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(54) **COSMETIC AND PHARMACEUTICAL FOAM**

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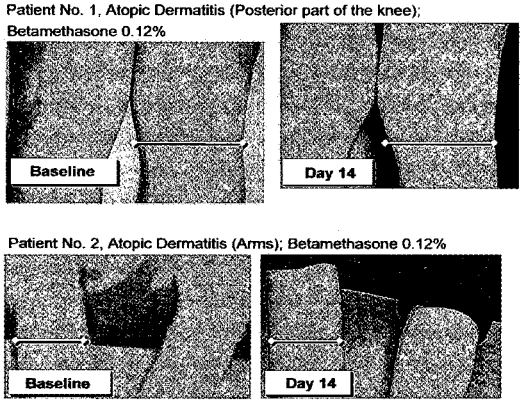
(57) **ABSTRACT**

The invention relates to uses of an alcohol-free cosmetic or pharmaceutical foam carrier comprising water, a hydrophobic solvent, a foam adjuvant agent, a surface-active agent and a water gelling agent as a flame retardant or flame resistant foam. The hydrophobic solvent is preferably mineral oil; medium chain triglycerides; isopropyl myristearate or octyl dodecanol, silicone oil or vegetable oil or mixtures thereof. The cosmetic or pharmaceutical foam carrier does not contain aliphatic alcohols, also making it non-irritating and non-drying. The alcohol-free foam carrier is suitable for inclusion of both water-soluble and oil-soluble pharmaceutical and cosmetic agents.

Picture No. 2:
Improvement in the treatment of atopic dermatitis, using Bethasone 0.12% foam



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A61K 47/06	(2006.01)
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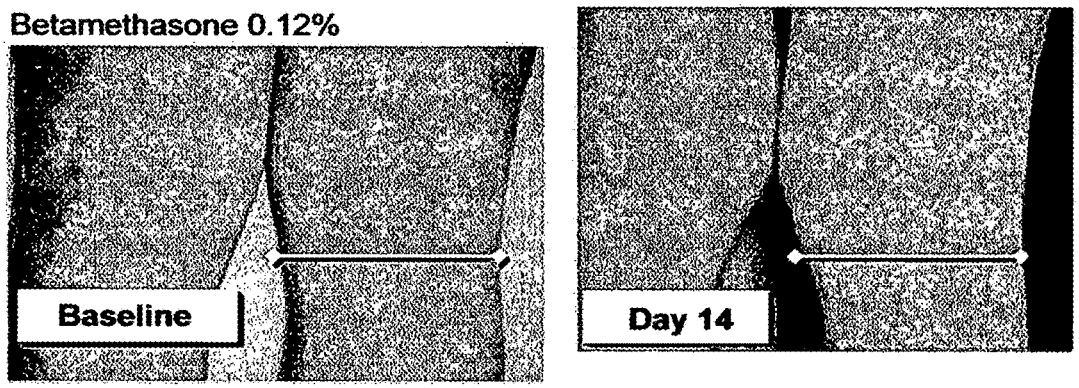
Picture No. 2:
Improvement in the treatment of atopic dermatitis, using Bethasone 0.12% foam

Patient No. 1, Atopic Dermatitis (Posterior part of the knee);
Betamethasone 0.12%



Patient No. 2, Atopic Dermatitis (Arms); Betamethasone 0.12%

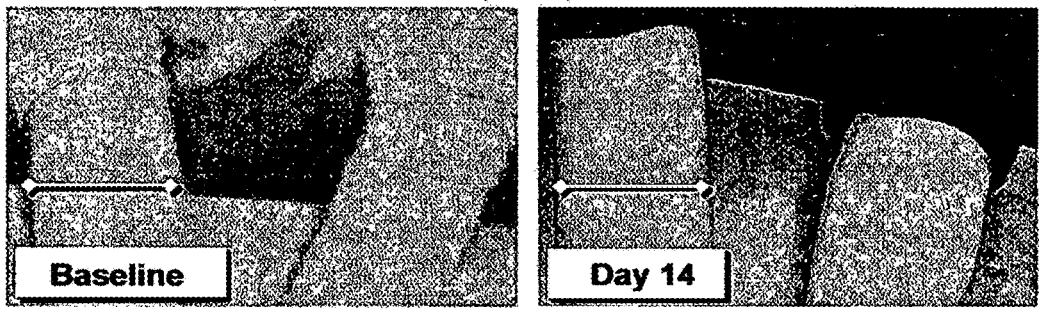


FIG. 1

Picture No. 1:
Improvement in the treatment of psoriasis, using Bethasone 0.12% foam

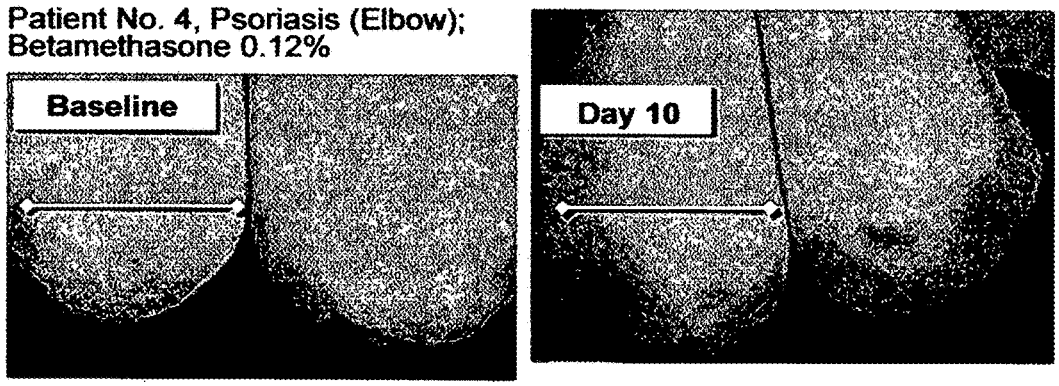


FIG. 2

COSMETIC AND PHARMACEUTICAL FOAM

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is a continuation-in-part application of co-pending U.S. patent application Ser. No. 10/532,618, filed Dec. 22, 2005, entitled "Cosmetic and Pharmaceutical Foam" which is a 371 of PCT Application No. PCT/IB/05527, filed on Oct. 24, 2003, which claims priority to both Israeli Patent Application No. 152486, filed Oct. 25, 2002, entitled "Alcohol-free Cosmetic and Pharmaceutical Foam Carrier" and U.S. Provisional Patent Application No. 60/429,546, filed Nov. 29, 2002, entitled "Cosmetic and Pharmaceutical Foam," all of which are incorporated herein in their entirety.

FIELD OF THE INVENTION

[0002] The invention relates to an alcohol-free, cosmetic or pharmaceutical foam carrier and its use. More specifically, the invention relates to a cosmetic or pharmaceutical foam carrier suitable for inclusion of both water soluble and oil soluble pharmaceutical and cosmetic agents.

BACKGROUND OF THE INVENTION

[0003] External topical administration is an important route for the administration of drugs in disease treatment. In external topical administration, the drug is absorbed into and/or through skin, mucous membrane or wound tissue. Many groups of drugs, including, for example, antibiotic, anti-fungal, anti-inflammatory, anesthetic, analgesic, anti-allergic, corticosteroid, retinoid and anti-proliferative medications are preferably administered in hydrophobic media, e.g. ointments or oils. However, due to the undesirable consistency of these hydrophobic carriers, their use is limited. For instance, ointments containing white petrolatum, e.g., Vaseline petroleum jelly, as the carrier often form an impermeable barrier, so that metabolic products and excreta from the wounds to which they are applied are not easily removed or drained away. Furthermore, it is difficult for the active drug dissolved in the carrier to pass through the white petrolatum barrier layer into the wound tissue, so the efficacy of the drug is reduced.

[0004] In addition, ointments and creams often do not create an environment for promoting respiration of the wound tissue and it is not favorable to the normal respiration of the skin. An additional disadvantage of petroleum jelly-based products relates to the greasy feeling left following their topical application onto the skin, mucosal membranes and wounds. Besides petroleum jelly, hydrophobic pharmaceutical carriers now in use include liquid paraffin, lanolin, beeswax, vegetable oil, glycerin monostearate, higher alcohols, polyethylene glycol and some emulsifying agents, which also have undesirable flow properties and skin feel.

[0005] Several hydrophobic liquid and semi-solid oils, e.g., mono- and poly-unsaturated oils from vegetable and marine sources, mineral oils, silicone oils, and liquid hydrophobic plant-derived oils, are known for their therapeutic benefits when applied topically, yet, their application in liquid form is not practical. Oils can also contain essential nutritional constituents, such as oil-soluble vitamins (e.g., vitamin A and vitamin E), minerals and other therapeutically beneficial constituents. Another class of therapeutic oils includes mineral and silicon oils useful for the treatment of skin dehydration and other medical disorders, which oils are liquid at ambient temperature. Such therapeutic oils unfortunately, cannot be applied by users in amounts sufficient to exert therapeutic affects because they typically are liquid at use temperatures.

[0006] Other pharmaceutical active ingredients are water-soluble and require a water component in the carrier.

[0007] While semi-solid cosmetic and pharmaceutical formulations, such as creams, lotions, gels and ointments are commonly used by consumers, new forms are desirable, in order to achieve better control of the application, while maintaining or bestowing the skin beneficial properties of such products. Thus, the development of a new composition, having breakable foam consistency when extruded out of a container and liquid properties when applied onto the skin is advantageous. Ideally a foam should contain hydrophobic substances (solvents), which can act as emollients and provide the skin with soothing and nourishing properties. However, such hydrophobic solvents are difficult to formulate into a lather-producing or foam-producing product because the hydrophobic solvents interfere with the lather forming ability of the surfactant. Furthermore, addition of oils and other emollients to topical formulations can result in an unpleasant or annoying skin residue.

[0008] Use of emulsions in foam compositions is known. Emulsion systems provide a two-phase system including lipophilic or hydrophobic components in one phase and hydrophilic components in the second phase. The foamed emulsion typically is an oil-in-water emulsion in which the hydrophobic component is dispersed in the aqueous continuous phase. Surfactants for reducing surface tension and emulsifiers for improving foam stability are included in the foam composition.

[0009] Foams and, in particular, foam emulsions are complicated systems which do not form under all circumstances. Slight shifts in foam emulsion composition, such as by the addition of active ingredients, may destabilize the foam. Furthermore, many emulsions do not provide the high foam capacity, foam stability and/or fast-breaking action under stress or temperatures that are desired in a topical foam composition.

[0010] A particularly desirable type of oil-containing foam is such wherein all or part of the oil phase comprises silicone oil. Silicone oil is known for its skin protective features and its incorporation in topical products is beneficial. However, it is not obvious to produce silicone oil-based foams, since many silicone oils possess anti-foaming properties.

[0011] U.S. Pat. No. 6,126,920 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. U.S. Pat. No. 6,126,920 is typical of many compositions that use aliphatic alcohols in the foam composition. The alcohol promotes fast drying and thereby attempts to address 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 defatting agents and may cause skin to become dry and cracked. Hence, the presence of aliphatic alcohol in a therapeutic foam for external topical administration as taught in U.S. Pat. No. 6,126,920 is undesirable.

[0012] U.S. Pat. No. 5,536,743 to Borgman describes a buffered non-flowing composition suitable for the treatment of bacterial vaginosis which contains metronidazole. Suitable formulations include oil-in-water emulsions including an internal oil phase of about 10-40 wt % oil and anionic, cationic or nonionic surfactants. Suitable components of the oleaginous phase include long chain alcohols, esters, and acids, vegetable and animal oils and waxes. No other stabilizing agents are disclosed for use in foam aerosol compositions.

[0013] EP Patent No. 0598412 describes a composition that is useful for skin protection against drying and harsh environmental substances. The protection is derived from the inclusion of poly(tetrafluoroethylene) (PTFE) in the composition. The composition includes low levels of both hydrophilic emollients and hydrophobic emollients. The compositions include high levels of surfactants, including ionic surfactants, and co-emulsifiers resulting in thick emulsions which are not flowable, and thus providing products which are inefficient foamers (or non-foaming) and too thick for spreading over large skin areas.

[0014] U.S. Pat. No. 6,423,323 describes an aqueous foam emulsion. The composition includes a hydrophobic phase including fatty acids, emulsifiers and co-emulsifiers, and an aqueous phase containing hydrophilic moisturizers and emulsifiers. An optional ingredient according to U.S. Pat. No. 6,423,323 is one or more refatting substances, in preferable concentrations of 0.5 to 2%, if the product is to be used for normal skin; and 3 to 6% for dry skin. Addition of high levels of co-emulsifiers such as fatty alcohols and fatty acids suggest that the foam is not stable. No other stabilizing agents are disclosed.

[0015] U.S. Pat. No. 5,635,469 describes a foamable cleansing liquid composition comprising about 0.05% to about 10% of an emollient, in addition to cleansing surfactants, humectants and water soluble cationic or nonionic polymers, but no propellants. Low density foams are achieved using a novel non-aerosol foam dispenser. The foaming is achieved by operating a manual pump, which is not convenient for operation. Emollients and humectants are included to improve the level of hydration and/or lipid content of the skin. However, the patent notes that emollients and humectants interfere with the lather forming ability of the surfactant.

[0016] U.S. Pat. No. 6,113,888 teaches a single water phase composition comprising a self-tanning agent, a nitrogen-free polymer, a nitrogen-free surfactant, and water.

[0017] U.S. Pat. No. 5,679,324 to Lisboa pertains to an aerosol foamable fragrance composition, translucent in its pre-dispensed state, which forms a fast breaking foam. Apparently the foam breaks spontaneously upon discharging from an aerosol container (with no need of any rubbing or sheer force application), thus, making is impractical for spreading over a skin surface. The composition contains surfactant, a propellant, a fragrance, a thickener, and a cosmetic vehicle (preferably water) wherein the ratio of the surfactant to propellant is from about 1:1 to about 1:10. Emollients including silicone oils, mineral oils and hydrocarbon oils may be included.

[0018] U.S. Pat. No. 6,251,369 discloses foamable dental fluoride compositions containing a water-soluble fluoride component, whereby said compositions include an oil in water emulsion. However, the patent fails to specify the identity or concentration of the oil component of the emulsion; and none of the compositions presented in the examples contain any oil component.

[0019] U.S. Pat. No. 5,961,957 describes a barrier foam composition comprising from 70 to 90% of water, from 7 to 9% of butane, from 2 to 4% of glyceryl monostearate, from 1.5 to 3.50% of dimethicone copolyol (a water-soluble silicone compound), from 1 to 3% of propane, from 0.5 to 2.5% of lanolin, from 0.5 to 2.5% of stearic acid and from 0.05 to 1.05% of at least one of methylchloroisothiazolinone and methylisothiazolinone.

[0020] U.S. Patent Publication No. 2006/238646 B1 discloses aqueous aerosol compositions for delivery of atomized oil as an atomised spray where the propellant is water soluble. The water based system is described as non-flammable. No foam is taught or exemplified.

[0021] U.S. Pat. No. 3,419,658 describes nonaqueous aerosol foams containing mineral oil and suggests using non-flammable propellants because of their lack of flammability.

[0022] U.S. Pat. No. 2,524,590 discloses an atomized oil emulsion spray with an emulsifying agent that preferably tends to suppress foam formation or is not foam forming. The gas stream is said to be practically non-inflammable due to presence of water particles and vapour in stream. The patent teaches away from foam formation.

[0023] Foams are considered a more convenient vehicle for topical delivery of active agents. There are several types of topical foams, including aqueous foams, such as commonly available shaving foams; hydroalcoholic foams, such as described in U.S. Pat. No. 6,126,920; emulsion-based foams, comprising oil and water components, such as described in U.S. Pat. No. 6,730,288 and PCT Application No. WO 2004/037225; and oleaginous foams, which consist of high oil content, such as described in US Patent Publication No. US 2005/0031547. In skin therapy, oil containing foams are preferred, since oil contribute to skin protection and moisturization, which improve the therapeutic effect of the formulation. Typically foams are made using liquefied hydrocarbon gas propellant, such a spropane, butane and isobutane, which are inflammable. The combination of the oil component of an oil-containing foam and a hydrocarbon propellant results in a foam that is typically inflammable. In several countries inflammable foams cannot be used, and in Europe there is a formal standard, namely European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test" which defines criteria to assess the inflammability of foam products.

[0024] One approach to avoid this problem is to use alternative halogenated propellants, such as chloro-fluoro carbons (CFCs) and hydrofluorocarbon (HFC) propellants; however, CFCs are know as ozone-depleting propellants and HFCs are expensive, making their use impractical in the case of consumer products and drugs.

[0025] A few dermatological foam products are available on the market.

[0026] Olux™ Foam, produced by Connetics, Inc., contains clobetasol propionate. Each gram of Olux™ Foam contains 0.5 mg clobetasol propionate, USP, in a thermolabile 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). Luxig™ is another corticostroid foam medication, containing 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.

[0027] Cortifoam, a hydrocortisone acetate rectal foam is produced by Schwartz Pharma GmbH, wherein the hydrocortisone is present at 10% in a foam vehicle. Nonmedicinal ingredients of Cortifoam include cetyl alcohol, ethoxylated stearyl alcohol, methylparaben, polyoxyethylene-10 stearyl ether, propylene glycol, propylparaben, triethanolamine, water, and inert propellants, isobutene, and propane.

[0028] Thus, foam compositions for topical treatment, containing higher concentrations of oils, but which do not comprise alcohol are still desirable. Foam compositions that are robust and suitable for inclusion of a wide range of active ingredients are desired. Furthermore, foam compositions for topical treatment containing oils and particularly higher concentrations of oils, which are flame retardant are desirable.

SUMMARY OF THE INVENTION

[0029] Despite the commonly known fact that hydrophobic solvents are difficult to formulate into a lather-producing or foam-producing product and that addition of conventional hydrophobic solvents interferes with the lather forming ability of the surfactant, we have surprisingly discovered a series of foamable carrier compositions, which, upon admixing with a liquefied gas propellant in an aerosol container, produces a foamable composition that is suitable for topical administration. Upon discharge from an aerosol container, the composition forms a breakable foam, which is rich and creamy in appearance, and show very fine bubble structure. The foam does not break down immediately upon discharge, however, it collapses to spread easily onto a skin area upon slight rubbing.

[0030] In one or more embodiments of the present invention, the alcohol-free cosmetic or pharmaceutical foamable carrier composition includes water, a liquid, non-volatile hydrophobic solvent, a foam adjuvant agent selected from the group consisting of fatty acids and fatty alcohols, a surface-active agent and a water gelling agent. Such foamable carriers, when placed in an aerosol container and combined with a liquefied gas propellant, create an oil in water emulsion, which, upon release from the aerosol container, provides a therapeutically beneficial foam product. The foam retains its structure for a time sufficient for a user to apply and to rub the foam into the skin. The foam has a very low yield strength and, hence, it breaks upon touch and makes rubbing easy and efficient, and its application even.

[0031] In one or more embodiments of the present invention, the foamable carrier composition the hydrophobic solvent content is about 2-5% and has a composition as follows:

[0032] Class A Composition:

- **[0033]** about 2-5% hydrophobic solvent;
- **[0034]** about 80-98% water;
- **[0035]** about 0.1% to 5% foam adjuvant agent;
- **[0036]** about 0.1% to 5% surface-active agent; and
- **[0037]** about 0.1% to 5% water gelling agent.

[0038] In one or more embodiments of the present invention, the foamable composition the hydrophobic solvent content is about 5-10% and has a composition as follows:

[0039] Class B Composition:

- **[0040]** about 5-10% hydrophobic solvent;
- **[0041]** about 75-95% water;
- **[0042]** about 0.1% to 5% foam adjuvant agent;
- **[0043]** about 0.1% to 5% surface-active agent; and
- **[0044]** about 0.1% to 5% water gelling agent.

[0045] In one or more embodiments of the present invention, the foamable composition the hydrophobic solvent content is about 10-20% and has a composition as follows:

[0046] Class C Composition:

- **[0047]** about 10-20% hydrophobic solvent;
- **[0048]** about 60-90% water;
- **[0049]** about 0.1% to 5% foam adjuvant agent;
- **[0050]** about 0.1% to 5% surface-active agent; and
- **[0051]** about 0.1% to 5% water gelling agent.

[0052] In one or more embodiments of the present invention, the foamable composition the hydrophobic solvent content is about 20-75% and has a composition as follows:

[0053] Class D Composition:

- **[0054]** about 20-75% hydrophobic solvent;
- **[0055]** about 25-75% water;
- **[0056]** about 0.1% to 5% foam adjuvant agent;
- **[0057]** about 0.1% to 5% surface-active agent; and
- **[0058]** about 0.1% to 5% water gelling agent.

[0059] All % values are provided on a weight (w/w) basis, based on the composition without propellant (unless otherwise specified).

[0060] The cosmetic or pharmaceutical foamable carrier composition is liquid. The foamable of the present invention does not contain short chain aliphatic alcohols, making it non-irritating and non-drying. Alcohols penetrate the skin's protective barrier and break down the intercellular matrix. In a recent publication by the American Academy of Dermatology (AAD), titled "Facing the Facts about Skin Care Products" it is stated "[i]ndividuals with dry skin should avoid astringents and any product with alcohol because they easily strip away moisture from the skin" (see: www.aad.org/PressReleases FacingFacts.html). Another AAD publication, titled "Sensitive About Your Skin?" recommends to "[a]void solvents that penetrate the skin including propylene glycol and ethanol" (see:www.aad.org/PressReleases/sensitive.html).

[0061] The alcohol-free foam carrier is formulated as an oil-in-water or water-in-oil emulsion, so that it is suitable for inclusion of either water-soluble and oil soluble active agents (or both). The foamable carrier composition of the present invention, when admixed with a propellant substance in an amount of about 5-25% by weight of the total composition in an aerosol container, produces lightweight breakable foam, suitable for facile application onto the skin, and other body areas, which may accept topically-applied products. Since the propellant, in the pressurized container is in liquid state, upon admixing the foamable carrier composition with the propellant, a stable emulsion, comprising the oil and the propellant (jointly as the "oil phase" component of such emulsion) is formed.

[0062] In one or more embodiments of the present invention, an alcohol-free cosmetic or pharmaceutical product is provided. The product includes a foam carrier composition according to one or more embodiments of the present invention and an active cosmetic or pharmaceutical ingredient in a therapeutically effective concentration. Cosmetic and pharmaceutical agents can be included in each of the compositions described above and in the detailed description that follows. Pharmaceutical products are intended for topical treatment of human and animal skin disorders, or any

other disorder, that requires topical application of a drug. Cosmetic products are intended for beautifying the skin and improving its appearance.

[0063] Cosmetic and medical disorders that are best treated using the alcohol-free foam carrier and the alcohol-free cosmetic or pharmaceutical product are identified, and the advantages of such carrier and products is demonstrated as compared to currently available options.

[0064] The foam of the present invention is advantageous to current options, for one or more of the following reasons:

[0065] (1) The foam is lightweight and thus, economical;

[0066] (2) The foam contains a hydrophobic solvent, in any desirable concentration, which provides a refatting and skin soothing effect, as well as a carrier for hydrophobic active agents;

[0067] (3) The foam contains silicone oil in a therapeutically effective concentration;

[0068] (4) The foam includes active agent, both water soluble and oil soluble;

[0069] (5) The foam is easily spreadable, allowing treatment of large areas such as the arms, back, legs and the breast;

[0070] (6) Due to its flow properties, it spreads effectively into folds and wrinkles, providing uniform distribution of the active agent without the need of extensive rubbing and absorbs into the skin; and

[0071] (7) In certain formulations the foam is flame retardant or flame resistant and in certain more specific embodiments it does not ignite.

[0072] Certain emulsions of the present invention surprisingly display the additional inherent property of being flame retardant or resistant, although the propellant is itself highly flammable. As the foamed composition according to one or more embodiments may spread over large surface areas, the attributes of flame retardancy or flame resistant is particularly desirable.

[0073] In one or more embodiments of the present invention, foamable carrier composition comprises:

[0074] about 2% to about 75% by weight hydrophobic solvent, said hydrophobic solvent comprising at least one of mineral oil, MCT oil, isopropyl oil, octyl dodecanol silicone oil and vegetable oil;

[0075] about 25 to about 98% by weight water;

[0076] about 0.1% to about 5% by weight foam adjuvant agent;

[0077] about 0.1% to about 5% by weight surface-active agent;

[0078] about 0.1% to about 5% by weight water gelling agent; and

[0079] a liquefied or compressed gas propellant, wherein the resultant foam is non-flammable, flame retardant or flame resistant.

[0080] In certain embodiments of the present invention, the foamable carrier composition is flame retardant or resistant. More specifically, flame retardant, flame resistant or non-flammable carrier compositions include a hydrophobic solvent comprising at least one of mineral oil, medium chain triglyceride (MCT) oil, isopropyl myristate, octyl dodecanol, silicone oil and soybean oil. Mineral oil, particularly light mineral oil is classified by manufacturers as a combustible material, Surprisingly, foamable compositions containing substantial amounts of mineral oil provide a foam foam with flame resistant or retardant properties without using non flammble propellants. Moreover it is effective even at high concentrations when there is phase reversal where the emulsion transitions form an oil in water emulsion to a water in oil emulsion.

[0081] Vegetable oil, particularly soybean oil is classified by manufacturers as a combustible material, Soybean oil is used in candles. Surprisingly, foamable compositions containing substantial amounts of soybean oil provide a foam with flame resistant or retardant properties without using non flammble propellants. Moreover it is effective even at higher concentrations.

[0082] Medium chain triglycerides (MCT's) also classified by manufacturers as combustible materials, provide the resultant foam with flame resistant or retardant properties. MCT formulations demonstrated flame retardance and flame resistance up to about their phase reversal limit. MCT foamable compositions containing MCT oil above the phase reversal composition; e.g., the composition becomes a water in oil emulsion are, thought less effective in retarding flammability.

[0083] Silicone oil, particularly dimethicone, is classified by manufacturers as a combustible material, Soybean oil is used in candles. Surprisingly, foamable compositions containing substantial amounts of soybean oil provide a foam with flame resistant or retardant properties without using non flammble propellants. Moreover it is effective even at significant concentrations.

[0084] Foamable compositions containing isopropyl myristate or ocytel dodecanol can provide the resultant foam with flame resistant or retardant properties. However, such oil like substances are more sensitive to the type of inflammable propellant mixture used. One possible way of reducing such sensitivity is to use a mixture of inflammable and non-flammable propellants. A non-limiting example is butane and dymel, although many other mixtures could be used. Using non-flammable propellants increases the flame retardant and resistant properties of the present invention.

[0085] In one or more embodiments the hydrophobic solvent is mineral oil and preferably light mineral oil.

[0086] In one or more embodiments the hydrophobic solvent is vegetable oil and preferably soybean oil.

[0087] In one or more embodiments the hydrophobic solvent is silicone oil and preferably dimethicone.

[0088] In one or more other embodiments MCT's are the hydrophobic solvent.

[0089] In one or more other embodiments octyl dodecanol or isopropyl myristearate are the hydrophobic solvents.

[0090] In one or more embodiments of the present invention, combinations of two or more of a mineral oil, MCT oil, octyl dodecanol and isopropyl myristearate may be used to prepare a foam that is flame resistant or retardant. Preferably the mineral oil is the major component (>50% by weight) of the foam composition.

[0091] In one or more embodiments of the present invention, combinations of two or more of a mineral oil, MCT oil, octyl dodecanol, isopropyl myristearate silicone oil and vegetable oil may be used to prepare a foam that is flame resistant or retardant. Preferably the mineral oil is the major component (>50% by weight) of the foam composition.

[0092] In one or more embodiments there is provided foamable carrier composition for use in the manufacture of a non-flammable, a flame retardant or a flame resistant foam, said carrier comprising:

[0093] about 2% to about 75% hydrophobic solvent, said hydrophobic solvent comprising at least one of mineral oil, MCT oil, isopropyl oil, octyl dodecanol, silicone oil and vegetable oil;

[0094] about 25 to about 98% by weight water;

[0095] about 0.1% to about 5% by weight foam adjuvant agent;

[0096] about 0.1% to about 5% by weight surface-active agent; and

[0097] about 0.1% to about 5% by weight water gelling agent, and

[0098] a liquefied or compressed gas propellant,

[0099] which is contained in a container, and

[0100] which upon release provides a breakable foam suitable for topical or mucosal administration that is non-flammable, flame retardant or flame resistant.

[0101] In one or more embodiments there is also provided use of said foamable carrier composition in the manufacture of a non-flammable or a flame retardant or a flame resistant foam.

[0102] In one or more embodiments there is also provided a method of administration to a subject in need a foam produced from a foamable carrier composition said carrier and foam comprising:

[0103] about 2% to about 75% by weight hydrophobic solvent; said hydrophobic solvent comprising at least one of mineral oil, MCT oil, isopropyl oil, octyl dodecanol, silicone oil and vegetable oil;

[0104] about 25 to about 98% water;

[0105] about 0.1% to about 5% foam adjuvant agent;

[0106] about 0.1% to about 5% surface-active agent;

[0107] about 0.1% to about 5% water gelling agent; and

[0108] a liquefied or compressed gas propellant, wherein the foam is applied to a surface of the subject and at a convenient time shortly thereafter the foam is subjected to shear forces, which causes it to collapse onto one or more surfaces of the subject and wherein the foam and the resultant collapsed composition are non-flammable, flame retardant or flame resistant and provide a non-flammable, a flame retardant or a flame resistant coating to said surface.

[0109] In one or more embodiments there is also provided a foamable carrier, composition and method of administration wherein the foam is non-flammable, when tested according to a simplified test based on the European Standard prEN 14851 or is flame resistant or flame retardant.

[0110] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the hydrophobic solvent is mineral oil, which is present in the composition in a concentration in the range of about 5 wt % to about 70 wt %.

[0111] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the hydrophobic solvent is MCT oil, and MCT oil is present in the composition in a concentration that is less than or about the phase transition composition amount for transitioning from an oil in water emulsion to a water in oil emulsion.

[0112] In one or more embodiments there is also provided foamable carrier, composition and method of administration, wherein MCT oil is present in an amount in the range of about 3 wt % to about 50 wt %.

[0113] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the hydrophobic solvent is vegetable oil, which is present in the composition in a concentration in the range of about 20 wt % to about 40 wt %.

[0114] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the vegetable oil is soybean oil.

[0115] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the hydrophobic solvent is silicone oil, which is present in the composition in a concentration in the range of about 10 wt % to about 25 wt %.

[0116] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the silicone oil is dimethicone.

[0117] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the the hydrophobic solvent is octyl dodecanol and which is present in the composition in a concentration that is less than or about the phase transition composition amount.

[0118] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the the hydrophobic solvent is isopropyl myristate, and which is present in the composition in a concentration that is less than or about the phase transition composition amount for transitioning from an oil in water emulsion to a water in oil emulsion.

[0119] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the hydrophobic solvent comprises a mixture of two or more of, MCT oil, isopropyl oil and octyl dodecanol.

[0120] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the propellant comprises about 5-25% by weight liquefied or compressed gas propellant.

[0121] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the propellant comprises at least one of propane, isobutane and n-butane.

[0122] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein birefringence can be observed in the foam.

[0123] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the foam has a substantially structured order.

[0124] In one or more embodiments there is also provided a foamable carrier, composition and method of administration, wherein the foam does not ignite.

[0125] In one or more embodiments the foamable carrier is for use in the manufacture of a non-flammable, a flame resistant or a flame retardant medicament for and having a topical, mucosal or body cavity use or effect. In one or more embodiments the foamable carrier is for use in the manufacture of a non-flammable, a flame resistant or a flame retardant pharmaceutical for and having a topical, mucosal or body cavity use or effect.

[0126] In one or more embodiments the foamable carrier is for use in the manufacture of a non-flammable, a flame resistant or a flame retardant cosmetic for and having a topical use or effect. In one or more other embodiments there is provided the use of the foamable carrier in the manufacture of a of a non-flammable a flame resistant or a flame

retardant medicament, pharmaceutical or cosmetic for and having a topical use or effect.

BRIEF DESCRIPTION OF THE DRAWINGS

[0127] A more complete appreciation of the present invention and many of its advantages will be understood by reference to the following detailed description when considered in connection with the following drawings, which are presented for the purpose of illustration only are not intended to limit the scope of the appended claims, and in which:

[0128] FIG. **1** illustrates the improvement in the treatment of psoriasis using Bethasone valerate 0.12% foam; and

[0129] FIG. **2** illustrates the improvement in the treatment of atopic dermatitis using Bethasone valerate 0.12% foam.

DETAILED DESCRIPTION OF THE INVENTION

Foam Flammability

[0130] Foamable compositions comprise of one or more flammable components. Upon being released from a pressurized canister usually by depression of an actuator valve the flowable composition expands rapidly to form a foam. Most or essentially all of the propellant immediately becomes a gas and dissipates into the atmosphere. A good to excellent foam, can be rich to very rich and creamy in appearance with a very fine to small bubble size. Propellant gas can to some extent be entrapped in such bubbles. Relatively small amounts of propellant may initially remain dissolved in the foam. The amount may vary according to the foam composition. For example, if the foam comprises a hydrophobic solvent and the propellant is hydrophobic a higher amount of propellant may remain in the foam immediately after release when compared to a hydrophillic foam. So it can be appreciated that the amount of propellant available to ignite in or about the surface of the foam shortly after expansion is variable and can depend extensively on the components of the foam.

[0131] Ideally, non-flammable propellants should be used so that the propellant does not contribute to the flammability of the foam. However, non-flammable CFC's are no longer being used due to the overriding concern of damage to the ozone layer and global warming consequent on uncontrolled use of such environmentally unfriendly substances. Other non-flammable gases like carbon dioxide do not deliver sufficient pressure and are more suitable for preparation of mouse cream. Other non-flammable gases like Dymel are currently not approved for use in the United States. Thus, many foamable compositions utilize hydrocarbon propellants especially one or more of propane, isobutene, and or butane on their own or more preferably in various mixtures thereof. Such propellants are clearly flammable and to the extent that a significant amount remains in or about the foam, it can readily ignite when exposed to a naked flame. Some of the other ingredients readily used in foam compositions are themselves flammable, alcohol being a classic example.

[0132] The flammability of the compositions originally disclosed in parent application U.S. patent application Ser. No. 10/532,618 was evaluated. Many were surprisingly found to be non-flammable or flame retardant, despite the fact that the foamable compositions contained significant amounts of liquid propellant and 'combustible' hydrophobic solvents.

[0133] Surprisingly, it has been discovered that mineral oils reduce flammability of a foam, as demonstrated in a simplified standard inflammability test based on the European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test", which was performed on mineral oil foam compositions. According to this simplified standard, a product is considered flammable if a stable flame appears following ignition, which is at least 4 cm high and which is maintained for at least 2 seconds. In additional embodiments, the concentration of the mineral oil is sufficient to reduce the degree of inflammability, when compared with the same composition where the oil component comprises a different oil, or other oil like substance, such as petrolatum or an ester of a fatty acid. In a further embodiment the the mineral oil is combined in substantial or significant amounts with a different oil, or other oil like substance, and acts to reduce the degree of inflammability of the resultant foam, when compared with the same composition with the different oil, or other oil like substance.

[0134] Mineral oil and MCT oil were discovered to be consistently flame retardent in the test ranges measured with different hydrocarbon propellant mixtures. The initial results showed that neither appeared to be significantly influenced by the propellant mixture used nor the amount of oil or oil like substance in the emollient foam.

[0135] Mineral oil appeared to be preferred and foam compositions comprising mineral oil at 15%, 25%, 35%, 50%, and 60% by weight were all flammable retardant. Moreover, none of the 15% and none of the 35% by weight mineral oil foam compositions with three different propellant mixtures ignited.

[0136] Surprisingly, it has been discovered that MCT's also reduce the flammability of a foam, as demonstrated in a simplified standard inflammability test based on European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test", which was performed on MCT foam compositions. In additional embodiments, the concentration of the MCT is sufficient to reduce the degree of inflammability, when compared with the same composition where the oil component comprises a different oil, or other oil like substance, such as petrolatum or an ester of a fatty acid. In a further embodiment the the MCT is combined in substantial or significant amounts with a different oil, or other oil like substance, and acts to reduce the degree of inflammability of the resultant foam, when compared with the same composition with the different oil, or other oil like substance.

[0137] Similarly foam compositions comprising MCT oil at 15%, 35% and 50% by weight were all flammable retardent. Higher MCT oil concentrations (e.g., 60 wt %) did not pass the flammability test used. Without being bound to any particular theory this may have been a consequence of and due to the formation of a water in oil emulsion. Moreover, none of the 15% and only one of the 35 wt % MCT foam compositions with three different propellant mixtures ignited.

[0138] Surprisingly, it has been discovered that vegetable oils also reduce the flammability of a foam, as demonstrated in a simplified standard inflammability test based on European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test", which was performed on

soybean oil foam compositions. In additional embodiments, the concentration of the soybean oil is sufficient to reduce the degree of inflammability, when compared with the same composition where the oil component comprises a different oil, or other oil like substance, such as petrolatum or an ester of a fatty acid. In a further embodiment the the soybean oil is combined in substantial or significant amounts with a different oil, or other oil like substance, and acts to reduce the degree of inflammability of the resultant foam, when compared with the same composition with the different oil, or other oil like substance.

[0139] Notably, foam compositions comprising soybean oil at 20%, 30.5% and 40% by weight were all flammable retardent and did not ignite at 30.5% or 20%.

[0140] Surprisingly, it has also been discovered that silicone oils also reduce the flammability of a foam, as demonstrated in a simplified standard inflammability test based on European Standard prEN 14851, titled "Aerosol containers—Aerosol foam flammability test", which was performed on dimethicone foam compositions. In additional embodiments, the concentration of the dimethicone is sufficient to reduce the degree of inflammability, when compared with the same composition where the oil component comprises a different oil, or other oil like substance, such as petrolatum or an ester of a fatty acid. In a further embodiment the the dimethicone oil is combined in substantial or significant amounts with a different oil, or other oil like substance, and acts to reduce the degree of inflammability of the resultant foam, when compared with the same composition with the different oil, or other oil like substance.

[0141] Notably, foam compositions comprising dimethicone at 10% and 25% by weight were all flammable retardent and did not ignite at 10%.

[0142] Foam compositions comprising other oil like substances namely, either octyl dodecanol or isopropyl myristate as hydrophobic solvent were found to be variable in behavior. In certain circumstances compositions containing significant amounts of octyl dodecanol or isopropyl myristate in addition to water were not flammable according to the simplified AFNOR like test, whereas in other certain circumstances they burnt with a flame too large and or for too long. Octyl dodecanol or isopropyl myristate appear to demonstrate similar flammability properties.

[0143] Turning to non-aqueous solvent components it was observed that petrolatum compositions were flammable. Possibly, and without being tied to any particular theory, apart from any flammability properties of the petrolatum itself, it may be that more of the propellant can remain either dissolved in the solvent or be entrapped in the bubble structure and therefore be available for ignition.

[0144] In contrast, flammability tests of compositions with 15% and 35% PPG 15 stearyl ester with different hydrocarbon propellant mixtures were found to ignite on most occasions with a flame higher than that permitted under the simplified AFNOR like test.

Hydrophobic Solvent

[0145] A hydrophobic solvent according to the present invention is a liquid material having solubility in distilled water at ambient temperature of less than about 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. It is liquid at ambient temperature.

[0146] The total content of hydrophobic solvent may vary from 2% to 75% (w/w) of the foamable composition. However, different ranges (herein "composition classes A-D") have been designated, in order to facilitate a choice of an appropriate class, according to the anticipated cosmetic or pharmaceutical need. As a rule of thumb, higher hydrophobic solvent concentrations are more appropriate for the treatment of dry skin, and/or for the treatment of a disease, which is more responsive to drugs delivered in an oily vehicle. Likewise, the higher oil-content composition classes provide an enhanced occlusive effect, which in turn induces the skin penetration of an active agent. Another consideration relates to user acceptance of a product containing a high concentration of the hydrophobic solvent (from about 25% of the composition), which would leave some oily feeling post-application. Thus, a particular composition of the present invention is selected having a hydrophobic solvent concentration in view of the target population and its specific needs.

[0147] In one or more embodiments of the present invention, the hydrophobic solvent is mineral oil. Mineral oil (Chemical Abstracts Service Registry number 8012-95-1) is a mixture of aliphatic, naphthalenic, and aromatic liquid hydrocarbons that are derived from petroleum. It is typically liquid; its viscosity is in the range of about 35 CST to about 100 CST (at 40° C.), and its pour point (the lowest temperature at which an oil can be handled without excessive amounts of wax crystals forming) is below 0° C. By contrast, white petrolatum, also termed "Vaseline", is disadvantageous, due to its waxy nature. It is known to leave waxy and sticky feeling after application and occasionally stain cloths. Thus, white petrolatum and other semi-solid oils are not a preferred hydrophobic solvent according to the present invention.

[0148] Yet another preferred hydrophobic solvents are liquid oils from vegetable, marine or animal sources. By way of example, the unsaturated oil may be selected from the group consisting of olive, corn, soybean, canola, cottonseed, coconut, sesame, sunflower, borage seed, *syzigium aromaticum*, hempseed, herring, cod-liver, salmon, flaxseed, wheat germ and evening primrose oils and mixtures thereof, at any proportion.

[0149] A particularly preferred class of oils includes polyunsaturated oils, e.g., esters, and in particular glyceryl esters, 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). Thus, in one or more embodiments of the present invention the hydrophobic solvent includes at least 6% by weight foamable composition of an oil selected from omega-3 oil, omega-6 oil, and mixtures thereof.

[0150] Another class of oils suitable for use as a phydrophobic solvent is liquid hydrophobic plant-derived oils, or essential oils, e.g. "therapeutic oils" containing active biologically occurring molecules that have a therapeutic effect when applied topically. Examples of such 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 basil, camphor, cardamom, carrot, citronella, clary sage, clove, cypress, frankincense, ginger, grapefruit, hyssop, jasmine, lavender, lemon, mandarin, marjoram, myrrh, neroli, nutmeg, petitgrain, sage, tangerine,

vanilla, *verbena*, as well as any other therapeutically beneficial oil, know in the art of herbal medication.

[0151] Medium-chain triglycerides ("MCT's") have an average molecular weight of about =500. They are sometimes referred to as MCT oil or thin vegetable oil. They take the form of a colorless to slightly yellowish oily liquid that is practically odorless and tasteless and which solidifies at about 0° C. They are miscible with long-chain hydrocarbons and triglycerides but are practically insoluble in water. They consist of a mixture of triglycerides of saturated fatty acids, mainly of caprylic acid and of capric acid and contain not less than 95% of saturated fatty acids.

[0152] In one or more embodiments of the present invention, the hydrophobic solvent is an "emollient". An emollient is a hydrophobic agent that softens, smoothens and improves lipid content of the skin or other mucous membranes. In one or more embodiments of the present invention, the emollient is a liquid. Without derogating the generality of this definition, examples of suitable emollients for use include isostearic acid derivatives, isopropyl palmitate, lanolin oil, diisopropyl dimerate, diisopropyl adipate, dimethyl isosorbide, maleated soybean oil, octyl palmitate, isopropyl isostearate, cetyl lactate, cetyl ricinoleate, tocopheryl acetate, acetylated lanolin alcohol, cetyl acetate, phenyl trimethicone, glyceryl oleate, tocopheryl linoleate, wheat germ glycerides, arachidyl propionate, myristyl lactate, decyl oleate, propylene glycol ricinoleate, isopropyl lanolate, pentaerythrityl tetrastearate, neopentylglycol dicaprylate/dicaprate, hydrogenated coco-glycerides, isononyl isononanoate, isotridecyl isononanoate, myristyl myristate, triisocetyl citrate, octyl dodecanol, octyl hydroxystearate and mixtures thereof. Other examples of other suitable emollients can also be found in the Cosmetic Bench Reference, pp. 1.19-1.22 (1996). In one or more embodiments, the hydrophobic solvent is a mixture of a mineral oil or silicone oil and an emollient.

[0153] In one or more embodiments of the present invention, silicone oil is a component of the hydrophobic solvent. Silicone oils are used in the foamable compositions due to their known skin protective and occlusive properties. Suitable silicone oils for use in the invention include non-volatile silicones, such as polyalkyl siloxanes, polyaryl siloxanes, polyalkylaryl siloxanes and polyether siloxane copolymers, polydimethylsiloxanes (dimethicones) and poly (dimethylsiloxane)-(diphenyl-siloxane) copolymers. These are preferably chosen from cyclic or linear polydimethylsiloxanes containing from about 3 to about 9, preferably from about 4 to about 5, silicon atoms. Volatile silicones such as cyclomethicones can also be used. Water-soluble silicones, such as dimethicone copolyol are not included in the definition of silicone oils (as hydrophobic solvents) according to the present invention.

[0154] In one or more embodiments of the present invention, the composition comprises at least 2% (w/w foamable composition) silicone oil, alone or as part of the hydrophobic solvent. Yet, in other embodiments, the composition comprises at least 5% (w/w) silicone oil alone or as part of the hydrophobic solvent.

[0155] The hydrophobic solvent of the present invention may comprise a mixture of two or more of the above hydrophobic solvents in any proportion.

Foam Adjuvant Agents

[0156] Foam adjuvants are 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 agents 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, 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 according to the present invention. The concentration of the fatty alcohol, required to support the foam system is inversely related to the length of its carbon chains.

[0157] In one or more embodiments of the present invention, the foam adjuvant agent 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.

[0158] Optionally, the carbon atom chain of the fatty alcohol or the fatty acid may have at least one double bond. A further class of foam adjuvant agent according to the present invention comprises a long chain fatty alcohol or fatty acid, wherein the carbon atom chain is branched. The carbon chain of the fatty acid or fatty alcohol can be substituted with a hydroxyl group, such as 12-hydroxy stearic acid.

[0159] The foam adjuvant agent according to one or more embodiments of the present invention includes a mixture of fatty alcohols, fatty acids and hydroxy fatty acids and derivatives thereof in any proportion, providing that the total amount is 0.1% to 5% (w/w) of the carrier mass. More preferably, the total amount is 0.4%—2.5% (w/w) of the carrier mass.

[0160] While fatty alcohols and fatty acids serve to stabilize the resultant foam composition, they often provide additional therapeutic properties. Long chain saturated and mono unsaturated fatty alcohols, e.g., stearyl alcohol, erycyl alcohol, arachidyl alcohol and docosanol have been reported to possess antiviral, anti infective, anti-proliferative and anti-inflammatory properties (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. Thus, the pharmaceutical or cosmetic carrier, containing the foam adjuvant agent of the present invention provides an extra therapeutic benefit in comparison with currently used vehicles, which are inert and non-active.

Surface-Active Agents

[0161] Surface-active agents, according to the present invention include any agent linking oil and water in the composition.

[0162] The surface-active agent is suitably selected from anionic, cationic, nonionic, zwitterionic, amphoteric and ampholytic surfactants, as well as mixtures of these surfactants. Such surfactants are well known to those skilled in the

pharmaceutical 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 and Myrj 59; poly(oxyethylene) alkylyl ethers, such as poly(oxyethylene) cetyl ether, poly(oxyethylene) palmityl 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.

[0163] A combination of surface active agents is possible. Any surface-active agent or combinations thereof may be used as surface-active agent. According to one or more embodiments of the present invention, the surface-active agent (or agents) has an HLB of higher than 9.

[0164] In one or more embodiments of the present invention, the surface-active agent is selected from the groups of non-ionic surfactants, cationic surfactants, amphoteric and zwitterionic surfactants, and, in particular, the surface-active agent is a non-ionic surfactant. Ionic surfactants (including cationic, anionic, amphotheric and zwitterionic surfactants) are known to be skin irritants. Therefore, non-ionic surfactants are preferred in applications including sensitive skin such as found in most dermological disorders. 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 below.

[0165] In one or more embodiments of the present invention, the surface active agent is solely non-ionic, comprising one or more non-ionic surfactants.

[0166] In one or more embodiments of the present invention, the surface active agent include a ratio of non-ionic surfactants to ionic surfactants in the range of 100:1 to 6:1; in some embodiments the non-ionic to ionic surfactant ratio is greater than 6:1, or greater than 8:1; or greater than 14:1, or greater than 16:1, or greater than 20:1.

[0167] Exemplary non-ionic surfactants include polyethoxylated fatty acids, fatty acid diesters, polyethylene glycol glycerol fatty acid esters, alcohol-oil transesterification products, polyglycerized fatty acids, sterol and sterol derivatives, polyethylene glycol sorbitan fatty acid esters, polyethylene glycol alkyl ethers, sugar esters, polyethylene glycol alkyl phenols, polyoxyethylene-polyoxypropylene block copolymers, sorbitan fatty acid esters and lower alcohol fatty acid esters.

[0168] Although polyethylene glycol (PEG) itself does not function as a surfactant, a variety of PEG-fatty acid esters have useful surfactant properties. Exemplary monoesters include esters of lauric acid, oleic acid, and stearic acid, e.g., PEG-8 laurate, PEG-8 oleate, PEG-8 stearate, PEG-9 oleate, PEG-10 laurate, PEG-10 oleate, PEG-12 laurate, PEG-12 oleate, PEG-15 oleate, PEG-20 laurate and PEG-20 oleate. Polyethylene glycol fatty acid diesters suitable for use as non-ionic surfactants in the compositions of the present invention include PEG-20 dilaurate, PEG-20 dioleate, PEG-20 distearate, PEG-32 dilaurate and PEG-32 dioleate. Suitable polyethylene glycol glycerol fatty acid esters include PEG-20 glyceryl laurate, PEG-30 glyceryl laurate, PEG-40 glyceryl laurate, PEG-20 glyceryl oleate, and PEG-30 glyceryl oleate.

[0169] A large number of surfactants of different degrees of hydrophobicity or hydrophilicity can be prepared by reaction of alcohols or polyalcohols with a variety of natural and/or hydrogenated oils. Most commonly, the oils used are castor oil or hydrogenated castor oil, or an edible vegetable oil such as corn oil, olive oil, peanut oil, palm kernel oil, apricot kernel oil, or almond oil. Preferred alcohols include glycerol, propylene glycol, ethylene glycol, polyethylene glycol, sorbitol, and pentaerythritol. Among these alcohol-oil transesterified surfactants, preferred hydrophilic surfactants are PEG-35 castor oil (Incrocas-35), PEG-40 hydrogenated castor oil (Cremophor RH 40), PEG-25 trioleate (TAGAT® TO), PEG-60 corn glycerides (Crovol M70), PEG-60 almond oil (Crovol A70), PEG-40 palm kernel oil (Crovol PK70), PEG-50 castor oil (Emalex C-50), PEG-50 hydrogenated castor oil (Emalex HC-50), PEG-8 caprylic/capric glycerides (Labrasol), and PEG-6 caprylic/capric glycerides (Softigen 767). Preferred hydrophobic surfactants in this class include PEG-5 hydrogenated castor oil, PEG-7 hydrogenated castor oil, PEG-9 hydrogenated castor oil, PEG-6 corn oil (Labrafil® M 2125 CS), PEG-6 almond oil (Labrafil® M 1966 CS), PEG-6 apricot kernel oil (Labrafil® M 1944 CS), PEG-6 olive oil (Labrafil® M 1980 CS), PEG-6 peanut oil (Labrafil® M 1969 CS), PEG-6 hydrogenated palm kernel oil (Labrafil® M 2130 BS), PEG-6 palm kernel oil (Labrafil® M 2130 CS), PEG-6 triolein (Labrafil® b M 2735 CS), PEG-8 corn oil (Labrafil® WL 2609 BS), PEG-20 corn glycerides (Crovol M40), and PEG-20 almond glycerides (Crovol A40). The latter two surfactants are reported to have HLB values of 10, which are generally considered to be the approximate border line between hydrophilic and hydrophobic surfactants.

[0170] Alcohol-oil transesterification derivatives of oil soluble vitamins (e.g., vitamins A, D, E, K, etc.), such as tocopheryl PEG-100 succinate (TPGS, available from Eastman), are also suitable surfactants.

[0171] Polyglycerol esters of fatty acids are also suitable non-ionic surfactants for the present invention. Among the polyglyceryl fatty acid esters, exemplary use hydrophobic surfactants include polyglyceryl oleate (Plurol Oleique), polyglyceryl-2 dioleate (Nikkol DGDO), and polyglyceryl-10 trioleate. Preferred hydrophilic surfactants include polyglyceryl-10 laurate (Nikko) Decaglyn 1-L), polyglyceryl-10 oleate (Nikkol Decaglyn 1-0), and polyglyceryl-10 mono, dioleate (Caprol® PEG 860), Polyglyceryl polyricinoleates (Polymuls) are hydrophilic and hydrophobic surfactants of this class.

[0172] Sterols and derivatives of sterols are suitable surfactants for use in the present invention. These surfactants can be hydrophilic or hydrophobic. Preferred derivatives include the polyethylene glycol derivatives. An exemplary hydrophobic surfactant in this class is cholesterol. An exemplary hydrophilic surfactant in this class is PEG-24 cholesterol ether (Solulan C-24).

[0173] A variety of PEG-sorbitan fatty acid esters are suitable for use as non-ionic surfactants in the present invention. In general, these surfactants are hydrophilic, although several hydrophobic surfactants of this class can be used. Among the PEG-sorbitan fatty acid esters, exemplary hydrophilic surfactants include PEG-20 sorbitan monolaurate (Tween-20), PEG-20 sorbitan monopalmitate (Tween-40), PEG-20 sorbitan monostearate (Tween-60), and PEG-20 sorbitan monooleate (Tween-80).

[0174] Ethers of polyethylene glycol and alkyl alcohols are suitable non-ionic surfactants for use in the present invention. Exemplary hydrophobic ethers include PEG-3 oleyl ether (Volpo 3) and PEG-4 lauryl ether (Brij 30).

[0175] The polyoxyethylene-polyoxypropylene (POE-POP) block copolymers are a unique class of polymeric surfactants. The unique structure of the surfactants, with hydrophilic POE and hydrophobic POP moieties in well-defined ratios and positions, provides a wide variety of surfactants suitable for use in the present invention. These surfactants are available under various trade names, including Synperonic PE series (ICI), Pluronic® series (BASF), Emkalyx, Lutrol (BASF), Supronic, Monolan, Pluracare, and Plurodac. The generic term for these polymers is "poloxamer" (CAS 9003-11-6). Exemplary hydrophilic surfactants of this class include Poloxamers 108, 188, 217, 238, 288, 338, and 407. Exemplary hydrophobic surfactants in this class include Poloxamers 124, 182, 183, 212, 331, and 335.

[0176] Sorbitan esters of fatty acids are suitable non-ionic surfactants for use in the present invention. Among these esters, preferred hydrophobic surfactants include sorbitan monolaurate (Arlacel 20), sorbitan monopalmitate (Span-40), sorbitan monooleate (Span-80), sorbitan monostearate, and sorbitan tristearate.

[0177] Esters of lower alcohols (C_2 to C_4) and fatty acids (C_8 to C_{18}) are suitable non-ionic surfactants for use in the present invention. Among these esters, preferred hydrophobic surfactants include ethyl oleate (Crodamol EO), isopropyl myristate (Crodamol IPM), and isopropyl palmitate (Crodamol IPP).

[0178] In one or more embodiments of the present invention, the surface-active agent comprise mono-, di- and tri-esters of sucrose with food fatty acids (sucrose esters), prepared from sucrose and methyl and ethyl esters of food fatty acids or by extraction from sucroglycerides. Exemplary sucrose esters include sucrose monopalmitate and sucrose monolaurate. Suitable sucrose esters include those having a high monoester content, which have higher HLB values.

[0179] In one or more embodiments of the present invention, a combination of a non-ionic surfactant and an anionic surfactant (such as sodium lauryl sulphate) is employed, at a ratio of between 1:1 and 20:1, or at a ratio of 4:1 to 10:1. The resultant foam has a low specific gravity, e.g., less than 0.1 g/ml, which upon rubbing (shear stress) onto the skin collapses easily, to allow facile absorption.

[0180] Unlike prior art foamable compositions, the total surfactant employed to obtain a foam that is stable, of low specific gravity and has a fine bubble structure is low. Lower surfactant levels, particularly of ionic surfactants, are preferred to reduce skin irritations. Total surfactant is in the range of 0.1 to 5.0 wt % of the foamable composition, and is typically less than 2 wt %, or even less than 1 wt %.

Water Gelling Agents

[0181] The water gelling agent according to one or more embodiments of the present invention stablizes the aqueous phase by, for example, increasing viscosity and linking capability. Exemplary water gelling agents that can be used in accordance with one or more embodiments of the present invention include for example, but are not limited to, naturally-occurring polymeric materials such as, locust bean gum, sodium alginate, sodium caseinate, egg albumin, gelatin agar, carrageenin gum sodium alginate, xanthan gum, quince seed extract, tragacanth gum, starch, chemically modified starches and the like, semi-synthetic polymeric materials such as cellulose ethers (e.g. hydroxyethyl cellulose, methyl cellulose, carboxymethyl cellulose, hydroxy propylmethyl cellulose), polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum, soluble starch, cationic celluloses, cationic guars and the like and synthetic polymeric materials such as carboxyvinyl polymers, polyvinylpyrrolidone, polyvinyl alcohol polyacrylic acid polymers, polymethacrylic acid polymers, polyvinyl acetate polymers, polyvinyl chloride polymers, polyvinylidene chloride polymers and the like. Mixtures of the above compounds are contemplated.

[0182] Further exemplary water gelling agents include the acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers sold, for example, by the B.F. Goodrich Company under the trademark of Carbopol Registered™ resins. These resins consist essentially of a colloidal water-soluble polyalkenyl polyether crosslinked polymer of acrylic acid crosslinked with from 0.75% to 2% of a crosslinking agent such as polyallyl sucrose or polyallyl pentaerythritol. Examples include Carbopol 934, Carbopol 940, Carbopol 950, Carbopol 980, Carbopol 951 and Carbopol 981. Carbopol 934 is a water-soluble polymer of acrylic acid crosslinked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule.

[0183] The gelling agent is present in an amount in the range of about 0.1% to about 5.0 wt % of the foamable composition. In one or more embodiments, it is typically less than 1 wt % of the foamable composition.

"Alcohol Free"

[0184] Unlike the composition disclosed in U.S. Pat. No. 6,126,920, which contains a 40-90 wt % aliphatic alcohol, the composition of the present invention does not contain such amount alcohols. For the purpose of the present application, the term "alcohol free" shall mean that the composition contains no more than an incidental amount of an aliphatic alcohol, e.g. less than about 7.5% of any aliphatic alcohol, having one to six carbon atoms in their carbon backbone, or no more than 7.5% of any mixture of such aliphatic alcohols. Alcohols at these low levels are not considered to have a negative effect on skin or mucous membranes. In one or more embodiments, the foamable compositions do not contain any alcohol.

Optional Ingredients

[0185] The pharmaceutical or cosmetic foam carrier of the present invention may further optionally comprise a variety of pharmaceutical or cosmetic ingredients, which are added in order to fine-tune the consistency of the formulation, protect the formulation components from degradation and oxidation and bestow their cosmetic acceptability. Such excipients, may be selected, for example, from the group consisting of diglycerides, triglycerides, stabilizing agents, antioxidants, humectants, flavoring, colorant and odorant agents and other formulation components, used in the art of pharmaceutical and cosmetic formulary. A pharmaceutical or cosmetic composition manufactured using the foam carrier according to the present invention is very easy to use. When applied onto the afflicted body surface of 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.

Propellant Aerosol

[0186] Aerosol propellants are used to generate and administer the foamable composition as a foam. The total composition including propellant, foamable compositions and optional ingredients is referred to as the foamable carrier. The propellant makes up about 5-25 wt % of the foamable carrier. Examples of suitable propellants include volatile hydrocarbons such as butane, propane, isobutane or mixtures thereof, and fluorocarbon gases.

[0187] Compositions of commercially available highly flammable hydrocarbon propellants are listed in the table below.

TABLE B

Propellant	Propane %		Iso-Butane %		n-Butane %	
Propellant	mol	mass	mol	mass	mol	mass
5515	~55	~47	~15	~18	~30	~35
1681	~16	~13	~81	~84	~3	~3
Pinto*	NL	~8	NL	~30	NL	~60

*Plus very small amounts of other gasses including ~2% isopentane;
NL = Not listed in the certificate of analysis.
~= approximately.

Composition and Foam Physical Characteristics

1. Composition Flow Properties:

[0188] It is important to have a composition, including water, hydrophobic solvents, formulation excipients and propellant, in a stable emulsion, which ascertain acceptable shelf-life of the product.

[0189] Yet, another crucial property is that said composition has to be free flowing, since otherwise, it cannot flow through the dip-tube of the aerosol container and create acceptable foam. It has been noted that in the context of the composition of the present invention, compositions comprising semi-solid hydrophobic solvents, e.g., white petrolatum, are excessively viscous and demonstrate poor flowability.

[0190] The combination of a surface active agent, foaming adjuvant and water gelling agent according to one or more embodiments of the invention provides a low specific gravity foam having superior flow properties and sheer breakability (among other attributes). According to one or more embodiments of the present invention, the total amount of surface active agent, foaming adjuvant and water gelling agent, in combination does not exceed 8% (w/w) of foamable composition. In other embodiments, the combined amounts of surface active agent, foaming adjuvant and water gelling agent is less than 5% (w/w) of foamable composition. The low solids content improves the flow properties of the foam, reduces unpleasant skin residue and reduces the cost of manufacture. As is demonstrated herein, the foam quality and foam breakability is excellent, despite the low levels of these components in the foam.

2. Foam Properties:

[0191] The following scale for foam quality is used to evaluate foams:

[0192] E (excellent): very rich and creamy in appearance, does not show any bubble structure or shows a very fine (small) bubble structure;

[0193] G (good): rich and creamy in appearance, very small bubble size, "dulls" more rapidly than an excellent foam;

[0194] FG (fairly good): a moderate amount of creaminess noticeable, bubble structure is noticeable;

[0195] F (fair): very little creaminess noticeable, larger bubble structure than a "fairly good" foam;

[0196] P (poor): no creaminess noticeable, large bubble structure; and

[0197] VP (very poor): dry foam, large very dull bubbles, difficult to spread on the skin.

[0198] Foams, adequate for topical administration according to the present invention have to be of quality grade E or G upon release from the aerosol container. Smaller bubbles mean 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.

[0199] A crucial aspect of foam properties, according to the present invention is breakability. Sheer-force breakability of the foam, as attained by the composition of the present invention is clearly advantageous to thermally-induced breakability, present, for example in U.S. Pat. No. 6,126,920, and the respective Olux and Luxiq products, as demonstrated by the fact that according to the use instructions of Olux and Luxiq, the foam cannot be applied on the hand and afterwards delivered to the afflicted area, since it immediately collapses upon exposure to skin temperature.

[0200] Yet, another important property is specific gravity of the foam, as measured upon release from the aerosol can. Typically, foams according to the present invention have specific gravity of less than 0.1 g/mL and more preferably, less than 0.05 g/mL.

Fields of Pharmaceutical Applications

[0201] By including an appropriate therapeutic agent in the foamable carrier, the foam composition of the present invention is useful in the therapy of a variety of dermatological disorders (also termed "dermatoses") including, in a non-limiting exemplary manner:

[0202] Dermatitis
- **[0203]** Contact Dermatitis
- **[0204]** Atopic Dermatitis
- **[0205]** Seborrheic Dermatitis
- **[0206]** Nummular Dermatitis
- **[0207]** Chronic Dermatitis Of The Hands And Feet
- **[0208]** Generalized Exfoliative Dermatitis
- **[0209]** Stasis Dermatitis
- **[0210]** Lichen Simplex Chronicus

[0211] Bacterial Infections
- **[0212]** Cellulitis
- **[0213]** Acute Lymphangitis
- **[0214]** Lymphadenitis
- **[0215]** Erysipelas
- **[0216]** Cutaneous Abscesses
- **[0217]** Necrotizing Subcutaneous Infections
- **[0218]** Staphylococcal Scalded Skin Syndrome

[0219] Folliculitis
[0220] Furuncles
[0221] Hidradenitis Suppurativa
[0222] Carbuncles
[0223] Paronychial Infections
[0224] Erythrasma
[0225] Fungal Infections
[0226] Dermatophyte Infections
[0227] Yeast Infections
[0228] Parasitic Infections
[0229] Scabies
[0230] Pediculosis
[0231] Creeping Eruption
[0232] Viral Infections
[0233] Disorders of Hair Follicles and Sebaceous Glands
[0234] Acne
[0235] Rosacea
[0236] Perioral Dermatitis
[0237] Hypertrichosis (Hirsutism)
[0238] Alopecia, including male pattern baldness, alopecia areata, alopecia universalis and alopecia totalis
[0239] Pseudofolliculitis Barbae
[0240] Keratinous Cyst
[0241] Scaling Papular Diseases
[0242] Psoriasis
[0243] *Pityriasis Rosea*
[0244] *Lichen Planus*
[0245] *Pityriasis Rubra* Pilaris
[0246] Benign Tumors
[0247] Moles
[0248] Dysplastic Nevi
[0249] Skin Tags
[0250] Lipomas
[0251] Angiomas
[0252] Pyogenic Granuloma
[0253] Seborrheic Keratoses
[0254] Dermatofibroma
[0255] Keratoacanthoma
[0256] Keloid
[0257] Malignant Tumors
[0258] Basal Cell Carcinoma
[0259] Squamous Cell Carcinoma
[0260] Malignant Melanoma
[0261] Paget's Disease Of The Nipples
[0262] Kaposi's Sarcoma
[0263] Reactions to Sunlight
[0264] Sunburn
[0265] Chronic Effects of Sunlight
[0266] Photosensitivity
[0267] Bullous Diseases
[0268] Pemphigus
[0269] Bullous Pemphigoid
[0270] Dermatitis Herpetiformis
[0271] Linear Immunoglobulin A Disease
[0272] Pigmentation Disorders
[0273] Hypopigmentation
[0274] Vitiligo
[0275] Albinism
[0276] Post-inflammatory hypopigmentation
[0277] Hyperpigmentation
[0278] Melasma (chloasma)
[0279] Drug-induced hyperpigmentation
[0280] Post-inflammatory hyperpigmentation
[0281] Disorders of Cornification
[0282] Ichthyosis
[0283] Keratosis Pilaris
[0284] Calluses And Corns
[0285] Actinic keratosis
[0286] Pressure Sores
[0287] Disorders of Sweating
[0288] Inflammatory Reactions
[0289] Drug Eruptions
[0290] Toxic Epidermal Necrolysis
[0291] Erythema Multiforme
[0292] Erythema Nodosum
[0293] Granuloma Annulare

[0294] In one or more embodiments of the present invention, the foam composition of the present invention is useful in the therapy of non-dermatological disorders, which respond to transdermal delivery of an active agent. By way of example, such disorders include localized pain in general, as well as joint pain, muscle pain, back pain, rheumatic pain, arthritis, ostheoarthritis and acute soft tissue injuries and sports injuries. Other disorders of this class include conditions, which respond to hormone therapy, such as hormone replacement therapy, transdermal nicotine administration, and other respective disorders, known in the art of drug delivery. The foam composition of the present invention is also useful in the delivery of local anesthetic agents.

Active Pharmaceutical Agents (Drugs)

[0295] The active pharmaceutical agents, also referred to as "drug(s)", may consist of a single drug or a combination of drugs that can be dissolved in the water phase or the hydrophobic phase of the carrier composition. Examples of such drugs are antibiotic, antibacterial, antifungal, antiviral, antiinflammatory, anesthetic, analgesic, antiallergic, corticosteroid, retinoid and antiproliferative medications and mixtures thereof at any proportion. The concentration of drugs may be adopted to exert a therapeutic effect on a disease when applied to an afflicted area.

Antibacterial Agents

[0296] One important class of drugs comprises antibacterial agents. It is well known that bacterial infections are involved in a variety of superficial disorders of the skin, eye, mucosal membrane, oral cavity, vagina and rectum.

[0297] The antibacterial drug can be active against gram positive and gram-negative bacteria, protozoa, aerobic bacteria and unaerobic ones.

[0298] By way of example, the antibacterial drugs can be selected from the group of chloramphenicol, tetracyclines, synthetic and semi-synthesic penicillins, beta-lactames, quinolones, fluoroquinolnes, macrolide antibiotics, metronidazlole and its derivatives and analogs, dicarboxylic acids, such as azelaic acid, slicylates, peptide antibiotics, cyclosporines and any combination thereof at a therapeutically effective concentration. Another group of antibacterial agents which is non-specific, comprises 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.

[0299] Antibacterial compositions according to the present invention may be used to treat infections of the skin. An example of a very common skin infection is acne, which involve infestation of the sebaceous gland with *p. acnes*, as

well *staphylococus aurus* and *pseudomonas*. Various antibacterial agents have been utilized to treat acne, however, their efficacy is limited due to their low penetration into the hydrophobic environment of the skin layers and sebaceous glands. The composition of the present invention, comprising a hydrophobic component, would facilitate an enhanced rate of penetration. Furthermore, the intrinsic antibacterial and antiinflammatory effects of the foam adjuvant agents, i.e., fatty alcohols and acids, provides a combined effect that should result in a better therapeutic response to treatment.

[0300] The composition of the present invention is particularly useful and beneficial in the prevention and treatment of secondary infections, accompanying skin-structure damage, such as in cuts, wounds, burns and ulcers. In all such cases, the present formulation is easy to use, being in foam state when applied and becoming liquid instantly upon rubbing onto the skin.

[0301] While being useful in the prevention and treatment of infections, the antibacterial foam of the present invention is also applicable for decontaminating areas, afflicted with bacterial warfare organisms, such as anthrax and smallpox.

[0302] The same advantage is expected when the composition of the present invention is topically applied to mucosal membranes, the oral cavity, the vagina and the rectum.

Anti-Fungal Agents

[0303] Fungal infections are another object of treatment using the composition of the present invention. Superficial fungal infection of the skin is one of the commonest skin diseases seen in general practice. Dermatophytosis is probably the most common superficial fungal infection of the skin. It is caused by a group of fungi, which are capable of metabolizing the keratin of human epidermis, nails or hair. There are 3 genera of dermatophytes causing dermatophytosis, i.e, *microsporum, trichophyton* and *epidermophyton.*

[0304] Candidiasis is an infection caused by the yeast like fungus *candida albicans* or occasionally other species of *candida*. Clinical syndromes of candidiasis include: (a) oral candidiasis (oral thrush); (b) candidiasis of the skin and genital mucous membrane; and (c) *candida* paronychia, which inflicts the nail.

[0305] The pharmaceutical composition may comprise an antifungal drug, which is active against dermatophytes and *candida*, selected from the group of, but not limited to azoles, diazoles, triazoles, miconazole, fluconazole, ketoconazole, clotrimazole, itraconazole griseofulvin, ciclopirox, amorolfine, terbinafine, Amphotericin B, potassium iodide, flucytosine (5FC) and any combination thereof at a therapeutically effective concentration.

[0306] It is useful, for example for the treatment of tinea corporis, tinea pedis, tinea *rubrum*, tinea unguium, tinea cruris, tinea barbae and tinea *versicolor*, as well as yeast Infections, such as candidiasis, and candidal vaginitis.

Anti-Viral Agents

[0307] The composition of the present invention is particularly beneficial in the case of viral infections. Cold sores are caused by the herpes simplex Type 1 virus and are sometimes referred to as facial herpes. Mollusca are small viral growths that appear singly or in groups on the face, trunk, lower abdomen, pelvis, inner thighs, or penis. Shingles (herpes zoster), which usually only occurs once in a lifetime, appears as a rash (clusters of blisters with a red base). It is caused by the same virus responsible for chickenpox. Warts are a common, benign skin tumor caused by viral infection.

[0308] Viral infections are currently treated with various antiviral agents, as summarized in the following table:

Drug	Viruses	Chemical Type
Vidarabine	Herpesviruses	Nucleoside analogue
Acyclovir	Herpes simplex (HSV)	Nucleoside analogue
Gancyclovir	Cytomegalovirus (CMV)	Nucleoside analogue
Nucleoside-analog reverse transcriptase inhibitors (NRTI): AZT (Zidovudine), ddI (Didanosine), ddC (Zalcitabine), d4T (Stavudine), 3TC (Lamivudine)	Retroviruses (HIV)	Nucleoside analogue
Non-nucleoside reverse transcriptase inhibitors (NNRTI): Nevirapine, Delavirdine	Retroviruses (HIV)	Nucleoside analogue
Protease Inhibitors: Saquinavir, Ritonavir, Indinavir, Nelfinavir	HIV	Peptide analogue
Ribavirin	Broad spectrum: HCV, HSV, measles mumps, Lassa fever	Triazole carboxamide
Amantadine/Rimantadine	Influenza A strains	Tricyclic amine
Interferons	Hepatitis B and C	Protein

[0309] Any of the above antiviral drugs, in a therapeutically effective concentration, can be incorporated in the foam composition of the present invention. The composition of the present invention, which comprises a hydrophobic solvent, would facilitate an enhanced rate of penetration and better topical distribution of any of the above listed antiviral drugs. Furthermore, the intrinsic antiviral effects of the foam adjuvant agents, i.e., fatty alcohols and acids, provides a combined effect that should result in a better therapeutic response to treatment.

Antiinflammatory or Antiallergic Agents

[0310] Yet, according to another embodiment according to the present invention the drug is an antiinflammatory or antiallergic agent. Antiinflammatory or antiallergic agent can be selected from the group of corticosteroids, nonsteroidal antiinflammatory drugs (NSAIDs), anti-histamines, immunosuppressants and any combination thereof at a therapeutically effective concentration.

[0311] The following table provides a summary of currently available corticosteroid agent and their typical therapeutically effective concentration.

Potency	Compound	Formulation
Very high	Clobetasol proprionate	Cream or ointment 0.05%
	Halobetasol proprionate	Cream or ointment 0.05%
High	Betamethasone diproprionate	Cream or ointment 0.05%
	Betamethasone valerate	Ointment 0.1%
	Fluocinolone acetonide	Cream 0.02%
	Halcinonide	Cream or ointment 0.1%
Medium	Betamethasone valerate	Cream 0.1%
	Fluocinolone acetonide	Cream or ointment 0.020%
	Hydrocortisone valerate	Cream or ointment 0.2%
	Triamcinolone acetonide	Cream, ointment, or lotion 0.1% or 0.020%

-continued

Potency	Compound	Formulation
Low	Hydrocortisone	Cream, ointment, or lotion 1.0% or 2.5%

[0312] The concentrations of corticosteroid drugs, as presented in the above table are provided herein only as example, and any therapeutically effective concentration of such corticosteroids can be incorporated in the composition of the present invention.

[0313] Since all corticosteroid drugs are typically hydrophobic, the carrier of the present invention, comprising a hydrophobic solvent, is most suitable as a vehicle to facilitate better topical distribution and an enhanced rate of penetration of any of the above listed drugs. Furthermore, the intrinsic antiviral, antibacterial and antiinflammatory effects of the foam adjuvant agents; i.e., fatty alcohols and acids, provides a combined effect that should result in a better therapeutic response to treatment.

[0314] Psoriasis is a very common chronic skin disease, which may be the target of treatment using the composition of the present invention. It is marked by periodic flare-ups of sharply defined red patches covered by a silvery, flaky surface.

[0315] Corticosteroid ointments, greasy preparations containing little or no water, are commonly used for treating psoriasis. Their main disadvantage is in their sticky feeling, which remains so long after treatment is over. By contrast, the foam of the present invention, while comprising considerable concentration of an oil (hydrophobic solvent), spreads very easily throughout the afflicted area and absorbs into the skin without leaving any untoward sensation or look. Examples of other inflammatory disorders, which can be treated by the composition of the present invention, wherein the drug is a steroid are atopic dermatitis, seborrhea, seborrheic dermatitis of the face and trunk, seborrheic blepharitis, contact dermatitis, stasis dermatitis (gravitational eczema; varicose eczema), exfoliative dermatitis (erythroderma), lichen simplex chronicus, *pityriasis rosea* and pemphigus.

[0316] Topical antihistaminic preparations currently available include 1% and 2% diphenhydramine (Benadlyl® and Caladryl®), 5% doxepin (Zonalon®) cream, phrilamine maleate, chlorpheniramine and tripelennamine, phenothiazines, promethazine hydrochloride (Phenergan®) and dimethindene maleate. These drugs, as well as additional antihistamins can also be incorporated in the composition of the present invention.

[0317] It is 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.

[0318] A second class of anti-inflammatory agents, which is useful in the foam of the present invention, includes the nonsteroidal 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:

[0319] 1) Oxicams, such as piroxicam, isoxicam, tenoxicam, sudoxicam;

[0320] 2) Salicylates, such as salicylic acid, ethyl salicylate, methyl salycilate, aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal;

[0321] 3) Acetic acid derivatives, such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acematacin, fentiazac, zomepirac, clindanac, oxepinac, felbinac, and ketorolac;

[0322] 4) Fenamates, such as mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acids;

[0323] 5) Propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indopropfen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic; and

[0324] 6) Pyrazoles, such as phenylbutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

[0325] Any further steroidal and nonsteroidal 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.

[0326] The pharmaceutical composition of the present invention may also comprise an antiinflammatory or antiallergic agent, wherein said agent reduces the occurrence of pro-inflammatory cytokines or inhibits the effect of pro-inflammatory cytokines.

[0327] Mixtures of such anti-inflammatory agents may also be employed, as well as the dermatologically acceptable salts, esters, amides, prodrugs and derivatives of these agents.

[0328] Topical application of a foam, comprising a safe and effective dose of an NSAID can be useful in the prevention and/or alleviation of the symptoms of rheumatoid arthritis, osteoarthritis and pain. Topical NSAIDs, incorporated in the foam of the present invention can be also used in the treatment of dermatological disorders, such as acne, rosacea, hair growth disorders, actinic keratosis and certain skin cancer conditions.

Topical Anesthetics

[0329] The compositions of the present invention may contain a safe and effective amount of a topical anesthetic. Examples of topical anesthetic drugs include benzocaine, lidocaine, bupivacaine, chlorprocaine, dibucaine, etidocaine, mepivacaine, tetracaine, dyclonine, hexylcaine, procaine, cocaine, ketamine, pramoxine, phenol, and pharmaceutically acceptable salts thereof. Mixtures of such anesthetic agents may be synergistically beneficial.

Keratolytically Active Agents

[0330] The term "keratolytically active agent" is used herein to mean a compound which loosens and removes the stratum corneum of the skin, or alters the structure of the keratin layers of skin.

[0331] Keratolytically active agents are used in the treatment of many dermatological disorders, which involve dry skin, hyperkeratiinization (such as prsoriasis), skin itching (such as xerosis), acne and rosacea.

[0332] Suitable keratolytically active agent include phenol and substituted phenolic compounds. Such compounds are known to dissolve and loosen the intracellular matrix of the

hyperkeratinized tissue. As such, they are used in the treatment of dermatological disorders. 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. These compounds also exhibit antiseptic properties. Cresols also possess bactericidal and keratolytic properties.

[0333] Vitamin A and its derivatives, such as retinoic acid, isoretinoic acid, retinol and retinal are another preferred class of keratolytically active agents.

[0334] 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 pharmaceutically acceptable derivatives, which typically possess anti-inflammatory, as well as keratolytic, activity.

[0335] Yet, another class of preferred keratolytically active agents includes urea and its derivatives.

Retinoids

[0336] Another preferred group of active agents comprise retinol, retinal, all trans retinoic acid and derivatives, isomers and analogs thereof, collectively termed "retinoids." Etretinate, actiretin, isotretinoin, adapalene and tazarotene are further examples of said retinoid isomers and analogs. Compositions according to the present invention, which contain retinoids as the active drug, can be used for the treatment of acne, seborrhea, various dermatoses, inflammation of the skin, mucosal membranes, vagina and the rectum, psoriasis, actinic keratosis and skin cancers, by application onto the affected area.

Insecticide and Insect Repellents Agents

[0337] Insects, such as mosquitoes, biting flies, mites, gnats, fleas, chiggers, punkies, sand flies, lice and ticks can be annoying and sometimes pose a serious risk to human and animal health. In certain areas of the United States, mosquitoes can transmit diseases like equine and St. Louis encephalitis. Biting flies can inflict a painful bite that can persist for days, swell, and become infected. Ticks can transmit serious diseases like Lyme disease and Rocky Mountain Spotted Fever.

[0338] There are several types of insect repellents to use when protecting people and animals from flying or biting insects, spiders, ticks and mites. By way of example, these may include DEET (N, N-diethyl-m-toluamide), dimethyl phthalate, piperonyl butoxide and permethrin. Insect repelling terpenoids, have been reported by Hwang, et al., J. Chem. Ecol., 11, 1297 (1985); and Ruledge, J. Am. Mosquito Control Assoc. 4, 414 (1988).

[0339] A particularly preferred group of insect repellents includes the terpenoid compounds, described in U.S. Pat. No. 5,411,992, including:

[0340] (1) Terpenoid-alcohol or terpene-ols are terpenoids which have at least one hydroxyl group. Examples of terpene-ols include: $C_{10}H_{16}O$ compounds, perillyl alcohol, carveol, myrtenol, and cis-verbenol; $C_{10}H_{18}O$ compounds, myrtanol, iso-pinocampheol, dihydrocarveol, isopulegol, terpineol, terpinen-4-ol, nerol, geraniol, and linalool, and $C_{10}H_{20}O$ compounds, menthol, beta-citronellol, and dihydro-myrcenol;

[0341] (2) Terpenoid-esters are terpenoids, which have at least one ester group which is the product of the bonding of the hydroxyl group of a terpene-ol with an aliphatic carboxylic acid that can contain functional groups such as the hydroxyl or amine on the aliphatic chain. Examples of suitable aliphatic carboxylic acids include acetic acid, propionic acid, lactic acid, and various amino acids. Examples of terpenoid-esters include: carvyl acetate, carvyl propionate, and menthyl lactate; and

[0342] (3) Essential oils which contain terpenoids and perfumes which contain terpenoids. Non-limiting examples of essential oils which have high content of terpene-ols and esters include bergamot (62% terpenoids); sage (>50% terpenoids); styrax (>50% terpenoids); peppermint (>50% terpenoids); and pine Siberian (75% terpenoids %). Terpenes, aldehydes and ketones vary in their usefulness but as a general group have potential as insect-repellent.

[0343] The foam of the present invention is particularly suitable for the effective uniform spreading of an insect repellent agent onto large areas of the skin of humans and animals. The hydrophobic solvent present in the foam composition helps retain the insect repellent on the skin surface for an extended period of time.

[0344] Yet, in a further embodiment, the foam is suitable for delivery of insect-killing agents (insecticides) to an afflicted external surface area of humans and animals. Thus, the pharmaceutical or cosmetic composition may comprise an insecticide, known in the art of parasitology. By way of example, such insecticide can be selected selected from the group of permethrin, hexachlorobenzene, carbamate, naturally occurring pyrethroids, permethrin, allethrin, malathion, piperonyl butoxide and any combination thereof at a therapeutically effective concentration. Its application is very convenient and it spreads easily, even over hairy areas. The hydrophobic solvent present in the foam composition helps retain the insecticide on the treated area for an extended period of time. Furthermore, the presence of a hydrophobic solvent in the foam eases mechanical removal of lice and nits with a comb.

Anti-Cancer Drugs

[0345] Anti-cancer drugs can also be used according to the present invention as the drug of choice from skin malignant tumors, such as basal cell carcinoma, squamous sell carcinoma, melanoma and Kaposi's sarcoma, as well as the pre-cancerous condition actinic keratosis. In certain cases, topical cytotoxic and antiproliferative drugs are used to treat or prevent such cancers, including 5-fluorouracil, also called 5-FU. 5-FU, as well as any other anti-cancer agents, know in the art of cancer medicine, can be incorporated in the foam at therapeutically effective levels.

[0346] A preferred family of anticancer drugs, suitable for usage in the foam of the present formulation comprises antiestrogens, such as tamoxifen. Tamoxifen blocks the effects of the hormone estrogen in the body. It is used to prevent or delay the return of breast cancer or to control its spread.

Photodynamic Therapy Agents

[0347] The foam composition of the present invention is also useful to deliver photo-sensitizing agents, known in the

art of photodynamic therapy. By way of example, such photosensitizers can be selected from the group comprising modified porphyrins, chlorins, bacteriochlorins, phthalocyanines, naphthalocyanines, pheophorbides, purpurins, m-THPC, mono-L-aspartyl chlorin e6, bacteriochlorins, phthalocyanines, benzoporphyrin derivatives, as well as photosensitiser precursors, such as aminolevulinic acid (ALA).

Active Agents for Burns, Wounds, Cuts and Ulcers

[0348] The treatment of burns, wounds, cuts and ulcers, using the composition of the present invention is particularly advantageous. The foam can include both anti-infective agents (against bacteria, fungi and/or viruses), antiinflammatory agents (steroidal and/or NSAIDs) and pain relieving components. Upon application, the foam spreads easily, covering the surface of the affected area, and without causing pain.

Skin Care Active Agents

[0349] The foam of the present invention is useful and advantageous for skin care and cosmetic care. The combination of oil and water, having moisture-retaining properties, in a spreadable foam form, can be used to substitute currently used cosmetic skin care creams, lotions, gels, etc. The cosmetic foam compositions of the present invention 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.

[0350] The CTFA Cosmetic Ingredient Handbook describes a wide variety of nonlimiting 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, antimicrobial agents (e.g., iodopropyl butylcarbamate), antioxidants, 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 eicosene 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 glycyrrhizinate), skin treating agents, thickeners, and vitamins and derivatives thereof.

[0351] In any embodiment of the present invention, however, the active agents useful herein can be categorized by the benefit they provide or by their postulated mode of action. 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 to that particular application or applications listed.

Anti-Acne Active Agents

[0352] The compositions of the present invention may contain a safe and effective amount of one or more pharmaceutically or cosmetically acceptable anti-acne active agents. 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 azelaic acid derivatives, antibiotic agents, such as erythromycin and clyndamycin, zinc salts and complexes, and combinations thereof, in a therapeutically effective concentration.

Anti-Wrinkle Active Agents/Anti-Atrophy Active Agents and Agents to Treat Dry and Scaly Skin (Xerosis and Ichthyosis)

[0353] The compositions of the present invention may further contain a safe and effective amount of one or more anti-wrinkle actives or anti-atrophy actives, which can be easily delivered by spreading a foam onto the skin. 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; thiols; hydroxy 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; lysophosphatidic 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, nicotinyl 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.

Anti-Oxidants/Radical Scavengers

[0354] A safe and effective amount of an anti-oxidant/radical scavenger may be added to the compositions of the subject invention, preferably from about 0.1% to about 10% (w/w), more preferably from about 1% to about 5% (w/w), of the composition.

[0355] 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 hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under the tradename Trolox.sup.®), gallic acid and its alkyl esters, especially propyl gallate, uric acid and its salts and alkyl esters, sorbic acid and its salts, lipoic acid, amines (e.g., N,N-diethylhydroxylamine, amino-guanidine), sulfhydryl

compounds (e.g., glutathione), dihydroxy fumaric acid and its salts, lycine pidolate, arginine pilolate, nordihydroguaiaretic acid, bioflavonoids, curcumin, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape skin/seed extracts, melanin, and rosemary extracts may be used.

[0356] The foam of the present invention is suitable for delivering skin protecting and revitalizing anti-oxidants/radical scavengers. 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 solvent comprises in full or in part, a solvent, selected from the group of emollients, silicone oil and oils, rich in unsaturated fatty acids, thus, affording a synergistic therapeutic effect of the anti-oxidants/radical scavenger agent and the vehicle components.

Self-Tanning Active Agents

[0357] The foam of the present invention is particularly suitable for the uniform delivery of a tanning active agent onto large areas of the skin. It is preferable that the compositions contain from about 0.1% to about 20%, more preferably from about 2% to about 7%, and still more preferably from about 3% to about 6%, of the composition, of dihydroxyacetone, or any other compound, know in the art as an artificial tanning active agent.

Skin Lightening and Whitening Agents

[0358] The foam of the present invention is particularly suitable for the uniform delivery of a skin lightening agent. When used, the compositions preferably contain from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, of the composition, of a skin-lightening agent. Suitable skin lightening or whitening agents include those known in the art, including hydroquinone, azelaic acid and other related dicarboxylic acids, and salts and derivatives thereof, retinoids, kojic acid, arbutin, nicotinic acid and its precursors, salts and derivatives, arbutin, ascorbic acid and salts and derivatives thereof (e.g., magnesium ascorbyl phosphate or sodium ascorbyl phosphate), and herbal extracts (e.g., licorice extract, mulberry extract, placental extract).

[0359] In one or more embodiments of the present invention, the foam composition comprises a combination of a skin whitening agent and a sunscreen agent.

[0360] In one or more embodiments of the present invention, the foam composition comprises a combination of a skin whitening agent and an inorganic sunscreen agent. When inorganic sunscreen agents, e.g. TiO_2, are rubbed onto the skin, they leave a white coating, which provides an immediate (although transient) whitening effect, which is highly desirable by the consumer, who wishes to see instant change in his/her appearance. The whitening agent, in combination with the inorganic sunscreen agent in the foam carrier can be easily and uniformly distributed on the skin surface, thereby affording an even instant whitening effect, unlike creams that are difficult to spread evenly on skin areas.

Sunscreens

[0361] Exposure to ultraviolet light can result in excessive scaling and texture changes of the stratum corneum. The foam of the present invention is advantageous for the delivery of sunscreen agents. Its application is very convenient and it spreads easily over large skin areas. The presence of a hydrophobic solvent in the foam ensures long lasting effect, even while bathing.

[0362] As used herein, "sunscreen active" or "sunscreen agent" includes both sunscreen agents and physical sunblocks. Suitable sunscreen actives may be organic or inorganic.

[0363] Inorganic sunscreens useful herein include the following metallic oxides; titanium dioxide having an average primary particle size of from about 15 nm to about 100 nm, zinc oxide having an average primary particle size of from about 15 nm to about 150 nm, zirconium oxide having an average primary particle size of from about 15 nm to about 150 nm, iron oxide having an average primary particle size of from about 15 nm to about 500 nm, and mixtures thereof. When used herein, the inorganic sunscreens are present in the amount of from about 0.1% to about 20%, preferably from about 0.5% to about 10%, more preferably from about 1% to about 5%, of the composition.

[0364] A wide variety of conventional organic sunscreen actives are suitable for use herein. Specific suitable sunscreen actives include, for example: p-aminobenzoic acid, its salts and its derivatives (ethyl, isobutyl, glyceryl esters; p-dimethylaminobenzoic acid); anthranilates (i.e., o-aminobenzoates; methyl, menthyl, phenyl, benzyl, phenylethyl, linalyl, terpinyl, and cyclohexenyl esters); salicylates (amyl, phenyl, octyl, benzyl, menthyl, glyceryl, and di-pro-pyleneglycol esters); cinnamic acid derivatives (menthyl and benzyl esters, a-phenyl cinnamonitrile; butyl cinnamoyl pyruvate); dihydroxycinnamic acid derivatives (umbelliferone, methylumbelliferone, methylaceto-umbelliferone); trihydroxy-cinnamic acid derivatives (esculetin, methylesculetin, daphnetin, and the glucosides, esculin and daphnin); hydrocarbons (diphenylbutadiene, stilbene); dibenzalacetone and benzalacetophenone; naphtholsulfonates (sodium salts of 2-naphthol-3,6-disulfonic and of 2-naphthol-6,8-disulfonic acids); di-hydroxynaphthoic acid and its salts; o- and p-hydroxybiphenyldisulfonates; coumarin derivatives (7-hydroxy, 7-methyl, 3-phenyl); diazoles (2-acetyl-3-bromoindazole, phenyl benzoxazole, methyl naphthoxazole, various aryl benzothiazoles); quinine salts (bisulfate, sulfate, chloride, oleate, and tannate); quinoline derivatives (8-hydroxyquinoline salts, 2-phenylquinoline); hydroxy- or methoxy-substituted benzophenones; uric and violuric acids; tannic acid and its derivatives (e.g., hexaethylether); (butyl carbotol) (6-propyl piperonyl) ether; hydroquinone; benzophenones (oxybenzene, sulisobenzone, dioxybenzone, benzoresorcinol, 2,2',4,4'-tetrahydroxybenzophenone, 2,2'-dihydroxy-4,4'-dimethoxybenzophenone, octabenzone; 4-isopropyldibenzoylmethane; butylmethoxydibenzoylmethane; etocrylene; octocrylene; [3-(4'-methylbenzylidene bornan-2-one), terephthalylidene dicamphor sulfonic acid and 4-isopropyl-di-benzoylmethane.

[0365] A safe and effective amount of the organic sunscreen active is used, typically from about 1% to about 20%, more typically from about 2% to about 10% of the composition. Exact amounts will vary depending upon the sunscreen or sunscreens chosen and the desired Sun Protection Factor (SPF).

Agents for Hair Growth Disorders

[0366] Agents, which affect the pattern of hair growth, can be suitably incorporated in the foam of the present invention. Male pattern baldness (MPB), the commonest cause of balding, is induced by the activity of the male hormone dihydrotestosterone (DHT), which converted from the hormone testosterone by the enzymes 5 alpha reductase. Current treatments of MPB include minoxidil and agents, which inhibit 5 alpha reductase, such as finasteride, spironolactone, azelaic acid and azelaic acid derivatives and salts. Such agents, as well as other agents known in the art, can be incorporated in the foam of the present invention.

[0367] It is further pointed out that polyunsaturated fatty acids, i.e., such which include any of the essential fatty acids (EFA's): linoleic and linolenic acid, gamma-linoleic acid (GLA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are also known to contribute to hair growth. Thus in a preferred embodiment, a hair growth foam is provided, wherein the hydrophobic solvent comprises in full or in part, an oil, rich in such unsaturated fatty acids.

[0368] Figure-Forming Agents; Agents to Treat Cellulite/Slimming

[0369] Figure forming agents such as used in the treatment of cellulite and in slimming products, can be suitably incorporated in the foam of the present invention. A non-limiting exemplary list of active agents, known in the treatment of cellulite and in the induction of a slimming effect include herbal extracts, such as baldderwack extract, butcher's, broom, cayenne, dandelion, red clover, *ginkgo biloba*, horse chestnut, witch hazel and borage oil, omega 3 and omega 6 oils, caffeic acid and salts and derivatives thereof, xanthine agents, such as caffeine, theophiline and pentoxyphilline, and nicotinic acid and salts and derivatives thereof.

Agents to Treat Sunburn, Heat Burn, Radiation Burn, Rash and Itch

[0370] Cosmetic and pharmaceutical ingredients which are known in the art of pharmacology and cosmetology to treat dermatitis, minor skin irritations, sunburn, heat burn, radiation burn, and inhibit inflammation can be beneficially incorporated in the foam of the present invention.

[0371] Examples of such active agents include chamomile extract (*matricaria recutitia*), cucumber distillate (*cucumis sativus*), lavender water (*lavendula angustifolia*), rose water (*rosa damascena*), witch hazel (*hamamelis virginiana*), allantoin, bisabolol, rosehip oil, calendula oil, azulaene, menthol and camphor.

Use of the Foam as a Lubricating and Protective Foam

[0372] There are several potential uses of the foam, particularly the silicone-oil based foam, as a lubricating foam. Typical examples are shaving foam, moisture protection foam and antifriction foam. For such purposes, the foam can be used in its basic composition (without additional formulation aids and active ingredients), or with the addition of such additives.

Foam for Neutralization and/or Decontamination of Hazardous Chemicals and Treatment of Heat Burns

[0373] It has been reported that povidone iodine antiseptic, a popular iodine product, can ameliorate damage to guinea pig skin exposed to mustard gas and other chemical irritants and further reduces, and many times prevents, damage to human skin after accidental heat burns caused by hot water, oil or hot steam.

[0374] Other active compound, having decontamination abilities, comprise strong oxidants and free radical liberating compounds, such as hydrogen oxide, bleaching agents (e.g., sodium, calcium or magnesium hypochloride and the like) iodine, chlorohexidine and benzoyl peroxide.

[0375] The alcohol-free foam of the present invention, comprising one or more of the above decontaminating and neutralizing agents can be applied onto the contaminated skin to form a preventive layer, prior to contamination measure or as a decontamination/neutralization means, right after contamination has occurred.

Penetration Enhancers

[0376] A penetration enhancer or permeation enhancer is an agent used to increase the permeability of the skin to a pharmacologically active agent to increase the rate at which the drug diffuses through the skin and enters the tissues and bloodstream. A chemical skin penetration enhancer increases skin permeability by reversibly altering the physiochemical nature of the stratum corneum to reduce its diffusional resistance. In a review of the technical and patent literature up to 1996, numerous chemical compounds were cited as skin penetration enhancers. Most of the compounds are generally recognized as safe (GRAS) ingredients that would often be considered inert by a formulator (Osborne, D. W., Henke, J. J., Pharmaceutical Technology, November 1997, pp 58-86).

[0377] Examples of penetration enhancers, according to the present invention include: polyols, such as propylene glycol, hexylene glycol, diethylene glycol, propylene glycol n-alkanols, terpenes, di-terpenes, tri-terpenes, terpen-ols, limonene, terpene-ol, 1-menthol, dioxolane, ethylene glycol, other glycols, and glycerol; sulfoxides, such as dimethylsulfoxide (DMSO), dimethylformanide, methyl dodecyl sulfoxide, dimethylacetamide; monooleate of ethoxylated glycerides (with 8 to 10 ethylene oxide units); Azone (1-dodecylazacycloheptan-2-one), 2-(n-nonyl)-1,3-dioxolane, esters, such as isopropyl myristate/palmitate, ethyl acetate, butyl acetate, methyl proprionate, capric/caprylic triglycerides, octylmyristate, dodecyl-myristate; myristyl alcohol, lauryl alcohol, lauric acid, lauryl lactate ketones; amides, such as acetamide oleates such as triolein; various surfactants, such as sodium lauryl sulfate; various alkanoic acids such as caprylic acid; lactam compounds, such as azone; alkanols, such as oleyl alcohol; dialkylamino acetates, and admixtures thereof.

[0378] Lower alcohols, such as ethanol, propanol, isopropanol, butanol, iso-butanol, t-butanol and pentanol are not considered appropriate penetration enhancers according to the present invention, due to their skin drying and irritation properties.

[0379] Yet, another preferred class of penetration enhancers is the cyclodextrins and related compounds. Cyclodextrins are structurally related cyclic oligomaltoses which form a new group of pharmaceutical excipients. These are torus-shaped molecules with a hydrophilic outer surface and a lipophilic central cavity. Cyclodextrins are capable of forming water-soluble inclusion complexes with a wide variety of lipophilic water-insoluble drugs by taking up a whole drug molecule, or some part of it, into the cavity. The cyclodextrin molecules are relatively large (molecular weight ranging from almost 1000 to over 1500), with a hydrated outer surface, and under normal conditions, cyclodextrin molecules will only permeate the skin barrier with considerable difficulty. It is generally believed that the cyclodextrin molecules act as true carriers by keeping lipophilic drug molecules in solution and deliver them to the skin surface where they partition from the cyclodextrin cavity into the skin.

Further Technical Parameters

[0380] The composition of the present invention may be contained in and dispensed from a container capable of withstanding the pressure of the propellant gas and having an appropriate valve/nozzle for dispensing the composition as foam under pressure. A customary liquefied or compressed gas propellant can be added, in the amount of about 5-25% of the total composition. Liquefied propellants are gases that exist as liquids under pressure, including high purity hydrocarbons such as propane, isobutane and n-butane, dimethyl ether and chlorofluorocarbons (CFCs). Compressed gasses are exemplified by air, nitrogen and carbon dioxide.

[0381] A specific embodiment according to the present invention comprises placing the composition of the present invention on a patch, occlusive tape or the skin-contact compartment of a transdermal delivery apparatus and applying such object onto the skin, in order to attain effective superficial treatment or enhanced penetration of the drug into the skin or through the skin.

[0382] Utilizing such strategy, one can apply drugs, which are currently administered systemically or that require transdermal delivery, in the preferred therapeutic system of the present invention. Examples for such drugs are nicotine, testosterone and other male hormones and male hormone precursors, estrogen and other female hormones and hormone precursors, growth hormone, insulin, caffeine, steroidal and non-steroidal antiinflammatory agents and thyroid hormone substitutes.

[0383] Other foamable compositions are described in: U.S. Patent Publication No. 2005/0232869, published on Oct. 20, 2005, entitled NONSTEROIDAL IMMUNOMODULATING KIT AND COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2005/0205086, published on Sep. 22, 2005, entitled RETINOID IMMUNOMODULATING KIT AND COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2006/0018937, published on Jan. 26, 2006, entitled STEROID KIT AND FOAMABLE COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2005/0271596, published on Dec. 8, 2005, entitled VASOACTIVE KIT AND COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2006/0269485, published on Nov. 30, 2006, entitled ANTIBIOTIC KIT AND COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2007/0020304, published on Jan. 25, 2007, entitled NON-FLAMMABLE INSECTICIDE COMPOSITION AND USES THEREOF; U.S. Patent Publication No. 2006/0193789, published on Aug. 31, 2006, entitled FILM FORMING FOAMABLE COMPOSITION; U.S. patent application Ser. No. 11/732,547, filed on Apr. 4, 2007, entitled ANTI-INFECTION AUGMENTATION OF FOAMABLE COMPOSITIONS AND KIT AND USES THEREOF; U.S. Provisional Patent Application No. 60/789,186, filed on Apr. 4, 2006, KERATOLYTIC ANTIFUNGAL FOAM; U.S. Provisional Patent Application No. 60/815,948, filed on Jun. 23, 2006, entitled FOAMABLE COMPOSITIONS COMPRISING A CALCIUM CHANNEL BLOCKER, A CHOLINERGIC AGENT AND A NITRIC OXIDE DONOR; U.S. Provisional Patent Application No. 60/818,634, filed on Jul. 5, 2006, entitled DICARBOXYLIC ACID FOAMABLE VEHICLE AND PHARMACEUTICAL COMPOSITIONS THEREOF; U.S. Provisional Patent Application No. 60/843,140, filed on Sep. 8, 2006, entitled FOAMABLE VEHICLE AND VITAMIN PHARMACEUTICAL COMPOSITIONS THEREOF, all of which are incorporated herein by reference in their entirety.

Stock Compositions

[0384] Non-limiting examples of how stock solutions are made up with and without active agent. Other stock solutions may be made using the same methodology by simply varying adding or omitting ingredients as would be appreciated by one of the ordinary skills in the art.

EXAMPLES

[0385] The invention is described with reference to the following examples. This invention is not limited to these examples and experiments. Many variations will suggest themselves and are within the full intended scope of the appended claims.

[0386] The general process, as typically exemplified in Example 1 may be applied in order to produce the composition of the present invention. The pharmaceutical carrier according to the present invention can also be used to prepare cosmetics for beauty purpose by adding into skin care agents and perfume.

Example 1—General Procedure for Preparing Foamable Composition

[0387] Aqueous Phase:

[0388] Water gelling agent and surface-active agent are dissolved in water, with agitation. The solution is warmed to 50-70° C. Water soluble cosmetic or pharmaceutical active ingredients and optional water soluble ingredients are added with agitation to the Aqueous Phase mixture.

[0389] Hydrophobic Phase:

[0390] The hydrophobic solvent is heated to same temperature. Foam adjuvant agent is added to preheated hydrophobic solvent. Oil soluble cosmetic or pharmaceutical active ingredients* and optional oil soluble formulation ingredients are added with agitation to the Hydrophobic Phase mixture.

[0391] The warm Hydrophobic Phase is gradually poured into the warm Aqueous Phase, with agitation, followed by Ultraturax homogenization. The mixture is allowed to cool down to ambient temperature. In case of heat sensitive active ingredients, the active ingredient is added with agitation to the mixture after cooling to ambient temperature. The mixture, at ambient temperature, is added to an aerosol container, the container is sealed and appropriate amount of propellant (5-25 w % of the composition mass) is added under pressure into the container.

Example 2—Vegetable Oil-Based Foam Carrier Composition

[0392]

	Ingredient	Version No. 1	Version No. 2	Version No. 3
		% (W/W)		
Hydrophobic solvent	Soybean oil	40	30.5	20
Water	Water	48.5	32.5	61
Foam adjuvant agent	Stearyl Alcohol	0.8	1.05	0.73
Surface-active agent	Sucrose ester SP70	0.64	0.45	0.8
Water gelling agent	Xanthan Gum	0.16	0.11	0.1
	Methocel ELV15	0.32	0.22	0.28
Other Ingredients	Antioxidant	0.02	0.02	0.02
	Preservatives	0.3	0.3	0.3
	Fragrance	0.2	0.2	0.2
Foam Specific gravity (gr/mL)		0.10	0.15	0.065

[0393] The compositions use a non-ionic surfactant and contain a combined amount of surface-active agent, foam adjuvant and water gelling agent ranging from 1.83% to 1.92% (w/w). The foam of this example is useful as a carrier of active pharmaceutical and/or cosmetic active ingredients, as exemplified below. It also can be used as a protective product. Additionally, it is also useful as lubricating foam, for various purposes.

Example 3—Silicone Oil-Based Foam Carrier Composition

[0394]

	Specific Ingredient	Version No. 1 % (W/W)	Version No. 2 % (W/W)
Hydrophobic solvent	Dimethicone 350*	25	10
Water	Water	72	87
Foam adjuvant agent	Stearyl Alcohol	0.2	0.2
Surface-active agent	Sucrose ester SP70	0.8	—
	Myrj 49P	—	0.8
Water gelling agent	Xanthan Gum	0.2	0.2
	Methocel ELV15	0.4	0.4
Other Ingredients	Antioxidant	0.02	0.02
	Preservatives	1	1
	Fragrance	0.2	0.2
Foam Specific gravity (gr/mL)		0.10	ND

*Dimethylpolysiloxane of 350 cps viscosity.

[0395] The compositions use only non-ionic surfactant and contain a combined amount of surface-active agent, foam adjuvant and water gelling agent of 1.6% (w/w). The foam of this example is useful as a carrier of active pharmaceutical and/or cosmetic active ingredients, as exemplified below. It also can be used as a protective product. Additionally, it is also useful as lubricating foam, for various purposes.

Example 4—Mineral Oil-Based Foam Carrier Composition

[0396]

	Ingredient	Version No. 1 % (W/W)	Version No. 2 % (W/W)	Version No. 3 % (W/W)	Version No. 4 % (W/W)	Version No. 5 % (W/W)
Hydrophobic solvent	Mineral oil	69	50	50	25	25
Water	Water	28.4	46.7	46.7	71.88	71.9
Foam adjuvant agent	Stearyl Alcohol	0.7	1	1	0.5	0.5
Surface-active agent	Sucrose ester SP70	0.4	0.64	0	0.8	0
	PEG S-40	0	0	0.64	0	0
	Polysorbate-60	0	0	0	0	0.8
Water gelling agent	Xanthan Gum	0.1	0	0.14	0.2	0.2
	Methocel ELV15	0.2	0.4	0.32	0.4	0.4
Other Ingredients	Antioxidant	0.02	0.02	0.02	0.02	0.02
	Preservatives	1	1	1	1	1
	Fragrance	0.2	0.2	0.2	0.2	0.2
Foam Specific gravity (gr/mL)		ND	ND	ND	ND	0.1

[0397] The compositions use only non-ionic solvents, and the total amount of surface active agent, foam adjuvants and water gelling agents ranges from 1.4 to 2.1% (w/w). The foam of this example is useful as a carrier of active pharmaceutical and/or cosmetic active ingredients, as exemplified in examples below. It is also useful as lubricating foam, for various purposes.

Example 5—Mixed Oils Foam Carrier Composition

[0398]

	Ingredient	Version No. 1 25% Oil	Version No. 2 12.5% Oil
Hydrophobic solvent	Mineral oil	11.2%	5.6%
	Isopropyl myristate	5.0%	2.5%
	MCT oil	7.5%	3.8%
Foam adjuvant agent	Stearyl Alcohol	0.5%	0.25%
Water	Water	73.0%	85.2%
Surface-active agent	Sucrose ester SP70	0.8%	0.8%
	Distilled monoglyceride	1.2%	0.6%
	Sodium lauryl sulphate	0.1%	0.1%
Water gelling agent	Xanthan Gum	0.3%	0.3%
	Methocel ELV15	0.6%	0.6%

[0399] The foams of this example have a non-ionic surfactant to ionic surfactant ratio (w/w) of 20:1 and 14:1 for versions 1 and 2, respectively. Total amounts of surface active agent foam adjuvant and water gelling agent is in the range of 1.75-3.5 (w/w). It is useful as a carrier of active pharmaceutical and/or cosmetic active ingredients, as exemplified in examples below. It is also useful as lubricating foam, for various purposes.

[0400] The following examples, representing optional drug-containing foams, are prototype formulations, which have not been optimized for stability and inter-component compatibility. Such optimization is a customary need, which can be done, using means, known to those skilled in the art of pharmaceutical formulation.

Example 6—Antibacterial Foam Composition

[0401]

Ingredient	Version 1 "Mupirocin"	Version 2 "Triple Antibiotic"	Version 3 "Fucidic Acid"	Version 4 "Metro-nidazole"	Version 5 "Triple Antibiotic"
Carrier Ingredients					
Mineral oil	48.8%	11.2%	48.8%	5.6%	5.6%
Isopropyl myristate		5.0%		2.5%	2.5%
MCT oil		7.5%		3.8%	3.8%
Stearyl Alcohol	0.8%	0.5%	0.8%	0.25%	0.25%
Water	50%	73.0%	50%	85.2%	85.2%
Sucrose ester SP70	0.8%	0.8%	—		0.8%
Myrj 40	—		0.8%	—	—
Distilled monoglyceride		1.2%		0.6%	0.6%
Tween 60				0.8%	
Sodium lauryl sulphate	0.05%	0.1%	0.1%		
Xanthan Gum	0.2%	0.3%	0.2%	0.3%	0.3%
Methocel ELV15	0.2%	0.6%	0.2%	0.6%	0.6%
Active Ingredients					
Mupirocin	2%				
Polymyxin B Sulfate		10,000 Units/gr			10,000 Units/gr
Bacitracin Zinc		500 Units/gr			500 Units/gr
Neomycin Sulfate*		0.05%			0.05%
Pramoxine HCl		1%			1%
Fucidic acid			2%		
Metronidazole				1%	

[0402] The foams of this example contain 100% non-ionic surfactant or have a non-ionic surfactant to ionic surfactant ratio ranging from 20:1 to 8:1. Total amounts of surface active agent, foam adjuvant and water gelling agent ranges from 2.05-3.5% (w/w). It is useful for the treatment of bacterial skin infection (general), cellulites, open wounds, cutaneous abscesses, furuncles, insect bite, impetigo, acne, acne-rosacea, and *trichomonas* vaginitis.

[0403] In certain embodiments, the foam of this example is useful for the prevention, decontamination and/or neutralization hazardous bacterial infestation (such as warfare organisms).

Example 7—Antifungal Foam Composition

[0404]

Ingredient	Version 1 "Terbinafine"	Version 2 "Clotrimazole"	Version 3 "Nystatin"	Version 4 "Nystatin"
Carrier Ingredients				
Mineral oil	48.8%	11.2%	48.8%	5.6%
Isopropyl myristate		5.0%		2.5%
MCT oil		7.5%		3.8%
Stearyl Alcohol	0.8%	0.5%	0.8%	0.25%
Water	50%	73.0%	50%	85.2%
Sucrose ester SP70	0.8%	0.8%	—	0.8%
Myrj 40	—		0.8%	—
Tween 80				0.8%
Distilled monoglyceride		1.2%		0.6%
Sodium lauryl sulphate	0.05%	0.1%	0.1%	
Xanthan Gum	0.2%	0.3%	0.2%	0.3%
Methocel ELV15	0.2%	0.6%	0.2%	0.6%
Active Ingredients				
Terbinafine	1%			
clotrimazole		2%		
Nystatin			100,000 Units/gr	100,000 Units/gr

[0405] The foams of this example have 100% non-ionic surfactant or have a non-ionic surfactant to ionic surfactant ratio ranging from 20:1 to 8:1. Total surface active agent, foaming adjuvant and water gelling agent ranges from 2.05 to 3.5% (w/w). It is useful in the treatment of dermatophyte infections, Tinea corporis, Tinea pedis, Tinea *rubrum*, Tinea unguium, Tinea cruris, Tinea barbae, and yeast infections, such as Candidiasis, *Tinea versicolor* and Candidal vaginitis.

Example 8—Corticosteroid Foam Composition

[0406]

Ingredient	Version 1 "Hydrocortisone"	Version 2 "Betamethasone"	Version 3 "Dexamethasone"
Carrier Ingredients			
Mineral oil	48.8%	11.2%	5.6%
Isopropyl myristate		5.0%	2.5%
MCT oil		7.5%	3.8%
Stearyl Alcohol	0.8%	0.5%	0.25%
Water	50%	73.0%	85.2%
Sucrose ester SP70	0.8%	0.4%	0.8%
Tween 80		0.4%	
Distilled monoglyceride		1.2%	0.6%
Sodium lauryl sulphate	0.05%		0.1%
Xanthan Gum	0.2%	0.3%	0.3%
Methocel ELV15	0.2%	0.6%	0.6%
Active Ingredients			
Hydrocortisone	1%		
Betamethasone dipropionate		0.05%	
Dexamethasone acetate			0.1%

Ingredient	Version 4 "Triamcinolone"	Version 5 "Flumetasone"
Carrier Ingredients		
Mineral oil	48.8%	48.8%
Stearyl Alcohol	0.8%	0.8%
Water	50%	50%
Sucrose ester SP70	0.8%	0.8%
Sodium lauryl sulphate	0.05%	0.05%
Xanthan Gum	0.2%	0.2%
Methocel ELV15	0.2%	0.2%
Active Ingredients		
Triamcinolone acetonide	0.1%	
Flumetasone pivalate		0.02%

[0407] The foams of this example have either 100% non-ionic surfactant or have a non-ionic surfactant to ionic surfactant ratio ranging from 20:1 to 16:1. Total surface active agent, foaming adjuvant and water gelling agent ranges from 2.05 to 3.5% (w/w), Indications include psoriasis, contact dermatitis, atopic dermatitis, seborrheic dermatitis, nummular dermatitis, inflammatory acne, chronic dermatitis of the hands and feet, generalized exfoliative dermatitis, stasis dermatitis, lichen simplex chronicus, herpes gestationis and pruritic urticarial papules and plaques of pregnancy.

Example 9—Antiviral Foam Composition

[0408]

Ingredient	Version 1 "Acyclovir"	Version 2 "Acyclovir"	Version 3 "α-Interferon"
Carrier Ingredients			
Mineral oil	48.8%	11.2%	5.6%
Isopropyl myristate		5.0%	2.5%
MCT oil		7.5%	3.8%
Stearyl Alcohol	0.8%	0.5%	0.25%
Water	50%	73.0%	85.2%
Sucrose ester SP70		0.8%	0.8%
Tween 80	0.8%		
Distilled monoglyceride		1.2%	0.6%
Sodium lauryl sulphate			0.1%
Xanthan Gum	0.2%	0.3%	0.3%
Methocel ELV15	0.2%	0.6%	0.6%
Active Ingredients			
Acyclovir	5%	5%	
α-Interferon			105 IU/g

[0409] The foams of this example have either 100% non-ionic surfactant or have a non-ionic surfactant to ionic surfactant ratio of 14:1. Total surface active agent, foaming adjuvant and water gelling agent ranges from 2.05 to 3.5% (w/w). Indications include Herpes simplex, Herpes zoster, Herpes gestationis and Herpes simplex genital ulcers.

Example 10—Insect Repellent Foam Composition

[0410]

Ingredient	%
Isopropyl myristate	2.0%
MCT oil	2.0%
Stearyl Alcohol	1.2%
Water	64.0%
Sucrose ester SP70	0.8%
Sodium lauryl sulphate	0.1%
Xanthan Gum	0.3%
Methocel ELV15	0.6%
Propylene glycol	15%
DEET	15%

Example 11—Comparative Tolerability and Acceptability Study of a Corticosteroid Foam Composition Vs. a Conventional Ointment

[0411] A panel of eight testers was requested to apply about 0.5 gr. of the foam preparation of example 10, Version 2 on one arm and 0.5 gr. of commercial Betamethasone valerate ointment, in a double blind fashion. They were asked to describe their feeling about the ease of application, ease of spreading, spreadability and penetrability of each of the products and to give their general rating for each of the products on a scale of 0-3 (0=poor; 1=barely acceptable; 2=acceptable and 3=excellent).

[0412] As demonstrated in the following table, the foam preparation of example 10, Version 2 obtained higher rates in all aspects of the test.

Property	Foam Preparation Mean Rating	Commercial Betamethasone Valerate Ointment Mean Rating
Ease of application	2.3	1.6
Ease of spreading	2.5	1.9
Spreadability	2.9	1.2
Penetrability	2.0	1.5
Lack of sticky feeling	2.4	1.0
Lack of greasy feeling	2.2	1.0
Lack of shiny look	1.9	1.4
Overall rating	2.5	1.4

Example 12: Human Safety and Efficacy Study of a Corticosteroid Composition in Psoriasis Patients

[0413] Two patients with mild to moderate psoriasis were administered topically a Betamethasone 0.12% foam (example 10, Version 2) twice daily for two weeks. Both patients improved significantly, as manifested by clearance of the psoriatic plaques flattening of the thickened lesions. FIG. **1** provides an exemplary response to treatment in the elbows of one of these patients. While betamethasone is know for its effect in psoriasis, such a beneficial effect after 14 days treatment is exceptional. The accelerated effect was attributed to the improved convenience and therefore, improved compliance.

Example 13: Human Safety and Efficacy Study of a Corticosteroid Composition in Psoriasis Patients

[0414] Four patients with moderate to severe, disseminated atopic dermatitis were administered topically a Betamethasone 0.12% foam (example 10, Version 2) twice daily for two weeks. All patients improved significantly, as manifested by complete clearance of all treated lesions. FIG. **2** provides exemplary responses to treatment in different body areas, after 10 days of treatment. While betamethasone is know for its effect in atopic dermatitis, such a beneficial effect after 10 days treatment is exceptional. The patients claimed that the use of the foam of the present invention was significantly more convenient than the corresponding cream and ointment. Thus, the accelerated effect was attributed to the improved convenience and therefore, improved compliance.

Example 14—Foam Compositions with Urea

[0415]

Component	% w/w			
Mineral oil	6.00	6.00	6.00	6.00
Isopropylmeristat	6.00	6.00	6.00	6.00
Glyceryl monostearate	0.50	0.50	0.50	0.50
Stearyl alcohol	0.20	0.20	0.20	1.00
Urea	10.00	10.00	10.00	10.00
Xantan gum	0.30	0.30	0.30	0.30
Methocel K100M	0.30	0.30	0.30	0.30
Myrj 52				3.00
TWEEN 80				1.00
Myrj 49p			3.00	
TWEEN 60	1.00	1.00	1.00	
Cocamidopropylbetain	0.50	0.50		
Phenonip	0.30	0.30	0.30	0.30
Water	to 100.0	to 100.0	to 100.0	to 100.0

-continued

Component	% w/w			
Butane/propane	8.00	8.00	18.00	18.00
Foam Quality	E	E	E	E
Density	n/a	0.023	n/a	0.024

Example 15—Compositions with Various Penetration Enhancers

[0416]

Part A					
Component	% w/w				
Mineral oil	6.00	6.00	6.00	6.00	6.00
Isopropyl myristate	6.00	6.00	6.00	6.00	6.00
Glyceryl monostearate	0.50	0.50	0.50	0.50	0.50
Stearyl alcohol	1.00	1.00	1.00	1.00	1.00
Xantan gum	0.30	0.30	0.30	0.30	0.30
Methocel K100M	0.30	0.30	0.30	0.30	0.30
TWEEN 60	1.00				
TWEEN 80		1.00	1.00	1.00	1.00
MYRJ 49p	3.00	3.00	3.00	3.00	3.00
Propylene glycol		5.00			
Glycofurol			1.00	10.00	
Urea					10.00
Cocoamidopro-pylbethaine	0.50	0.50	0.50	0.50	0.50
Lidocain base	4.00	4.00	4.00	4.00	4.00
Phenonip	0.30	0.30	0.30	0.30	0.30
Water	to 100	to 100	to 100	to 100	to 100
Butane/propane	8	8	8	16	10
Foam Quality	E	E	E	E	E
Density	0.020	0.018	0.019	0.019	0.018

Part B		
Component	% w/w	% w/w
Isopropyl myristate	30.00	30.00
Glyceryl monostearate	0.50	0.50
Stearic acid	0.45	0.45
Xantan gum	0.30	0.30
Methocel K100M	0.30	0.30
TWEEN 80	1.00	1.00
MYRJ 49p	3.00	3.00
Cocoamidopropylbethaine	0.50	0.50
Transcutol p	20.00	20.00
Hydrophilic drug	Effective concentration	
Hydrophobic drug		Effective concentration
Phenonip	0.30	0.30
Water	to 100.0	to 100.0
Butane/propane	8.00	8.00
Foam Quality	E	E
Density	0.020	0.020

Example 16—Inflammability Test

[0417] According to European Standard prEN 14851 (sometimes referred to as the "AFNOR test"—AFNOR is Association Francaise de Normalisation) a product is considered inflammable if a stable flame appears following ignition, which is at least 4 cm high and which is maintained for at least 2 seconds. For the purpose of testing non-flammability a simplified test based on the European Standard test (titled "Aerosol containers—Aerosol foam flammability test") was used. Formulations that ignited for less

than 2 seconds and which showed a flame of up to 4 cm above the height of the foam or less were passed as were formulations that simply did not ignite. However, formulations where the flame was clearly greater than 4 cms were failed even if the flame burnt for less than 2 seconds. Formulations that burnt for longer than 2 seconds likewise failed.

[0418] 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±5° C. and relative humidity in the range of 30% to 80%.

[0419] Interestingly, it appears that the formulations, which burnt for longer than this period also burnt with a larger flame than 4 cms. Another initial trend observed was that apparently formulations that were not stabilized at 20 C may be more likely to ignite.

[0420] In setting up a system to measure flammability along the lines of the AFNOR test, a number of initial and minor but possibly potentially significant trends were observed. The first was that variability in results was noted when tests were undertaken without allowing the formulation to reach a settled equilibrium. In passing, it should be mentioned that from observations of foamable formulations in pressurized glass bottles such formulations take time to reach equilibrium and for example may thicken up considerably in texture overnight. Thus, results were more reproducible after formulations were allowed to reach equilibrium overnight in an incubator. Reproducibility was likewise improved by using larger canisters. Also, the incidence of ignition and flammability appeared to increase when the temperature was higher.

Example 17

[0421]

Part A -Formulations with different oil or oil like substance at 35% w/w

Ingredients	PFT002	PFT003	PFT004	PFT005
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)				35.00
light mineral oil			35.00	
Octyl dodecanol		35.00		
IPM (ISOPROPYL MYRISTATE)	35.00			
Glyceryl Monostearate	0.49	0.49	0.49	0.49
Sorbitane Stearate	0.65	0.65	0.65	0.65
Stearyl Alcohol	0.92	0.92	0.92	0.92
Steareth-21	2.17	2.17	2.17	2.17
PEG-40 Stearate	2.83	2.83	2.83	2.83
Methocel A4M	0.33	0.33	0.33	0.33
Xanthan gum	0.28	0.28	0.28	0.28
Polysorbate 80	0.98	0.98	0.98	0.98
Water purified	56.35	56.35	56.35	56.35
Total	100.00	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture *	8.00	8.00	8.00	8.00
Results				
Appearance				
Quality	G-E	G-E	G-E	G-E
Color	white	white	white	white
Odor	no odor	no odor	no odor	no odor
Shakability	good	good	good	good

* Three different propellant mixtures were used and tested and all the formulations provided good to excellent quality foam.

Part B - Flammability Test Results

	PFT002 35% IPM (ISOPROPYL MYRISTATE)	PFT003 35% Octyl dodecanol	PFT004 35% light mineral oil	PFT005 35% MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)
	8% 5515	8% 5515	8% 5515	8% 5515
sample weight (g)	6.00	7.40	7.60	5.80
Ignite	Y	Y	N	Y
Pass	Y	N	Y	Y
Fail*	N	Y	N	N
	8% 1681	8% 1681	8% 1681	8% 1681
sample weight (g)	10.00	6.60	7.40	8.90
Ignite	Y	Y	N	N

-continued

Pass	Y	N	Y	Y
Fail*	N	Y	N	N
	8% pinto	8% pinto	8% pinto	8% pinto
sample weight (g)	5.90	5.80	6.20 6.30	5.60
Ignite	N	N	N	N
Pass	Y	Y	Y	Y
Fail*	N	N	N	N

*Flame is for longer and or higher than the test limit; N = no; Y = yes

[0422] All the compositions were identical other than for the oil or emollient, which was 35% of the formulation. The foam compositions comprising light mineral oil, isopropyl myristate or MCT at 35% were all found to be non-inflammable according to the test parameters used irrespective of which propellant mixture was used. The octyl dodecanol formulation was apparently surprisingly sensitive to changes in the proportion of propane butane iso-butane mixture. Also surprising is that the octyl dodecanol formulation is sensitive to propellant at 35% w/w but not at 15% w/w and further unexpectedly it is noted that when octyl dodecanol is sensitive IPM is not sensitive. The same formula with 35% PPG 15 stearyl ether ignited with a flame that was higher than the test limit. Replacing the solid surfactants and foam adjuvants with liquid surfactants Laureth 4 (2%) and Span 80 (2%) and increasing the Polysorbate 80 to 2% did not reduce flammability of the 35% PPG formulation.

[0423] The foams produced with 1681 propellant mixture were viewed under the microscope and without being bound by any particular theory birefringence was observed and further in general terms non ignition coincided with some sort of structured order in the foam. By structured order, relatively repeatble cells of various sizes separated by a relatively similar interconnecting network is loosly intended.

Example 18

[0424]

Part A - Formulations -with different oil or oil like substance at 15% w/w

Ingredients	PFT007	PFT008	PFT009	PFT010
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)				15.00
light mineral oil			15.00	
Octyl dodecanol		15.00		
IPM (ISOPROPYL MYRISTATE)	15.00			
Glyceryl Monostearate	0.49	0.49	0.49	0.49
Sorbitane Stearate	0.65	0.65	0.65	0.65
Stearyl Alcohol	0.92	0.92	0.92	0.92
Steareth-21	2.17	2.17	2.17	2.17
PEG-40 Stearate	2.83	2.83	2.83	2.83
Methocel A4M	0.33	0.33	0.33	0.33
Xanthan gum	0.28	0.28	0.28	0.28
Polysorbate 80	0.98	0.98	0.98	0.98
Water purified	76.35	76.35	76.35	76.35
Total	100.00	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture*	8.00	8.00	8.00	8.00
Appearance				
Quality	G-E	G-E	G-E	G-E
Color	white	white	white	white
Odor	No odor	no odor	no odor	no odor
Shakability	good	good	good	good

*Three different propellant mixtures were used and tested and all the formulations provided good to excellent quality foam.

Part B - Flammabilty Test Results

	PFT007 15% IPM (ISOPROPYL MYRISTATE)	PFT008 15% Octyl dodecanol	PFT009 15% light mineral oil	PFT010 15% MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)
	8% 5515	8% 5515	8% 5515	8% 5515
sample weight (g)	7.20	5.10	7.50	7.30
Ignite	Y	Y	N	N

-continued

Pass	Y	Y	Y	Y
Fail*	N	N	N	N
	8% 1681	8% 1681	8% 1681	8% 1681
sample weight (g)	8.40	5.00	8.90	8.40
Ignite	Y	Y	N	N
Pass	N	Y	Y	Y
Fail*	Y	N	N	N
	8% pinto	8% pinto	8% pinto	8% pinto
sample weight (g)	9.60	8.00	7.20	6.70
Ignite	Y	Y	N	N
Pass	N	Y	Y	Y
Fail*	Y	N	N	N

*Flame is for longer and or higher than the test limit; N = no; Y = yes

[0425] All the compositions were identical other than for the oil or emollient phase, which was 15% of the formulation. The foam compositions comprising light mineral oil, octyl dodecanol or MCT were all found to be non-flammable according to the test parameters used irrespective of which propellant mixture was used. The isopropyl myristate formulation apparently may be surprisingly sensitive to changes in the proportion of propane butane iso-butane mixture.

[0426] Also surprising is that IPM is sensitive to propellant at 15% w/w but not at 35% w/w and further unexpectedly it is noted that when IPM is sensitive octyl dodecanol is not sensitive. The same formula with 15% PPG 15 stearyl ether ignited and the flame was higher than the test limit.

[0427] The foams produced with 1681 propellant mixture were viewed under the microscope and without being bound by any particular theory birefringence was observed and further in general terms non ignition coincided with some structured order in the foam. In contrast the flammable formulation appeared more random. By structured order, relatively repeatble cells of various sizes separated by a relatively similar interconnecting network is loosly intended.

Example 19—Aqueous Formulation with and without 5% IPM

[0428]

	PPG001	PPG003
IPM (ISOPROPYL MYRISTATE)	—	5.00
Glyceryl Monostearate	0.49	0.49
Sorbitane Stearate	0.65	0.65
Stearyl Alcohol	0.92	0.92
Steareth-21	2.17	2.17
PEG-40 Stearate	2.83	2.83
Methocel A4M	0.33	0.33
Xanthan gum	0.28	0.28
Polysorbate 80	0.98	0.98
Water purified	91.35	86.35
Total	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture (1681)	8.00	8.00
Results		
Foam quality	E	E
Color	White	White

-continued

	PPG001	PPG003
Odor	No	No
Shakability	Good	Good
Flammability test:		
Ignite	N	Y
Pass	Y	Y
Fail*	N	N

*Flame is for longer and or higher than the test limit; N = no; Y = yes

[0429] Comments: The compositions were identical other than for the presence or absence of the emollient isopropyl myristate. When present, isopropyl myristate was at a concentration of 5% w/w of the formulation prior to addition of propellant. When absent, IPM was replaced by water. Both foam compositions were found to be non-flammable according to the test parameters used. The formulation without IPM did not ignite. So the underlying carrier formulation without oil or with only 5% is non-flammable. However, the same formulation with 15% PPG 15 stearyl ether and 76.35% water ignited with a flame higher than the test limit.

Example 20—Aqueous Emulsions with 15% to 50% Oil

[0430]

Ingredients	PPG008	PPG009	PPG011	PPG012
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)		15.00		
light mineral oil	15.00		25.00	50.00
Glyceryl Monostearate	0.49	0.49	0.49	0.49
Sorbitane Stearate	0.65	0.65	0.65	0.65
Stearyl Alcohol	0.92	0.92	0.92	0.92
Steareth-21	2.17	2.17	2.17	2.17
PEG-40 Stearate	2.83	2.83	2.83	2.83
Methocel A4M	0.33	0.33	0.33	0.33
Xanthan gum	0.28	0.28	0.28	0.28
Polysorbate 80	0.98	0.98	0.98	0.98
Water purified	76.35	76.35	66.35	41.35
Total	100.00	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture (1681)	8.00	8.00	8.00	9.00
Foam quality	E	E	E	E
Color	White	White	White	White

-continued

Ingredients	PPG008	PPG009	PPG011	PPG012
Odor	No	No	No	No
Shakability	Good	Good	Good	Good
Flammability test:				
Ignite	Y	Y	Y	Y
Pass	Y	Y	Y	Y
Fail*	N	N	N	N

*Flame is for longer and or higher than the test limit; N = no; Y = yes

[0431] These compositions all produced excellent quality foam. They were identical other than for the presence or absence of the emollient or oil, which was 50%, 25% or 15% of the formulation. When reduced, the oil or emollient was replaced by water. All the foam compositions were found to be non-flammable according to the test parameters used. Increasing the amount of oil from 15% to 50% did not significantly affect flammability. However, the same formulation comprising 15% PPG 15 stearyl ether and 76.35% water ignited with a flame higher than the test limit.

Example 21—Aqueous Emulsions with 10% to 50% Oil

[0432]

	PPG013	PPG015	PPG017	PPG018	PPG019
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)	50.00				35.00
light mineral oil				35.00	
Octyl dodecanol		10.00	35.00		
Glyceryl Monostearate	0.49	0.49	0.49	0.49	0.49
Sorbitane Stearate	0.65	0.65	0.65	0.65	0.65
Stearyl Alcohol	0.92	0.92	0.92	0.92	0.92
Steareth-21	2.17	2.17	2.17	2.17	2.17
PEG-40 Stearate	2.83	2.83	2.83	2.83	2.83
Methocel A4M	0.33	0.33	0.33	0.33	0.33
Xanthan gum	0.28	0.28	0.28	0.28	0.28
Polysorbate 80	0.98	0.98	0.98	0.98	0.98
Water purified	41.35	81.35	56.35	56.35	56.35
Total	100.00	100.00	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture (1681)	10.00	8.00	9.00	10.00	11.00
Foam quality	E	E	E	E	E
Color	White	White	White	White	White
Odor	No	No	No	No	No
Shakability	Good	Good	Good	Good	Good
Flammability test:					
Ignite	N	N	N	N	N
Pass	Y	Y	Y	Y	Y
Fail*	N	N	N	N	N

*Flame is for longer and or higher than the test limit; N = no; Y = yes

[0433] These compositions all produced excellent quality foam. They were identical other than for the presence or absence of the emollient or oil, which was 50%, 35% or 10% of the formulation. When reduced the oil or emollient was replaced by water. All the foam compositions were found to be non-flammable according to the test parameters used. Increasing the amount of oil from 10% to 50% did not significantly affect flammability. However, the same formulations comprising 10% PPG 15 stearyl ether and 81.35% water and comprising 35% PPG 15 stearyl ether and 56.35% water each ignited with a flame higher than the test limit.

Example 22—Aqueous Emulsion with 69% Oil

[0434]

	PFT048
light mineral oil	69.00
Stearyl Alcohol	0.70
Surphope 1816	0.40
Methocel ELV15	0.20
Xanthan gum	0.10
Water purified	29.60
Total	100.00
Propellant: [propane: iso-butane: n-butane] mixture* (1681)	8.00
Appearance	
Quality	FG
Color	white
Odor	no odor
Shakability	good
Flammability test	8% 1681
Sample weight (g)	5.10
Ignite	N
Pass	Y
Fail**	N

*Three different propellant mixtures were used and tested and all the formulations provided fairly good quality foam.
**Flame is for longer and or higher than the test limit; N = no; Y = yes.

[0435] This foam corresponds to the foam formulation of Example 6, No, 1., except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0436] This foam composition with a very high mineral oil concentration was non-flammable according to the test parameters. It is expected that by raising the sucrose ester surfactant (Surphope 1816) good to excellent foam quality can be achieved.

Example 23 - Oil Combinations	PFT050	PFT051	PFT052
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)	7.50		3.80
Light mineral oil	11.20	25.00	5.60
IPM (ISOPROPYL MYRISTATE)	5.00		2.50
Stearyl Alcohol	0.50	0.50	0.25
Surphope 1816	0.80		0.80
Methocel ELV15	0.60	0.40	0.60
Cocoglyceride	1.20		0.60
Xanthan gum	0.30	0.20	0.30
Sodium lauryl sulphate	0.10		0.10
Polysorbate 60		0.80	
Water purified	72.80	73.10	85.45
Total	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture* (1681)	8.00	8.00	8.00
Results			
Appearance			
Quality	G-E	FG	G-E
Color	white	white	white
Odor	no odor	no odor	no odor
Shakability	good	good	good

-continued

Flammability test	8% 1681	8% 1681	8% 1681
sample weight (g)	5.70	6.00	5.80
Ignite	N	N	N
Pass	Y	Y	Y
Fail**	N	N	N

*Three different propellant mixtures were used and tested. The oil mixture formulations all produced foam of good to excellent quality and the oil alone formulation foam was fairly good.
**Flame is for longer and or higher than the test limit; N = no; Y = yes.

[0437] Foam PFT051 corresponds to the foam formulation of Example 4, No. 5 except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0438] Foam PFT050 corresponds to the foam formulation of Example 5, No. 1.

[0439] Foam PFT052 corresponds to the foam formulation of Example 5, No. 2.

[0440] These compositions all produced excellent quality foam. They were identical other than for the presence or absence of the emollient or oil, which was 50%, 35% or 10% of the formulation. When reduced the oil or emollient was replaced by water. All the foam compositions were found to be non-flammable according to the test parameters used. Increasing the amount of oil from 10% to 50% did not significantly affect flammability.

Example 24 Soybean Oil Compositions

[0441]

Ingredients	PFT058	PFT059	PFT060
Soybean oil	40.00	30.50	20.00
Stearyl alcohol	0.80	1.05	0.73
Sucrose ester SP70	0.64	0.45	0.80
Xanthan Gum	0.16	0.11	0.10
Methocel ELV15	0.32	0.22	0.28
Water pur.	58.08	67.67	78.09
Total	100.00	100.00	100.00
Results			
Appearance			
Quality	G	E	E
Color	White	White	White
Odor	No Odor	No Odor	No Odor
Shakability	Good	Good	Good
Propellant	8% 1681	8% 1681	8% 1681
sample weight (g)	7.20	6.80	9.20
Ignite	Y	N	N
Pass	Y	Y	Y
Fail*	N	N	N

*Flame is for longer and or higher than the test limit.
N = no; Y = yes; G = good; E = excellent

[0442] Foam PFT058 corresponds to the foam formulation of Example 2, No, 1 except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0443] Foam PFT059 corresponds to the foam formulation of Example 2, No, 2., except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0444] Foam PFT060 corresponds to the foam formulation of Example 2, No, 3., except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0445] These compositions all produced good to excellent quality foam. They were identical other than for the presence or absence of the emollient or oil, which was 40%, 30.5% or 20% of the formulation. When reduced the oil or emollient was replaced by water. All the foam compositions were found to be non-flammable according to the test parameters used. Reducing the amount of oil from 40% to 30% and from 30% to 20% resulted in the foam not igniting.

Example 25 Silicone Oil Compositions

[0446]

Ingredients	PFT056	PFT057
Dimethicone 350	25.00	10.00
Stearyl alcohol	0.20	0.20
Sucrose ester SP70	0.80	
Myrj 49P		0.80
Xanthan Gum	0.20	0.20
Methocel ELV15	0.40	0.40
Water pur.	73.40	88.40
Total	100.00	100.00
Results		
Appearance		
Quality	G	G
Color	White	White
Odor	No Odor	No Odor
Shakability	Good	Good
Propellant	8% 1681	8% 1681
sample weight (g)	11.20	9.10
Ignite	N	Y
Pass	Y	Y
Fail*	N	N

*Flame is for longer and or higher than the test limit.
N = no; Y = yes; G = good; E = excellent.

[0447] Foam PFT056 corresponds to the foam formulation of Example 3, No. 1 except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0448] Foam PFT057 corresponds to the foam formulation of Example 3, No. 2 except that the anti-oxidant, preservatives and fragrance have been replaced by and the amount has been made up to 100% with water.

[0449] These compositions produced good quality foam. They were identical other than for the presence or absence of the emollient or oil, which was 25% or 10% of the formulation. When reduced the oil or emollient was replaced by water. All the foam compositions were found to be non-flammable according to the test parameters used. Reducing the amount of oil from 25% to 10% resulted in the foam not igniting.

Comparison Example 1—W/O 57% and 60% MCT Emulsion Formulations

[0450]

	PFT053	PFT054	PFT055
MCT (CAPRYLIC/CAPRIC TRIGLYCERIDE)	57.18	60.00	60.00

-continued

PPG 15 stearyl ether	1.01		
Glyceryl Monostearate	2.00	2.00	2.00
Hexilene glycol	10.03	10.00	
Stearyl Alcohol	4.71	5.00	5.00
Steareth-2	3.01		
PVP K-90		2.00	2.00
Span 60	2.00		
Lecithin	10.03	10.00	
Water purified	10.03	11.00	31.00
Total	100.00	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture* (1681)	8.00	8.00	8.00
Appearance			
Quality	G	G-E	G-E
Color	yellow	yellow	white
Odor	no odor	no odor	no odor
Shakability	good	good	moderate
Flammability test	8% 1681	8% 1681	10% 1681
Sample weight (g)	6.10	5.10	5.20
Ignite	Y	Y	Y
Pass	N	N	N
Fail**	Y ~15 sec. of fire!	Y ~15 sec. of fire!	Y ~15 sec. of fire!

*Three different propellant mixtures were used and tested. The high oil formulations produced foam of good quality.
**Flame is for longer and or higher than the test limit; N = no; Y = yes.

[0451] These formulations are flammable in the presence of hexylene glycol and of lecithin. When both were substituted by water the composition was still found to be flammable according to the test parameters used—suggesting (without being bound by this theory) that whilst MCT oil in water compositions are inherently non-flammable when there is a phase inversion such that there is a water in oil emulsion the MCT foam is more combustible and may not pass the test parameters.

Comparison Example 2-25% Petrolatum and 45% PPG Stearyl Ether Foam Formulations

[0452]

Ingredients	% w/w	% w/w
Water	70.00	45.00
PPG 15 Stearyl ether		45.00

-continued

Ingredients	% w/w	% w/w
Petrolatum	25.00	
Steareth-2	2.00	7.00
Steareth-21	3.00	3.00
Total	100.00	100.00
Propellant: [propane: iso-butane: n-butane] mixture (1681)	8.00	8.00
Results		
Quality	G	G-E
Color	White	White
Odor	Very Faint	No
Flammability		
sample weight (g)	5.3	5.5
Ignite	Y	Y
Pass	N	N
Fail*	Y	Y

*Flame is for longer and or higher than the test limit.
N = no G = good Y = yes E = excellent

[0453] 25% Petrolatum in a minimal formulation and 45% PPG stearyl ether in a minimal formulation were both flammable.

1. A foamable carrier composition for use in the manufacture of a non-flammable, a flame retardant or a flame resistant foam, said carrier comprising:

about 2% to about 75% by weight hydrophobic solvent, said hydrophobic solvent comprising at least one of mineral oil, MCT oil, isopropyl oil, octyl dodecanol, silicone oil and vegetable oil;

about 25% to about 98% by weight water;

about 0.1% to about 5% by weight foam adjuvant agent;

about 0.1% to about 5% by weight surface-active agent; and

about 0.1% to about 5% by weight water gelling agent, and

a liquefied or compressed gas propellant,

which is contained in a container, and

which upon release provides a breakable foam suitable for topical or mucosal administration that is non-flammable, flame retardant or flame resistant.

2-61. (canceled)

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