respiratory system, vagina or rectum.

(0163) By including an appropriate active agent in the compositions of the present invention, the composition are useful in treating a patient having any one of a variety of dermatological disorders, which include inflammation as one or their etiological factors (also termed “dermatoses”), such as classified in a non-limiting exemplary manner according to the following groups:

(0164) Dermatitis including contact dermatitis, atopic dermatitis, seborrheic dermatitis, nummular dermatitis, chronic dermatitis of the hands and feet, generalized exfoliative dermatitis, stasis dermatitis; lichen simplex chronicus; diaper rash;

(0165) Bacterial infections including cellulitis, acute lymphangitis, lymphadenitis, erysipelas, cutaneous abscesses, necrotizing subcutaneous infections, staphylococcal scalded skin syndrome, folliculitis, furuncles, hidradenitis suppurativa, carbuncles, paronychial infections, and erythrasma;

(0166) Fungal Infections including dermatophyte infections, yeast Infections; parasitic Infections including scabies, pediculosis, creeping eruption;

(0167) Viral Infections;

(0168) Disorders of hair follicles and sebaceous glands including acne, rosacea, perioral dermatitis, hypertrichosis (hirsutism), alopecia, including male pattern baldness, alopecia areata, alopecia universalis and alopecia totalis; psuedofolliculitis barbae, keratogenous cyst;

(0169) Scaling papular diseases including psoriasis, pityriasis rosea, lichen planus, pityriasis rubra pilaris;

(0170) Benign tumors including moles, dysplastic nevi, skin tags, lipomas, angiomas, pyogenic granuloma, seborrheic keratoses, dermatofibroma, keratoacanthoma, keloid;

(0171) Malignant tumors including basal cell carcinoma, squamous cell carcinoma, malignant melanoma, paget’s disease of the nipples, kaposis’s sarcoma;

(0172) Reactions to sunlight, including sunburn, chronic effects of sunlight, photosensitivity;

(0173) Bullous diseases including pemphigus, bullous pemphigoid, deramitis herpetiformis, linear immunoglobulin A disease;

(0174) Pigmentation disorders including hypopigmentation such as vitiligo, albinism and postinflammatory hypopigmentation and hyperpigmentation such as melasma (chloasma), drug-induced hyperpigmentation, postinflammatory hyperpigmentation;

(0175) Disorders of cornification including ichthyosis, keratosis pilaris, calluses and corns, actinic keratosis;

(0176) Pressure sores, open wounds, chronic wounds, open ulcers and burns; Disorders of sweating; and

(0177) Inflammatory reactions including drug eruptions, toxic epidermal necrolysis, erythema multiforme, erythema nodosum, and granuloma annulare.

(0178) The same advantage is expected when the composition is topically applied to a body cavity or mucosal surfaces, including, but not limited to the cranial cavity, the thoracic cavity, the abdominal cavity, the ventral cavity, the vagina, the rectum and penile cavities, the urinary tract, the nasal cavity, the mouth, the eye, the ear the peritoneum, the large and small bowel, the caecum, bladder, and stomach, the cavity between the uterus and the fallopian tubes, the ovaries and other body areas, which may accept topically-applied products. The composition of the present invention is suitable to treat conditions of a body cavity and a mucosal membrane, such as post-surgical adhesions, chlamydia infection, gonorrhea infection, hepatitis B, herpes, HIV/AIDS, human papillomavirus (HPV), genital warts, bacterial vaginosis, candidiasis, chancroid, granuloma inguinale, lymphogranuloma venereum, mucopurulent cervicitis (MPC), molluscum contagiosum, nongonococcal urethritis (NGU), trichomoniasis, vulvar disorders, vulvodynia, vulvar pain, yeast infection, vulvar dys trophy, vulvar intraepithelial neoplasia (VIN), contact dermatitis, pelvic inflammation, endometritis, salpingitis, oophoritis, genital cancer, cancer of the cervix, cancer of the vulva, cancer of the vagina, vaginal dryness, dyspareunia, anal and rectal disease, anal abscess/fistula, anal cancer, anal fissure, anal warts, Crohn’s disease, hemorrhoids, anal itch, pruritus ani, fecal incontinence, constipation, polyps of the colon and rectum.
According to one or more embodiments of the present invention, the compositions are also useful in the therapy of non-dermatological disorders by providing transdermal or trans-mucosal delivery of an active agent that is effective against non-dermatological disorders.

In one or more embodiments, the disorder is a health abnormality that responds to treatment with a hormone. A typical example of such abnormality is sexual dysfunction in men and women whereby androgen therapy is successfully used to restore sexual function. Other non-limiting examples of disorders/medical indications that are in the scope of treatment with a hormone according to the present invention are androgen deficiency, estrogen deficiency, growth disorders, hypogonadism, cancer, vasomotor symptoms, menopausal disorders, vulvar and vaginal atrophy, urethritis, hypoestrogenism, osteoarthritis, osteoporosis, uterine bleeding, Hirsutism, Virilization, ovarian tumors, hypothalamic pituitary unit diseases, testicular tumors, prostate cancer, hypopituitarism, Klinefelter’s syndrome, testicular feminisation, orchitectomy, vasomotor symptoms (such as “hot flashes”) associated with the menopause, metabolic abnormalities and mood disturbances.

The following examples further exemplify the, foamable carrier, the pharmaceutical and cosmetic compositions of the present invention, methods for preparing the same, and therapeutic uses of the compositions. The examples are for the purposes of illustration only and are not intended to be limiting of the invention. Many variations may be carried out by one of ordinary skill in the art and are contemplated within the full scope of the present invention.

A general procedure for preparing foamable compositions is set out in WO 2004/037225 which is incorporated herein by reference. Moreover, with respect to using one or more polar solvents, the polar solvent is added to the aqueous phase mixture in the course of preparation.

Example 1—Foamable Carrier, Containing Polar Solvent (Dimethyl Isosorbide) and Hydrophobic Carrier (Caprylic/Capric Triglyceride)

<table>
<thead>
<tr>
<th></th>
<th>Foam A % w/w</th>
<th>Foam B % w/w</th>
<th>Foam C % w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprylic/capric triglyceride (Hydrophobic carrier)</td>
<td>30.0</td>
<td>19.0</td>
<td>40.0</td>
</tr>
<tr>
<td>Dimethyl isosorbide (Polar solvent)</td>
<td>20.0</td>
<td>20.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Glycerol oleate (Surfactant)</td>
<td>1.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>PPG-15 stearyl ether (Surfactant)</td>
<td>5.0</td>
<td>15.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Lecithin (Surfactant)</td>
<td>20.0</td>
<td>20.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Sorbitan stearate (Surfactant)</td>
<td>—</td>
<td>20.0</td>
<td>—</td>
</tr>
<tr>
<td>Sucrose stearate (Surfactant)</td>
<td>5.0</td>
<td>5.0</td>
<td>—</td>
</tr>
<tr>
<td>PVP K-90 (Polymeric agent)</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Preservative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propane/Butane (Propellant)</td>
<td>8.00</td>
<td>8.00</td>
<td>8.00</td>
</tr>
<tr>
<td>Purified water</td>
<td>to100.00</td>
<td>to100.00</td>
<td>to100.00</td>
</tr>
</tbody>
</table>

Example 2—Foamable Carrier, Containing Polar Solvent (Dimethyl Isosorbide and Propylene Glycol) and Hydrophobic Carrier (Caprylic/Capric Triglyceride and Isopropyl Myristate)

<table>
<thead>
<tr>
<th></th>
<th>Foam D % w/w</th>
<th>Foam E % w/w</th>
<th>Foam F % w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprylic/capric triglyceride (Hydrophobic carrier)</td>
<td>5.00</td>
<td>5.00</td>
<td>5.00</td>
</tr>
<tr>
<td>Isopropyl myristate (Hydrophobic carrier)</td>
<td>5.00</td>
<td>5.00</td>
<td>5.00</td>
</tr>
<tr>
<td>Dimethyl isosorbide (Polar solvent)</td>
<td>55.50</td>
<td>62.00</td>
<td>59.00</td>
</tr>
<tr>
<td>Propylene glycol (Polar solvent)</td>
<td>2.50</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Glyceryl monostearate (Surfactant)</td>
<td>—</td>
<td>1.00</td>
<td>1.60</td>
</tr>
<tr>
<td>Sorbitan monostearate (Surfactant)</td>
<td>8.00</td>
<td>5.00</td>
<td>8.00</td>
</tr>
<tr>
<td>Sucrose stearate (Surfactant)</td>
<td>5.00</td>
<td>5.00</td>
<td>8.00</td>
</tr>
<tr>
<td>Hydroxypropyl-cellulose (Polymeric agent)</td>
<td>—</td>
<td>0.50</td>
<td>—</td>
</tr>
<tr>
<td>Cetostearyl alcohol (Foam adjuvant)</td>
<td>8.00</td>
<td>8.00</td>
<td>—</td>
</tr>
<tr>
<td>Stearyl alcohol (Foam adjuvant)</td>
<td>—</td>
<td>—</td>
<td>5.00</td>
</tr>
<tr>
<td>Oleyl alcohol (Foam adjuvant)</td>
<td>2.50</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Preservative</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Propane/Butane (Propellant)</td>
<td>8.00</td>
<td>8.00</td>
<td>8.00</td>
</tr>
<tr>
<td>Purified water</td>
<td>to100.00</td>
<td>to100.00</td>
<td>to100.00</td>
</tr>
</tbody>
</table>

Example 3—Foamable Carrier, in the Form of Emulsion, Containing Polar Solvent (Diethyl Isosorbide) and Hydrophobic Carrier (Caprylic/Capric Triglyceride)

<table>
<thead>
<tr>
<th></th>
<th>Foam G % w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caprylic/capric triglyceride (Hydrophobic carrier)</td>
<td>30.00</td>
</tr>
<tr>
<td>Dimethyl isosorbide (Polar solvent)</td>
<td>20.00</td>
</tr>
</tbody>
</table>
Example 4—Foamable Carrier, in the Form of Emulsion, Containing Polar Solvent (Ethanol) and Hydrophobic Carrier (Caprylic/Capric Triglyceride)

Example 5—Non-Flammable Foamable Carriers

Example 6—Inflammability Test

The following compositions were tested for inflammability according to European Standard prEN 14851: (1) Foam F; (2) Foam I; (3) Foam J; and (4) Foam K.

Procedure: Approximately 5 g of foam, mousse gel or paste is sprayed from the aerosol container on to a watchglass. An ignition source (a lighter) was placed at the base of the watchglass and any ignition and sustained combustion of the foam, mousse, gel or paste was observed. The test was carried out in a draught-free environment capable of ventilation, with the temperature controlled at 20°C ± 5°C and relative humidity in the range of 30% to 80%.

According to the standard, appearance of a stable flame which is at least 4 cm high and which is maintained for at least 2 seconds defines a product as “inflammable”.

Results:

[0190] Foam F and Foam I were found “inflammable”.

[0191] Foam J and Foam K were found “non-flammable”.

Example 7

Exemplary concentrations of active agents in foamable compositions are set out in Table 2. Each active agent is added into, for example, any of the carriers listed in any of Examples 1 to 5 above in a therapeutically effective concentration and amount. The methodology of addition is well known to those of the art. The composition is adjusted in each case so that it is made up to 100% w/w as appropriate by purified water.

### TABLE 2

<table>
<thead>
<tr>
<th>Class</th>
<th>Concentration</th>
<th>Exemplary Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone acetate</td>
<td>3%</td>
<td>Steroid responsive inflammation and psoriasis or atopic dermatitis</td>
</tr>
<tr>
<td>Betamethasone valerate</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td>Chlorinated propionate</td>
<td>0.05%</td>
<td></td>
</tr>
<tr>
<td>Acyclovir</td>
<td>5%</td>
<td>Viral infection, herpes</td>
</tr>
<tr>
<td>Ciclopirox</td>
<td>1%</td>
<td>Fungal infection, seborrhoea, dandruff,</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>2%</td>
<td>Bacterial infection, acne, rosacea,</td>
</tr>
<tr>
<td>Azelaic acid</td>
<td>15%</td>
<td>Acne, rosacea, pigmentation disorder and various dermatoses</td>
</tr>
</tbody>
</table>

Mineral oil (Hydrophobic carrier) 4.32
Isopropyl myristate (Hydrophobic carrier) 4.32
Ethanol (Polar solvent) 20.00
Glyceryl monostearate (Surfactant) 0.36
Polysorbate 80 (Surfactant) 0.72
PG-40 stearate (Surfactant) 2.16
Xanthan gum (Polymeric agent) 0.22
Hydroxypropyl methylcellulose (Polymeric agent) 0.22
Stearyl alcohol (Foam adjuvant) 0.72
Preservative 0.50
1,1,1,2-tetrafluoroethane (Dymel 134) 8.00
Purified water to100.00
TABLE 2-continued

<table>
<thead>
<tr>
<th>Class</th>
<th>Concentration</th>
<th>Exemplary Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>0.25%-2%</td>
<td>- R. nosocomial, bacterial infections and parasite infestations</td>
</tr>
<tr>
<td>Doxiflucan</td>
<td>1%</td>
<td>- Osteoarthropathies, joint pain</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>0.2%</td>
<td>- Atopic dermatitis, eczema and inflammation</td>
</tr>
</tbody>
</table>

[0193] The above examples represent different drug classes and it is to be understood that other drugs belonging to each of the classes represented above may be included and used in the compositions of the present invention in a safe and effective amount.

51. A foamy pharmaceutical composition comprising:

(a) an emulsion comprising:

(i) an organic carrier at a concentration of 10% to 70% by weight of the composition, wherein the organic carrier comprises:

a) a hydrophobic solvent comprising caprylic/capric triglyceride, isopropyl myristate, and/or mineral oil;

b) a polar solvent comprising dimethyl isosorbide and/or a short chain alcohol;

(ii) a surfactant;

(iii) a foam adjuvant at a concentration of about 0.01% to 5% by weight of the composition;

(iv) a polymeric agent at a concentration of about 0.01% to 5% by weight of the composition; and

(v) water;

(b) a liquefied or compressed gas propellant at a concentration of about 3% to 25% by weight of the composition; and

wherein the composition is provided in an aerosol container and upon release from the container, the composition forms a breakable foam.

52. The composition of claim 51, wherein the short chain alcohol comprises ethanol.

53. The composition of claim 51, wherein the short chain alcohol comprises ethanol.

54. The composition of claim 52, wherein the polar solvent comprises ethanol at a concentration of about 15% to about 20% by weight of the composition.

55. The composition of claim 53, wherein the polar solvent comprises ethanol at a concentration of about 15% to about 20% by weight of the composition.

56. The composition of claim 52, wherein the polar solvent comprises dimethyl isosorbide at a concentration of about 20% by weight of the composition.

57. The composition of claim 53, wherein the hydrophobic solvent is at a concentration of about 5% to about 30% by weight of the composition.

58. The composition of claim 53, wherein the emulsion further comprises an emollient.

59. The composition of claim 53, wherein the emulsion further comprises a preservative.

60. The composition of claim 53, wherein the surfactant is at a concentration of about 0.1% to about 5% by weight of the composition.

61. The composition of claim 53, wherein the surfactant comprises a non-ionic surfactant and an ionic surfactant, and wherein the ratio of the non-ionic surfactant to the ionic surfactant is greater than 6:1.

62. The composition of claim 53, wherein the surfactant is selected from the group consisting of glyceryl monostearate, sorbitan stearate, polysorbate 80, PEG-40 stearate, and a mixture of two or more thereof.

63. The composition of claim 53, wherein the foam adjuvant is at a concentration of about 0.01% to about 1% by weight of the composition.

64. The composition of claim 53, wherein the foam adjuvant comprises a fatty alcohol having 15 or more carbons in its carbon chain; a fatty acid having 16 or more carbons in its carbon chain; a fatty alcohol derived from beeswax; a mixture of alcohols, a majority of which has at least 20 carbon atoms in their carbon chain; a fatty alcohol having a double bond; a fatty acid having a double bond; a branched fatty alcohol; a branched fatty acid; a fatty acid substituted with a hydroxyl group; and a mixture of two or more thereof.

65. The composition of claim 64, wherein the fatty alcohol having 16 or more carbons in its carbon chain comprises stearyl alcohol.

66. The composition of claim 53, wherein the polymeric agent is selected from a biodegradable agent, a gelling agent, a film forming agent, and a phase change agent.

67. The composition of claim 53, wherein the polymeric agent is selected from the group consisting of a locust bean gum, sodium caseinate, an egg albumin, a gelatin agar, a carrageenan gum, sodium alginate, a xanthan gum, a quince seed extract, a tragacanth gum, a guar gum, a starch, a chemically modified starch, a cellulose ether, an alkyl cellulose, a hydroxyalkyl cellulose, a hydroxyethyl cellulose, a hydroxypropyl cellulose, a methyl cellulose, a carboxymethyl cellulose, a methylhydroxyethylcellulose, a methylhydroxypropylcellulose, a hydroxypropyl methylcellulose, a hydroxyethylcarboxymethylcellulose, a carboxyalkylhydroxyethylcellulose, a hydroxypropyl guar gum, a soluble starch, a carboxymethyl polymer, a polyvinylpyrrolidone, a polyvinyl alcohol, a polyacrylamid acid polymer, a polyacrylic acid polymer, a polyvinyl acetate polymer, a polyvinyl chloride polymer, a polyvinylidene chloride polymer, an acrylic acid/ethyl acrylate copolymer, a carboxyvinyl polymer, a silicone dioxide, a poly(acrylamid acid), a poly(methylvinyl ether/maleic anhydride) copolymer, a chitosan, an alginic acid, a hyaluronic acid, a pectin, a karaya gum, a cyclodextrin, a chemically modified cyclodextrin, a hydroxypropyl-3-cyclodextrin, a poly(N-isopropylamide), a poloxamer, and a mixture of any two or more thereof.

68. The composition of claim 53, wherein the liquefied or compressed gas propellant comprises propane and/or butane.

69. The composition of claim 53, wherein:

(a) the emulsion comprises:

(i) a hydrophobic solvent comprising caprylic/capric triglyceride at a concentration of about 30% by weight of the composition;

(ii) a polar solvent comprising dimethyl isosorbide at a concentration of about 20% by weight of the composition;

(iii) a surfactant comprising glyceryl monostearate and sorbitan stearate at a combined concentration of about 4% by weight of the composition;

(iv) a foam adjuvant comprising stearyl alcohol at a concentration of about 1% by weight of the composition;
(v) a polymeric agent comprising xanthan gum and hydroxypropyl methylcellulose at a combined concentration of about 0.3% by weight of the composition; and
(vi) water;
(b) a liquefied or compressed gas propellant comprising propane and butane at a concentration of about 8% by weight of the composition.

70. The composition of claim 53, wherein:
(a) the emulsion comprises:
   (i) a hydrophobic solvent comprising mineral oil and isopropyl myristate at a combined concentration of about 9.24% by weight of the composition;
   (ii) a polar solvent comprising ethanol at a concentration of about 15% by weight of the composition;
   (iii) a surfactant comprising glyceryl monostearate, polysorbate 80, and PEG-40 stearate at a combined concentration of about 3.37% by weight of the composition;
   (iv) a foam adjuvant comprising stearyl alcohol at a concentration of about 0.77% by weight of the composition;
   (v) a polymeric agent comprising xanthan gum and hydroxypropyl methylcellulose at a combined concentration of about 0.46% by weight of the composition; and
   (vi) water;
(b) a liquefied or compressed gas propellant comprising propane and butane at a concentration of about 8% by weight of the composition.

71. The composition of claim 53, wherein:
(a) the emulsion comprises:
   (i) a hydrophobic solvent comprising mineral oil and isopropyl myristate at a combined concentration of about 8.64% by weight of the composition;
   (ii) a polar solvent comprising ethanol at a concentration of about 20% by weight of the composition;
   (iii) a surfactant comprising glyceryl monostearate, polysorbate 80, and PEG-40 stearate at a combined concentration of about 3.24% by weight of the composition;
   (iv) a foam adjuvant comprising stearyl alcohol at a concentration of about 0.72% by weight of the composition;
   (v) a polymeric agent comprising xanthan gum and hydroxypropyl methylcellulose at a combined concentration of about 0.44% by weight of the composition; and
   (vi) water;
(b) a liquefied or compressed gas propellant comprising propane and butane at a concentration of about 8% by weight of the composition.

72. The composition of claim 53, wherein the breakable foam has a density of about 0.04 g/mL to about 0.12 g/mL.

73. The composition of claim 53, wherein the weight ratio between the polar solvent and the hydrophobic solvent is between about 1:4 and about 4:1.

74. The composition of claim 53, wherein the emulsion further comprises an active agent.

75. A method of treating, alleviating, or preventing a disorder, comprising topically administering a breakable foam produced from the composition of claim 74.

76. The method of claim 75, wherein the disorder is a steroid-responsive inflammation, a viral infection, a fungal infection, a bacterial infection, a parasite infestation, a pigment disorder, a dermatosis, psoriasis, atopic dermatitis, herpes, seborrhea, dandruff, acne, rosacea, osteoarthritis, a joint pain, or eczema.

77. The method of claim 75, wherein the active agent is hydrocortisone acetate, betamethasone valerate, clobetasol propionate, acyclovir, ciclopirox, clindomycin, azelaic acid, metronidazole, diclofenac, or tacrolimus.

* * * * *