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(54) Title: PHARMACEUTICALLY ELEGANT, TOPICAL ANHYDROUS AEROSOL FOAM

(57) Abrégé/Abstract:
A topical pharmaceutical aerosol foam containing liquid silicones to enhance cosmetic elegance. Although liquid silicones are inherent defoamers, a high quality, stable foam is produced.

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(54) Title: PHARMACEUTICALLY ELEGANT, TOPICAL ANHYDROUS AEROSOL FOAM

(57) Abstract: A topical pharmaceutical aerosol foam containing liquid silicones to enhance cosmetic elegance. Although liquid silicones are inherent defoamers, a high quality, stable foam is produced.

TITLE: PHARMACEUTICALLY ELEGANT, TOPICAL ANHYDROUS AEROSOL FOAM

FIELD OF THE INVENTION

This invention relates to topical pharmaceutical compositions.

BACKGROUND OF THE INVENTION

Topical pharmaceutical compositions are, of course, well known. They can be used as water proofing agents, sunscreens, skin conditioning agents, lip balms, wound dressings, hair pomades, etc. Regardless of the specific use, common to pharmaceutically satisfactory topical actives are that they must stay on the skin for a sufficient period of time to allow the active to perform; they must not irritate the skin; and, they must be perceived by the patient as pharmaceutically elegant or the patient will simply not use them. By "pharmaceutically elegant", as those skilled in the art know, one means the skin feel to the patient is good. It must not be too watery or too greasy. Some say it relates to the creaminess or lubricity properties as well as 'moisture retaining' properties.

There is a continual need for improvements in topical carrier systems, particularly for those that are lipophilic in nature, most of which are perceived by consumers as too waxy or too greasy when smeared on the skin. This invention relates to this need.

While aerosol delivery lipophilic systems have been used for topicals before, a problem with typical aerosol systems is to develop one that does not feel greasy and which is cosmetically superior. Known non-aerosol compositions which provide a nongreasy feel in topicals can include liquid silicones such as cyclomethicone, hexamethyldisiloxane, and dimethiconol. However, such liquid silicones are recognized in the art as defoaming agents. Defoaming agents are not something that one would want to add to a topical aerosol composition where foaming is an essential part of the delivery system since they act to defoam. Surprisingly, it has been found, however, that in the current invention, a topical aerosol foam composition has been created that does contain a large quantity of liquid silicones and yet it unexpectedly produces quality foam.

This invention offers a number of other benefits to the user which are also desirable objectives. The drug delivery system in the form of foam facilitates a novel, yet

efficient mode of topical drug delivery system. It also facilitates continuous product output thereby adding ease of application. When dispensed in small quantity, the drug delivery system in the form of a foam can also cover a larger surface area of application while also facilitating better product application in areas where conventional topical products cannot be as effective. The drug delivery system in the form of foam also facilitates the use of a lower dosage which can minimize adverse reactions. The other crucial benefit is that this foam form of delivery system is devoid of any contact with air, light, or any other form of contamination as this is a completely sealed system throughout the life of the product. Thus, light and oxidation prone topical actives can be preserved effectively in the aerosol system. The anhydrous system of the carrier further extends the preservation of topical actives that are otherwise easily degraded by presence of a water base.

Accordingly, it is a primary object of the present invention to prepare a topical application or pharmaceutical composition which is of widespread applicability (i.e. useful with many drug actives) and which is at the same time perceived by the user as pharmaceutically elegant.

Another objective of the present invention is to achieve the primary object with a composition especially adapted for lipophilic compounds and which can provide effective delivery in the form of a foam.

A yet further objective is to provide a method of preparation of a topical application or pharmaceutical composition in the form of a foam that achieves each of the above objectives or attributes.

The method and manner of achieving each of the above objectives as well as other objectives of the invention, will become apparent from the following detailed description of the invention.

SUMMARY OF THE INVENTION

A topical pharmaceutical aerosol foam composition containing a lipophilic compound, a liquid silicone, a foaming agent, a propellant and a topical pharmaceutical active. The composition may also contain rheology modifiers that serve as foam stabilizers. The composition exhibits excellent emollient and rub-in characteristics. The composition when expelled from an aerosolized container produces surprisingly good

quality foam from a composition consisting of large quantities of liquid silicones, which are normally inherently de-foamers.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

For describing the compositions certain definitional terms are appropriate. "Pharmaceutically elegant" has been previously defined. The "pharmaceutical composition" as used throughout the present specification and the accompanying claims is to be understood as defining the compositions of which the individual components or ingredients are themselves pharmaceutically acceptable, e.g. that is they are topically acceptable actives. Put another way, they are either FDA approved or on the GRAS safe list. The term "topically active pharmaceutical" is intended to be non-limiting and includes those pharmaceutical active agents that are commonly applied topically such as waterproofing agents, skinbarrier agents, skin conditioning agents, solvents, bio-adhesives, acne actives, analgesics, anesthetics, anorectics, antihistamines, anti-inflammatory agents, antibiotics, antifungals, antivirals, antimicrobials, scabicides, pediculicides, antineoplastics, antiperspirants, antipruritics, antipsoriatics, antiseborrheics, astringents, biologically active proteins and peptides, burn actives, cauterizing agents, depigmenting agents, diaper rash agents, enzymes, hair growth actives, hemostatics, keratolytics, canker sore actives, cold sore actives, photosensitizing actives, steroids, sunburn actives, sunscreens, vaginal actives, wart actives, wound care actives; and retinol, retinoic acid and retinoic acid derivatives. These may also include prescription and over-the-counter (OTC) drug products. It is understood that this list is by way of example and not a limitation with respect to the active. The term "pharmaceutically-effective amount of a topically active pharmaceutical" is intended to mean that a sufficient amount of the topically active pharmaceutical is present in the composition to perform its intended purpose.

In the present invention, there are five essential ingredients. The first is a lipophilic compound or combinations of lipophilic compounds selected from the group, including but not limited to, petrolatum, mineral oil, vegetable oils, fatty acids, glycerides, medium chain triglycerides, or combinations thereof. The amount of lipophilic compound or combinations of lipophilic compounds is from about 1% to about 80% by weight of the total composition. Preferably, the amount of lipophilic compound or combinations of

lipophilic compounds is from about 5% to about 65% by weight of the total composition. Various grades of Petrolatum exist, one of which is manufactured by Crompton under the grade Perfecta; a source of the medium chain triglycerides is Neobee® 1053 manufactured by Stepan; and a source of mineral oil is Kaydol White Mineral Oil manufactured by Crompton. An example of a medium chain triglyceride is caprylic/capric triglyceride.

The second essential ingredient is a liquid silicone or a combination of liquid silicones which are used to overcome the oily/greasy feel of the lipophilic compound during application to the skin and to provide good skin feel and rub in characteristics. The liquid silicone is selected from the group consisting of silicones, silicone derivatives, cyclomethicone, or combinations thereof. The amount of liquid silicone or combinations of liquid silicones is from about 1% to about 80% by weight of the total composition. Preferably, the amount of liquid silicone or combinations of liquid silicones is from about 5% to about 35% by weight of the total composition. Preferably, the liquid silicone used is Cyclomethicone, one source of which is ST-Cyclomethicone 5-NF manufactured by Dow Corning.

The third essential ingredient is a foaming agent, which is capable of foaming a product containing the above referenced liquid silicone. The foaming agent used is selected from the group consisting of mono, di, tri esters of Sorbitol and fatty acids. The amount of foaming agent used is from about 0.5% to about 25% by weight of the total composition. Preferably, the amount of the foaming agent used is from about 3% to about 7% by weight of the total composition. The preferred foaming agent used is Sorbitan Monooleate one source of which is Span 80V Pharma manufactured by Uniqema.

The fourth essential ingredient is a pharmaceutically-effective amount of a topically active pharmaceutical, or in other words, the drug active. Suitable drug active categories have been previously listed. Some of these in specific can be Hydrocortisone, Zinc Oxide, Titanium Dioxide, Retinol, Bacitracin Zinc, Polymyxin B Sulfate, Neomycin Sulfate, Tretinoin, Salicylic Acid, Lidocaine, Tetracaine, Sodium Sulfacetamide, Boric acid, Ketoconazole, Tolnaftate, Tretinoin, Anthralin, Zinc Pyrithione, Menthol, Thymol, Desonide, Methyl Salicylate, Camphor, Clobetasol Propionate, Aluminum Sulfate, Trypsin, etc. Generally, the drug actives are present in amount from about 0.01% to about 40% weight of the total composition.

And finally, the fifth essential ingredient is a propellant, which is used to expel the composition from the aerosol container. The propellant is selected from the group consisting of hydrocarbons like Butane, Propane, Pentane, Isopentane, Isobutane or Mixtures thereof supplied by Aeropres under the Trade name of A-70 and hydroflourocarbons like DuPont's Dymel 236fa, which is 1,1,1,3,3,3 hexafluoropropane or Dymel 227ea/P which is 1,1,1,2,3,3,3 heptafluoropropane or the propellant of choice here being Dymel 134a/P which is 1,1,1,2 Tetrafluoroethane. The amount of propellant used ranges from about 1% to about 30% by weight of the total composition. Preferably, the amount of propellant used ranges from about 5% to 20% by weight of the total composition.

The composition may further contain rheology modifiers, which are capable of sustaining the foam. The rheology modifier if used may be selected from the group consisting of polyoxyl 40 hydrogenated castor oil, beeswax, paraffin wax, or combinations thereof. Sources of the Polyoxyl 40 Hydrogenated Castor oil are Lipocol HCO 40 manufactured by Lipo Chemicals or Cremophor RH-40 manufactured by BASF. A source of the Beeswax is White Wax SP422P NF manufactured by Strahl and Pitsch, and a source of the Paraffin wax is SP-674 manufactured by Strahl and Pitsch. The amount of rheology modifier used in the composition ranges from about 0.05% to about 15% by weight of the total composition. Preferably, the amount of rheology modifier used in the composition ranges from about 1% to about 5% by weight of the total composition.

Critical to the invention, therefore, is the combination of all five of the essential ingredients listed above to create the desired pharmaceutically elegant foam. When these are used in combination with the surfactant system herein specified, the dispensed foam is stabilized and of good quality in the presence of what would otherwise be defoamer, i.e., the silicones.

The following examples are offered to further illustrate, but not necessarily limit both the process and the composition of the present invention.

Example 1: Vehicle

Ingredient	%w/w
Caprylic/Capric Triglyceride	20.00
Mineral Oil	8.00
Cyclomethicone	31.25
Sorbitan Oleate	5.00
Polyoxy1 40 Hydrogenated Castor Oil	4.00
Petrolatum	30.00
Beeswax	0.75
Hydrogenated Castor Oil	1.00

All ingredients are weighed in a vessel and it is heated to 70-75° C, and mixed well until uniform. It is then cooled to ambient and pressurized in an aerosol can with Hydroflourocarbon in the ratio: Base: 85%, Propellant: 15%.

Example 2: Diaper Rash

Ingredient	%w/w
Caprylic/Capric Triglyceride	25.50
Mineral Oil	8.00
Cyclomethicone	20.00
Beeswax	1.50
Sorbitan Monooleate	4.50
Hydrogenated Castor Oil	0.50
Zinc Oxide	40.00

All ingredients are weighed in a vessel except the Zinc Oxide and it is heated to 70-75° C, and mixed well until uniform. It is then cooled to 45° C and gradually added is dispersed Zinc Oxide, thus avoiding any lump formation. It is then cooled to ambient and pressurized in an aluminum aerosol can with Hydroflourocarbon in the ratio: Base: 80%, Propellant: 20%.

Example 3: Antipuritic

Ingredient	%w/w
Caprylic/Capric Triglyceride	24.50
Mineral Oil	10.00
Cyclomethicone	32.00
Beeswax	1.50
Sorbitan Monooleate	6.00
Petrolatum	25.00
Hydrocortisone	1.00

All ingredients are weighed in a vessel except Hydrocortisone and it is heated to 70-75° C and mixed well until uniform. It is then cooled to 35° C and then gradually added and dispersed is the Hydrocortisone. It is then cooled to ambient and pressurized in an aluminum aerosol can with Hydrofluorocarbon in the ratio: Base: 90%, Propellant: 10%.

For each of examples 1-3 the product when tested for foaming characteristics produces an elegant skin feel product with good and stable foam characteristics and the delivery was deemed excellent.

From the above examples, it can be seen that the invention accomplishes at least all of its stated objectives.

What is claimed is:

1. An anhydrous, topical pharmaceutical aerosol foam composition, comprising in pharmaceutically-elegant and effective amounts: a lipophilic compound or combinations of lipophilic compounds selected from the group consisting of petrolatum, mineral oil, vegetable oils, fatty acids, glycerides, medium chain triglycerides; a liquid silicone or combinations of liquid silicones; a foaming agent; a topically active pharmaceutical; and a propellant.

2. The composition of claim 1 wherein the lipophilic compound is mineral oil.

3. The composition of claim 1 wherein the lipophilic compound is a medium chain triglyceride.

4. The composition of claim 1 wherein the lipophilic compound is a mixture of petrolatum, mineral oil and a medium chain triglyceride.

5. The composition of claim 1 wherein the liquid silicone is selected from the group consisting of silicones and silicone derivatives or combinations thereof.

6. The composition of claim 1 wherein the foaming agent is selected from the group consisting of mono, di, tri esters of sorbitol, fatty acids, and combinations thereof.

7. The composition of claim 1 wherein the esters of sorbitol are selected from the group consisting of: sorbitan caprylate, sorbitan diisostearate, sorbitan dioleate, sorbitan isostearate, sorbitan laurate, sorbitan monooleate, sorbitan trioleate, sorbitan sesquioleate, and combinations thereof.

8. The composition of claim 7 wherein the foaming agent is sorbitan monooleate.

9. The composition of claim 8 wherein the amount of sorbitan monooleate ranges from about 0.5% to about 25% by weight of the total anhydrous, topical pharmaceutical aerosol foam composition.

10. The composition of claim 1 further comprising a rheology modifier.

11. The composition of claim 10 wherein the rheology modifier is selected from the group consisting of polyoxyl 40 hydrogenated castor oil, beeswax, paraffin wax, and combinations thereof;

12. The composition of claim 1 wherein the topically active pharmaceutical is selected from the group consisting of acne actives, analgesics, anesthetics, anorectics, antihistamines, anti-inflammatory agents, antibiotics, antifungals, antivirals, antimicrobials, scabicides, pediculicides, antineoplastics, antiperspirants, antipruritics, antipsoriatics, antiseborrheics, astringents, biologically active proteins and peptides, burn actives, cauterizing agents, depigmenting agents, diaper rash agents, enzymes, hair growth actives, hemostatics, keratolytics, canker sore actives, cold sore actives, dental actives, saliva actives, photosensitizing actives, skin protectant/barrier agents, steroids, sunburn actives, sunscreens, vaginal actives, wart actives, wound care actives; and retinol, retinoic acid and retinoic acid derivatives.

13. The composition of claim 1 wherein the propellant is a hydrocarbon.

14. The composition of claim 1 wherein the propellant is a hydroflourocarbon.

15. The composition of claim 5 wherein the liquid silicone is cyclomethicone.

16. The composition of claim 1 wherein the amount of liquid silicone or combinations of liquid silicones range from about 1% to about 80% by weight of the total anhydrous, topical pharmaceutical aerosol foam composition.

17. The composition of claim 13 wherein the hydrocarbon is selected from the group consisting of butane, isomers of butane, propane, isomers of propane, pentane, isomers of pentane, and combinations thereof.

18. The composition of claim 14 wherein the hydrofluorocarbon is selected from the group consisting of 1,1,1,2 tetrafluoroethane and 1,1,1,2,3,3,3 heptafluoropropane.

19. The composition of claim 1 wherein the amount of lipophilic compound or combinations of lipophilic compounds range from about 1% to about 80% by weight of the total anhydrous, topical pharmaceutical aerosol foam composition.