The invention relates to stable, rapid drying, non-aqueous topical compositions of mometasone furoate in the form of spray, the composition comprising one or more solubilizers, one or more non-aqueous volatile solvents and film formers or emollients. Methods of preparing such compositions are also provided. The present invention further relates to use of mometasone furoate topical spray compositions for the treatment of psoriasis, atopic dermatitis (atopic eczema) and other skin disorders or diseases.
TOPICAL SPRAY COMPOSITIONS OF MOMETASONE FUROATE

FIELD OF THE INVENTION

The present invention relates to a rapid drying, non-aqueous topical spray composition of mometasone furoate. Methods of preparing such compositions are also provided.

BACKGROUND OF THE INVENTION

Topical corticosteroids are a class of compounds that demonstrate anti-inflammatory, anti-pruritic and vasoconstrictive actions. They are generally used to relieve the redness, skin edema (swelling), itching, crusting, flaking, cracking, oozing, psoriasis, atopic dermatitis (atopic eczema) and other pathologies of the skin like contact dermatitis, seborrheic dermatitis, eczema, dermatitis herpetiformis, neurodermatitis or autoeczematization.

Mometasone furoate is a synthetic corticosteroid with anti-inflammatory activity. The chemical name of mometasone furoate is 9a, 21-dichloro-11β, 17-dihydroxy-16a-methylpregna-1,4-diene-3,20-dione 17-(2-furoate), with the empirical formula C27H30Cl2O6, a molecular weight of 521.4 and following structural formula:

![Structural formula of mometasone furoate]

Mometasone furoate is a white to off-white powder practically insoluble in water, slightly soluble in octanol, and moderately soluble in ethyl alcohol.
Mometasone furoate is commercially available as various topical dosage forms such as cream, ointment and lotion. It is marketed under the brand name ELOCON® and indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses in patients 2 years of age or older.

US4775529 discloses topical lotion compositions containing corticosteroids in a hydro-alcoholic base containing propylene glycol.

US4808610 discloses topical cream compositions comprising mometasone furoate, hexylene glycol, water, white wax, white petrolatum and other ingredients.

EP1 886686 (B1) discloses topical pharmaceutical compositions comprising mometasone furoate, water and a combination of at least an aromatic alcohol and at least a solvent selected from two different groups, and optionally further additives. The compositions include solution, microemulsion, gel, lotion, cream or ointment.

EP2575822 (A2) discloses topical pharmaceutical compositions comprising mometasone furoate, hexylene glycol, water, and oil phase. The composition is preferably formulated in the form of a cream.

Many formulations containing topical corticosteroids in the form of cream and ointment are greasy, and hence are unpleasant to apply on large areas of the skin. In addition, some conventional cream and ointment bases are irritating to the skin, particularly over the long exposure that is frequently required for efficacy, and the fluidity of lotions often makes the physical application difficult to control over a desired area. Several commercially available topical formulations are primarily incapable of providing the much needed soothing effect to the affected areas, particularly in conditions such as psoriasis and other skin disorders. Such formulations do not promote patient compliance. Therefore, a spray composition, which increases the ease of use for the patient is often preferred.
WO2000045795 discloses a topical medicinal spray composition comprising one or more medicaments in a volatile vehicle, and one or more film-forming polymers. When sprayed on to a topical site, the composition forms a stable, breathable film from which the medicaments are transdermal available.

WO2011026076 (A2) discloses a propellant free sprayable topical composition comprising steroids, emulsifying agents, polymer, water, water immiscible substance and penetration enhancer.

However, conventional topical spray formulations tend to remain at the application site for only a short time. For example, they are easily rubbed off, thus require frequent re-application. Further, some topical spray compositions often irritate the skin and require longer time for drying after application. In addition, some of the spray formulations do not provide uniform thin occlusive film after spraying, which is required for the treatment of psoriasis in order to maintain the skin hydration. There remains, therefore, an unmet need for improved patient compliant topical spray formulations that are effective in the treatment of skin disorders such as psoriasis and atopic dermatitis.

In an attempt to develop novel non-aqueous mometasone furoate topical compositions in the form of spray, the present inventors have surprisingly found that use of one or more solubilizers, one or more non-aqueous volatile solvents and one or more film formers or emollients resulted in compositions, which are stable, provide occlusive film, provide longer duration of action, have improved patient compliance, and exhibit efficacy comparable to mometasone furoate compositions currently available in the market. The compositions of the present invention provide rapid drying after application on to the skin. Such compositions are effective in the treatment of psoriasis, atopic dermatitis (atopic eczema) and other skin disorders or diseases.

**SUMMARY OF THE INVENTION**

The present specification relates to a rapid drying, non-aqueous topical spray composition of mometasone furoate and its process for preparation.
In one aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers, and
(iii) one or more non-aqueous volatile solvents.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers,
(iii) one or more non-aqueous volatile solvents, and
(iv) one or more film formers.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) hexylene glycol,
(iii) one or more non-aqueous volatile solvents, and
(iv) one or more film formers.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers,
(iii) one or more non-aqueous volatile solvents,
(iv) one or more emollients, and
(v) one or more acidifying agents.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers, and
(iii) one or more non-aqueous volatile solvents; wherein the composition forms a stable occlusive film.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1 % (w/w) mometasone furoate,
(ii) 1% to 15 % (w/w) of one or more solubilizers, and
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1 % (w/w) mometasone furoate,
(ii) 1% to 15 % (w/w) hexylene glycol,
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents, and
(iv) 1% to 10% (w/w) of one or more film formers.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1 % (w/w) mometasone furoate,
(ii) 1% to 15 % (w/w) hexylene glycol,
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents,
(iv) one or more emollients, and
(v) one or more acidifying agents.

In yet another aspect, the present specification provides a stable, rapid drying, non-aqueous topical spray composition of mometasone furoate.
In yet another aspect, the present specification relates to use of rapid drying, non-aqueous topical spray composition of mometasone furoate for the treatment of psoriasis, atopic dermatitis (atopic eczema) and other skin disorders or diseases.

**BRIEF DESCRIPTION OF FIGURES**

Figure: 1: Comparative pharmacokinetic study between the present invention (Example 2) and commercially available ELOCON® ointment.

**DESCRIPTION OF THE INVENTION**

The present specification relates to a rapid drying, non-aqueous topical spray composition of mometasone furoate and its process for preparation.

In one aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers, and
(iii) one or more non-aqueous volatile solvents.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers,
(iii) one or more non-aqueous volatile solvents, and
(iv) one or more film formers.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) hexylene glycol,
(iii) one or more non-aqueous volatile solvents, and
(iv) one or more film formers.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers,
(iii) one or more non-aqueous volatile solvents,
(iv) one or more emollients, and
(v) one or more acidifying agents.

In another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) mometasone furoate,
(ii) one or more solubilizers, and
(iii) one or more non-aqueous volatile solvents; wherein the composition forms a stable occlusive film.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1% (w/w) mometasone furoate,
(ii) 1% to 15% (w/w) of one or more solubilizers, and
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents.

In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1% (w/w) mometasone furoate,
(ii) 1% to 15% (w/w) hexylene glycol,
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents, and
(iv) 1% to 10% (w/w) of one or more film formers.
In yet another aspect, the present specification relates to a rapid drying, non-aqueous topical spray composition comprising:
(i) 0.01% to 1% (w/w) mometasone furoate,
(ii) 1% to 15% (w/w) hexylene glycol,
(iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents,
(iv) one or more emollients, and
(v) one or more acidifying agents.

As used herein, the term "rapid drying" means that the composition dries rapidly after application on to the skin. Suitably, the topical spray compositions have a drying time of less than ten minutes, preferably less than five minutes, e.g. less than two minutes.

As used herein, the term "non-aqueous" means that the composition is substantially free of water. In the present invention, "the composition being substantially free of water" means that: the composition is free of water; or, if the composition contains water, the level of water is very low. In the present invention, the level of water, if included, is 5% or less, preferably 3% or less, more preferably 2% or less, still more preferably 1% or less, even more preferably 0.5% by weight of the composition.

As used herein, the term "mometasone" includes mometasone or any pharmaceutically acceptable salts or esters or derivatives thereof, e.g. mometasone furoate. The amount of mometasone furoate employed in the composition is in the range of 0.01% to 5% (w/w), 0.01% to 1% (w/w) of total composition, e.g. 0.1% (w/w).

As used herein, the term "solubilizers" refer to components that help in solubilization of mometasone furoate. Suitable solubilizers include hexylene glycol, propylene glycol, polyethylene glycol or mixtures thereof. Preferred solubilizers include hexylene glycol. The amount of solubilizers employed in the composition is in the range of 1% to 20% (w/w) of total composition, e.g. 3% (w/w), 5% (w/w).
As used herein, the term "solvents" refer to components that aid in the dissolution of the drug in the formulation. The solvents are typically volatile in nature. One of the advantages of the inclusion of a volatile solvent or volatile carrier is that it facilitates the composition to dry rapidly. Suitable volatile solvents may be selected from non-aqueous solvents. The volatile non-aqueous solvents may be selected from ethanol, ethyl acetate, isopropyl alcohol, acetone, ethyl formate, methyl acetate, methyl ethyl ketone, cyclomethicone, dimethiconol, hexamethyldisiloxane or mixtures thereof. The amount of solvents employed in the composition is in the range of 50% to 99% (w/w) of total composition, e.g. more than 70%, 75% or 80%.

The topical spray compositions of the present specification may further comprise co-solvents. Particularly, the co-solvents are added to improve the solubilization of mometasone furoate in the volatile solvents. Suitable co-solvents include alkyl benzoates, benzyl alcohol, isopropyl palmitate, isopropyl myristate, diisopropyl adipate, diethylene glycol monoethyl ether, N-methyl pyrrolidone, or mixtures thereof. The amount of co-solvents employed in the composition is in the range of 1% to 20% (w/w) of total composition, e.g. 3% (w/w), 5% (w/w).

As used herein, the term "film former" refers to a substance that provides a smooth uniform thin occlusive film after evaporation of solvents. The film firmly adheres to the skin and thereby is able to retain on the skin for a suitable period of time. The film formers include but are not limited to acrylic polymers or copolymers, including methacrylic polymers and copolymers such as non-ionic copolymer of methyl methacrylate and butyl methacrylate (Plastoid® B), a copolymer of dimethylamine ethyl methacrylate and a neutral methacrylic acid ester (Eudragit® E100), ammonio methacrylate copolymer type B (Eudragit® RS), ammonio methacrylate copolymer type A (Eudragit® RL), methacrylic acid copolymer type A (Eudragit® LIOO), methacrylic acid copolymer type B (Eudragit® S100), Acrylates / Octylacrylamide copolymer (Dermacryl®), urethanes polymers or copolymers, polyvinyl acetate, polyvinyl alcohol, povidone, alkylated polyvinylpyrrolidones, vinylpyrrolidone-vinylacetate (Kollidon® VA), cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl ethyl cellulose,
hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, or mixtures thereof. The amount of film former employed in the composition is in the range of 1% to 15% (w/w), 1% to 10% (w/w), 1% to 5% (w/w) of total composition, e.g. 2% (w/w), 5% (w/w).

As used herein, the term "emollient" refers to a substance that softens and soothes the skin. Emollients are used to correct dryness, scaling of the skin and also provide an occlusive barrier. Suitable emollients include, for example, stearyl alcohol, glycercy monooleate, glycercy monoricinoleate, glycercy monostearate, cetyl alcohol, isopropyl isostearate, stearic acid, isobutyl palmitate, isocetyl stearate, oleyl alcohol, isopropyl laurate, hexyl laurate, decyl oleate, octadecan-2-ol, isocetyl alcohol, cetyl palmitate, dimethylpolysiloxane, di-n-butyl sebacate, isopropyl palmitate, isopropyl stearate, butyl stearate, polyethylene glycol, triethylene glycol, lanolin, sesame oil, coconut oil, arachis oil, castor oil, acetylated lanolin alcohols, petroleum, mineral oil, butyl myristate, isostearic acid, palmitic acid, isopropyl linoeiate, lauryl lactate, myristyl lactate, decyl oleate, myristyl myristate, and mixture thereof. The amount of emollient employed in the composition is in the range of 1% to 20% (w/w), 1% to 10% (w/w), 5% to 15% (w/w), e.g. 5% (w/w), or 10% (w/w).

The topical spray compositions of the present specification may include an acidifying agent. Various useful acidifying agents include but are not limited to citric acid, citric acid anhydrous, citric acid monohydrate, DL-lactic acid, DL-malic acid, DL-tartaric acid, fumaric acid, L-malic acid, L-tartaric acid, salicylic acid, glycol acid, potassium acid tartrate, potassium citrate, potassium DL-bitartarate, potassium gluconate, sodium lactate, sodium L-tartrate, sodium citrate, ascorbic acid, and mixtures thereof.

The topical spray compositions of the present specification may include one or more antioxidants. The antioxidant may be selected from DL-alpha-tocopherol, butylohydroxy toluene (BHT), butylohydroxy anisole (BHA), ascorbyl palmitate, ascorbic acid, propyl gallate, or mixtures thereof. The amount of antioxidant employed in the composition is in the range of 0.01 to about 0.5% (w/w) of total composition, e.g. 0.07% (w/w), or 0.09% (w/w).
The topical spray compositions of the present specification may contain additional ingredients to improve the composition. Such ingredients include plasticizers, surfactants, penetration enhancers, humectants, coloring agents, chelating agents. Examples of such ingredients are well known in the art.

The topical spray compositions of present specification may be prepared by any suitable conventional process. For example, the topical spray compositions may be prepared by the process steps comprising dissolving mometasone furoate in solubilizers and adding the resulting mixture to one or more non-aqueous volatile solvents. Subsequently, the film formers, emollients, other excipients are added sequentially and mixed well until clear solution is formed.

The topical spray compositions of present specification may be applied onto the skin by using a sprayable dispensing device. The dispensing device provides either a fixed or variable metered dose application such as a stored-energy metered dose pump or a manual metered dose pump.

The topical spray compositions of present specification form a stable occlusive film onto the skin after drying. The occlusive film is resistant to water and it does not get washed off easily and is retained on the skin for longer duration. The film can be removed easily by rubbing with a cotton plug after use.

The topical spray compositions of present specification may be used for the treatment or prevention of psoriasis or atopic dermatitis (atopic eczema) and other skin disorders or diseases.
The psoriasis could be chronic plaque psoriasis or palmoplantar psoriasis.

The topical spray compositions of present specification were subjected to accelerated and long term stability studies.
The specification will now be described in greater detail by reference to the following non-limiting examples.

**EXAMPLES**

**Example 1**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Amount (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>2.5</td>
</tr>
<tr>
<td>Hexylene glycol</td>
<td>7.5</td>
</tr>
<tr>
<td>Ammonio methacrylate copolymer type B (Eudragit® RS)</td>
<td>0.5</td>
</tr>
<tr>
<td>Ammonio methacrylate copolymer type A (Eudragit® RL)</td>
<td>2.5</td>
</tr>
<tr>
<td>Ethanol</td>
<td>86.9</td>
</tr>
</tbody>
</table>

**Process:**
1. Mometasone furoate was dissolved in hexylene glycol and the mixture was added to isopropyl myristate and ethanol mixture.
2. Ammonio methacrylate copolymer type B and ammonio methacrylate copolymer type A were added to the solution prepared in step 1 and stirred well until clear solution was formed.

**Example 2**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Amount (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>5</td>
</tr>
<tr>
<td>Hexylene glycol</td>
<td>5</td>
</tr>
<tr>
<td>Acrylates/octylacrylamide copolymer (Dermacryl® 79)</td>
<td>1</td>
</tr>
</tbody>
</table>
Vinylpyrrolidone-vinyl acetate copolymers (Kollidon® VA 64) | 1  
Dimethiconol-hexamethyldisiloxane (Silmogen carrier) | 45  
Isopropyl alcohol | 42.9

**Process:**
1. Mometasone furoate was dissolved in hexylene glycol and the mixture was added to isopropyl alcohol and isopropyl myristate mixture.
2. Acrylates/octylacrylamide Copolymer and vinylpyrrolidone-vinyl acetate copolymers were added to the solution prepared in step 1 and stirred well until clear solution was formed.
3. The above mixture was added slowly to dimethiconol-hexamethyldisiloxane carrier solvent under stirring and further stirred well until clear solution was formed.

### Example 3

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Amount (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>2.5</td>
</tr>
<tr>
<td>Hexylene glycol</td>
<td>5</td>
</tr>
<tr>
<td>Isopropyl alcohol</td>
<td>82.1</td>
</tr>
<tr>
<td>Glyceryl monooleate</td>
<td>10</td>
</tr>
<tr>
<td>Citric acid</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Process:**
1. Mometasone furoate was dissolved in hexylene glycol and the mixture was added to isopropyl alcohol and isopropyl myristate mixture.
2. Glyceryl monooleate and citric acid were added to the solution prepared in step 1 and stirred well until clear solution was formed.
Example 4

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Amount (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>1.5</td>
</tr>
<tr>
<td>Hexylene glycol</td>
<td>5</td>
</tr>
<tr>
<td>Vinylpyrrolidone-vinyl acetate copolymers (Kollidon® VA 64)</td>
<td>10</td>
</tr>
<tr>
<td>Diethylene glycol monoethyl ether</td>
<td>1</td>
</tr>
<tr>
<td>Ethanol</td>
<td>82.4</td>
</tr>
</tbody>
</table>

**Process:**
Dissolve mometasone furoate in hexylene glycol and add the mixture into a blend of isopropyl myristate, diethylene glycol monoethyl ether and ethanol. Finally add vinylpyrrolidone-vinyl acetate copolymer and mix well until clear solution is formed.

Example 5

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Isopropyl myristate</td>
<td>2</td>
</tr>
<tr>
<td>Hexylene glycol</td>
<td>5</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>2</td>
</tr>
<tr>
<td>Acrylates Copolymer (Avalure™ AC 120)</td>
<td>2</td>
</tr>
<tr>
<td>Ethanol</td>
<td>88.9</td>
</tr>
</tbody>
</table>

**Process:**
Dissolve mometasone furoate in hexylene glycol and add the mixture into a blend of isopropyl myristate, propylene glycol and ethanol. Finally add Acrylates copolymer and mix well until clear solution is formed.
Example 6:

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mometasone furoate</td>
<td>0.1</td>
</tr>
<tr>
<td>Acrylates/octylacrylamide copolymer (Dermacryl 2.0)</td>
<td>3</td>
</tr>
<tr>
<td>Vinylpyrrolidone-vinyl acetate copolymers (Kollidon® VA 64)</td>
<td>1</td>
</tr>
<tr>
<td>Hexylene Glycol</td>
<td>5</td>
</tr>
<tr>
<td>Isopropyl Myristate</td>
<td>2</td>
</tr>
<tr>
<td>Isopropyl alcohol</td>
<td>75.8</td>
</tr>
<tr>
<td>Cyclomethicone</td>
<td>13</td>
</tr>
<tr>
<td>Citric acid anhydrous</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Process:
1. Mometasone furoate was dissolved in hexylene glycol and the mixture was added to isopropyl alcohol and isopropyl myristate mixture.
2. Acrylates/octylacrylamide Copolymer and vinylpyrrolidone-vinyl acetate copolymers were added to the solution prepared in step 1 and stirred well until clear solution was formed. Then the Citric acid was added in the mixture and stirred well.
4. Cyclomethicone was added to the above mixture slowly under stirring and stirred well until clear solution was formed.

Stability study
The stability of the topical spray compositions of present specification were evaluated through accelerated stability studies. Two compositions were prepared according to the formula and process of example 3 and 6, and the compositions were subjected to stability study at various temperature and humidity conditions. The compositions were found to be stable at accelerated conditions. Table 2 represents the study result data.
Table 2:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Period</th>
<th>Assay Mometasone (%)</th>
<th>Total Impurity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Example 3</td>
<td>Example 6</td>
</tr>
<tr>
<td>Initial</td>
<td>Initial</td>
<td>102.0</td>
<td>101.0</td>
</tr>
<tr>
<td>25°C/60% RH</td>
<td>3 Months</td>
<td>101.4</td>
<td>101.5</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>102.0</td>
<td>101.5</td>
</tr>
<tr>
<td>30°C/65% RH</td>
<td>3 Months</td>
<td>102.6</td>
<td>101.6</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>102.5</td>
<td>102.7</td>
</tr>
<tr>
<td>40°C/75% RH</td>
<td>3 Months</td>
<td>100.3</td>
<td>101.9</td>
</tr>
<tr>
<td></td>
<td>6 Months</td>
<td>104.2</td>
<td>102.9</td>
</tr>
</tbody>
</table>

In-Vivo evaluation:
The safety and effectiveness of the topical spray compositions of present specification were evaluated through Dermatological safety evaluation and Rat skin Pharmacokinetic study.

I. Dermatological safety evaluation:
The dermatological safety of the compositions prepared in accordance with Example 2 and 3 were evaluated in a double blinded, non-comparative, multicentric study on palmoplantar psoriasis subjects. Total 30 subjects (including 9 males and 11 females), aged between 18 and 65 years, having mild to moderate psoriasis on both palms were included. The compositions were applied by spraying at an approximate distance 10 to 15 cm, 3-4 times on each palm uniformly. Safety of the compositions were assessed by the dermatologist, through the grading on the both palms of defined clinical signs (observed by the dermatologist) and functional signs (felt by the subjects and reported to the dermatologist), at TO, T immediate after product application, T+1 5 to 20 minutes after product application. Table 1 represents the physical characteristics of spray compositions and Table 2 represents the study assessment protocol and Observation by dermatologists. The compositions were dried within 2-3 minutes and formed smooth uniform film. No increase in the clinical and functional signs from baseline (TO) is observed 15-20 minutes after product application.
<table>
<thead>
<tr>
<th>Table 1:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tests</strong></td>
</tr>
<tr>
<td>Weight per actuation</td>
</tr>
<tr>
<td>Spray Volume</td>
</tr>
<tr>
<td>Uniformity of spray</td>
</tr>
<tr>
<td>Drying time</td>
</tr>
<tr>
<td>Density</td>
</tr>
<tr>
<td>Spray Angle</td>
</tr>
<tr>
<td>Dermal adhesion</td>
</tr>
<tr>
<td>/Flexibility of film</td>
</tr>
<tr>
<td>Film Thickness</td>
</tr>
<tr>
<td>(IR Microscopy)</td>
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</tbody>
</table>

+: poor; ++: Moderate; +++: Good

<table>
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<tr>
<th>Table 2:</th>
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<td><strong>Clinical Signs</strong></td>
</tr>
<tr>
<td>Erythema</td>
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<tr>
<td>Oedema</td>
</tr>
<tr>
<td>Scaling</td>
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<tr>
<td>Peeling</td>
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</table>

Both the compositions quickly formed a noticeable shiny coat/film on the skin surface of the subjects and average drying time was less than 3 minutes in both cases. The film formed was retained throughout the study duration and thereafter removed easily by rubbing with cotton. Throughout the study, no
occurrence of oedema and tingling was recorded by the dermatologist for the test site, on average, on the whole panel.

Nevertheless, the intensity of other studied parameters has not increased compared to baseline (TO) and is lower than grade 2 (corresponding to a moderate intensity), on average, on the whole panel, throughout the study for both compositions.

II. Rat skin Pharmacokinetic study:

A 0.1% mometasone furoate topical spray composition is prepared in accordance with Example 2. The composition is applied by spraying on to the skin of male rat. To another group of rats, a commercial 0.1% mometasone furoate topical ointment product, ELOCON® ointment, is applied in same manner and concentration similar to the spray composition. The rat skin is collected at 2 hours and 8 hours after application and the amount of mometasone is measured in the skin for both groups. Pharmacokinetic analyses indicate that mean mometasone concentration in the skin is superior in spray composition prepared in accordance with Example 2 as compared to the commercially available ELOCON® ointment (Figure 1).
CLAIMS

1. A rapid drying, non-aqueous topical spray composition comprising:
   (i) mometasone furoate,
   (ii) one or more solubilizers,
   (iii) one or more non-aqueous volatile solvents, and
   (iv) one or more film formers.

2. The topical spray composition as claimed in claim 1, wherein the solubilizers are selected from one or more of hexylene glycol, propylene glycol, polyethylene glycol or mixtures thereof.

3. The topical spray composition as claimed in claim 2, wherein the solubilizer is hexylene glycol.

3. The topical spray composition as claimed in claim 1, wherein the non-aqueous volatile solvents are selected from one or more of ethanol, ethyl acetate, isopropyl alcohol, acetone, ethyl formate, methyl acetate, methyl ethyl ketone, cyclomethicone, dimethiconol, hexamethyldisiloxane or mixtures thereof.

4. The topical spray composition as claimed in claim 1, wherein the film formers are selected from copolymer of methyl methacrylate and butyl methacrylate, a copolymer of dimethylamine ethyl methacrylate and a neutral methacrylic acid ester, ammonio methacrylate copolymer type B, ammonio methacrylate copolymer type A, methacrylic acid copolymer type A, methacrylic acid copolymer type B, Acrylates / Octylacrylamide copolymer, urethanes polymers or copolymers, polyvinyl acetate, polyvinyl alcohol, povidone, alkylated polyvinylpyrrolidones, vinylpyrrolidone-vinylacetate, cellulose acetate, hydroxypropyl methyl cellulose, hydroxypropyl ethyl cellulose, hydroxyethyl cellulose, methyl cellulose, ethyl cellulose, or mixtures thereof.
5. The topical spray composition as claimed in claim 1, wherein the composition further comprises a co-solvent selected from alkyl benzoate, benzyl alcohol, isopropyl palmitate, isopropyl myristate, diisopropyl adipate, diethylene glycol monoethyl ether, N-methyl pyrrolidone, or mixtures thereof.

6. The topical spray composition as claimed in claim 1, wherein the composition further comprises an acidifying agent.

7. The topical spray composition as claimed in claim 1, wherein the composition forms a stable occlusive film.

8. The topical spray composition as claimed in claim 1, comprising
   (i) 0.01% to 1% (w/w) mometasone furoate,
   (ii) 1% to 15% (w/w) hexylene glycol,
   (iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents, and
   (iv) 1% to 10% (w/w) of one or more film formers.

9. A rapid drying, non-aqueous topical spray composition comprising:
   (i) mometasone furoate,
   (ii) one or more solubilizers,
   (iii) one or more non-aqueous volatile solvents,
   (iv) one or more emollients, and
   (v) one or more acidifying agents; wherein the composition forms a stable occlusive film.

10. The topical spray composition as claimed in claim 9, wherein the solubilizers are selected from one or more of hexylene glycol, propylene glycol, polyethylene glycol or mixtures thereof.

11. The topical spray composition as claimed in claim 10, wherein the solubilizer is hexylene glycol.
12. The topical spray composition as claimed in claim 9, wherein the non-aqueous volatile solvents are selected from one or more of ethanol, ethyl acetate, isopropyl alcohol, acetone, ethyl formate, methyl acetate, methyl ethyl ketone, cyclomethicone, dimethiconol, hexamethyldisiloxane or mixtures thereof.

13. The topical spray composition as claimed in claim 9, wherein the composition further comprises a co-solvent selected from alkyl benzoate, benzyl alcohol, isopropyl palmitate, isopropyl myristate, diisopropyl adipate, diethylene glycol monoethyl ether, N-methyl pyrrolidone, or mixtures thereof.

14. The topical spray composition as claimed in claim 9, wherein the composition forms a stable occlusive film.

15. The topical spray composition as claimed in claim 9, comprising:
   (i) 0.01% to 1% (w/w) mometasone furoate,
   (ii) 1% to 15% (w/w) hexylene glycol,
   (iii) 75% to 95% (w/w) of one or more non-aqueous volatile solvents,
   (iv) one or more emollients, and
   (v) one or more acidifying agents.
Figure: 1
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
A61K31/58 Version=2016.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Patseer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<td>X</td>
<td>WO20000045795 A2 (CIPLA LTD, ) 10 August 2000 the whole document especially claims</td>
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<tr>
<td>X</td>
<td>US6231875 B1 (JOHNSON &amp; JOHNSON CONSUMER COMPANIES, INC) 15 May 2001 the whole document especially page 8, line 10; page 9, line 25; page 12, line 13-25; page 13, line 19</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

Date of the actual completion of the international search
15-07-2016

Date of mailing of the international search report
15-07-2016

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Dr. Manmeet Kumar
Telephone No. +91-1125300200

Form PCT/ISA/210 (second sheet) (January 2015)
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