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(54) Title: COMPOSITION HAVING IMPROVED SPRAYING CHARACTERISTICS COMPRISING VEGETABLE OILS AND TRIGLYCERIDES AND/OR MINERAL OILS

Spray pattern diameter (mm)

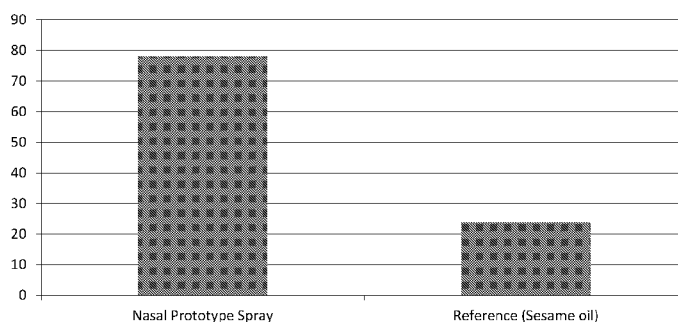


Fig. 1

(57) Abstract: A composition with improved spray characteristics consists of i) a lipophilic component comprising 40-60 % by weight of a medium to high viscosity vegetable oil or oil mixture and 40-60 % by weight of low viscous triglyceride(s) and/or mineral oil(s), and optionally ii) 0-5 % by weight of surfactant(s), iii) 0-5 % by weight of pharmaceutically active agent(s), and iv) 0-20 % by weight of propellant(s).

COMPOSITION HAVING IMPROVED SPRAYING CHARACTERISTICS COMPRISING VEGETABLE OILS AND TRIGLYCERIDES AND/OR MINERAL OILS

TECHNICAL FIELD

The present embodiments generally relate to compositions, such as intranasal compositions, and in
5 particular compositions having improved spraying characteristics.

BACKGROUND

There are several prior art oil-based nasal sprays available on the market. Many of these nasal sprays
use sesame oil as main lipophilic component due to its publically documented beneficial properties.
10 Examples of such prior art nasal sprays based on sesame oil are disclosed in WO 2005/048952.

As a nasal spray, sesame oil acts as a barrier to prevent the loss of moisture from the nasal lining (mucous
membrane), thereby restoring the natural moisture levels to nasal passages. Sesame oil also acts as a
softener which induces scabs, clots, hardened mucus, etc. to separate, thereby promoting their
15 manageability. The anti-inflammatory qualities of various naturally occurring minor components of
sesame oil have been noted. Individuals suffering from the discomforting effects of colds, sinusitis and
associated nasal inflammation (characterized by dry, irritated, crusty nasal passages, often accompanied
by bleeding or bloody discharges), have traditionally sought relief from such discomforts through the use
of isotonic saline solution. However, in a randomized crossover clinical study designed to compare the
20 quality of relief from the symptoms of dry mucosa, medical researchers tested isotonic saline solution
against pure sesame oil and found that sesame oil was significantly more effective than saline solution
at relieving the associated dryness, crustiness and stuffiness that afflict individuals suffering from dry
mucous membrane (Johnsen et al., *Arch Otolaryngol Head Neck Surg*, 2001, 127, pages 1353-1356.)

25 However, nasal sprays based on sesame oil and other medium to high viscosity vegetable oils or oil
mixtures have a less than optimal spraying pattern and characteristics. This is in part dependent on the
high viscosity of the used oils and sesame oil in particular. Sesame oil has a fairly high viscosity, 60
centipoise (cP) at room temperature (20°).

30 There is therefore a need for compositions, such as intranasal compositions, based on a medium to high
viscosity vegetable oil or oil mixture, such as sesame oil, that has improved spraying characteristics.

SUMMARY

It is a general objective to provide a composition having improved spraying characteristics.

This and other objectives are met by embodiments as disclosed herein.

An aspect of the embodiments relates to a composition consisting of a lipophilic component comprising
5 a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component.
The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 centipose (cP) at room
temperature (20°C). The medium to high viscosity vegetable oil or oil mixture comprises mono- and/or
polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.
The lipophilic component also comprises a low viscous triglyceride or a mixture of low viscous
10 triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils at 40-60 % by weight
of the lipophilic component. The composition optionally also consists of a surfactant or a mixture of
surfactants at 0-5 % by weight of the composition, a pharmaceutically active agent or a mixture of
pharmaceutically active agents at 0-5 % by weight of the composition, and a propellant or a mixture of
propellants at 0-20 % by weight of the composition.

15

Another aspect of the embodiments relates to a composition comprising a lipophilic component at 90-
99.9 % by weight of the composition. The lipophilic component comprises a medium to high viscosity
vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component. The medium to high viscosity
vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C). The medium to high
20 viscosity vegetable oil or oil mixture comprises mono- and/or polyunsaturated fats at at least 40 % by
weight of the medium to high viscosity vegetable oil or oil mixture. The lipophilic component also
comprises a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic
component. The composition also comprises a surfactant or a mixture of surfactants at 0.1-5 % by weight
of the composition.

25

A further aspect of the embodiments relates to a composition according to above for use in treating,
preventing and/or relieving symptoms of a nasal medical condition in a human subject. The nasal medical
condition is selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous
membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling.

30

A related aspect of the embodiments defines a method of treating, preventing and/or relieving a nasal
medical condition selected from a group consisting of dry nasal mucous membrane, irritated nasal
mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling in a human subject.

The method comprises intranasally administering a composition according to above to the human subject.

Yet another aspect of the embodiments relates to a composition comprising a lipophilic component at 5 80-100 % by weight of the composition for use in treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject. The lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C). The medium to high viscosity vegetable oil or oil mixture comprises mono- and/or polyunsaturated fats at at 10 least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture. The lipophilic component also comprises a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component. The nasal medical condition is selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling.

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A related aspect of the embodiments defines a method of treating, preventing and/or relieving a nasal medical condition selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling in a human subject. The method comprises intranasally administering a composition comprising a lipophilic component at 80- 20 100 % by weight of the composition to the human subject. The lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C). The medium to high viscosity vegetable oil or oil mixture comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture. The lipophilic component 25 also comprises a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component.

A further aspect of the embodiments relates to a nasal spray delivery device comprising a nozzle configured to be inserted into a nostril of a human subject and a composition container in fluid connection 30 with the nozzle. The composition container comprises a composition according to above.

Yet another aspect of the embodiments relates to use of a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils as an additive to a composition comprising a medium to high viscosity vegetable oil or oil mixture to improve spray

characteristics during administration of the composition as a spray or aerosol. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C). The medium to high viscosity vegetable oil or oil mixture comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

5

BRIEF DESCRIPTION OF THE DRAWINGS

The embodiments, together with further objects and advantages thereof, may best be understood by making reference to the following description taken together with the accompanying drawings, in which:

10 Fig. 1 is a diagram illustrating a comparison of spray pattern diameters of a reference nasal spray and a first test nasal spray (n=4);

Fig. 2 illustrates spray patterns from the reference nasal spray (Fig. 2A) and the first test nasal spray (Fig. 2B);

15

Fig. 3 is a diagram illustrating a comparison of vertical flow distances of the reference nasal spray and the first test nasal spray (n=4);

Fig. 4 illustrates vertical flow of the reference nasal spray (Fig. 4A) and the first test nasal spray (Fig. 4B)
20 on intact skin;

Fig. 5 illustrate spray patterns into paper cones for the reference nasal spray (Fig. 5A) and the first test nasal spray (Fig. 5B);

25 Fig. 6 illustrates spray patterns from the reference nasal spray (Fig. 6A) and a second test nasal spray (Fig. 6B);

Fig. 7 is a diagram illustrating a comparison of vertical flow distances of the reference nasal spray and the second test nasal sprays (n=4);

30

Fig. 8 illustrates vertical flow of the reference nasal spray (Fig. 8A) and the second test nasal spray (Fig. 8B) on intact skin;

Fig. 9 illustrate spray patterns into paper cones for the reference nasal spray (Fig. 9A) and the second test nasal spray (Fig. 9B); and

Fig. 10 illustrates results for spray pattern tests performed with test nasal sprays according to the
5 embodiments and reference nasal sprays.

DETAILED DESCRIPTION

The present embodiments generally relate to compositions, such as intranasal compositions, and in particular compositions having improved spraying characteristics.

10

Compositions, such as intranasal compositions, such as intranasal sprays and aerosols, comprising medium to high viscosity vegetable oil or oil mixture, such as sesame oil, and in particular consisting to a major part of sesame oil, have shortcomings due to the comparatively high viscosity of the oil. For instance, sesame oil typically has a viscosity of about 60 centipoise (cP) at room temperature (20°C).

15 The high viscosity results in non-optimal characteristics and properties of the composition including, for instance, low adsorption onto skin and mucous membrane and instead forming a running product on the skin or membrane surface. Furthermore, the spray pattern of compositions consisting of pure medium to high viscosity vegetable oil or oil mixture, such as sesame oil or substantially consisting of only sesame oil, will be a central jet of oil forming running droplets on the target surface.

20

The present embodiments solve at least some of the above mentioned shortcomings of compositions with medium to high viscosity vegetable oil or oil mixture. Thus, as compared to substantially pure oils, compositions of the embodiments have high degree of adsorption onto skin and mucous membrane and result in a spray mist onto a target surface.

25

The present embodiments use a lipophilic component not only comprising medium to high viscosity vegetable oil or oil mixture but also comprising low viscous triglyceride(s) and/or low viscous mineral oil(s). The addition of such low viscous triglyceride(s) and/or mineral oil(s) to the medium to high vegetable oil significantly lowers the viscosity of the resulting composition at room temperature. The
30 resulting reduction in viscosity of the composition is believed to be at least partly the basis for the improvements seen by the compositions of the embodiments over prior art compositions as shown in the experiment section.

As aspect of the embodiments relates to a composition consisting of a lipophilic component, a surfactant or a mixture of surfactants at 0-5 % by weight of the composition, a pharmaceutically active agent or a mixture of pharmaceutically active agents at 0-5 % by weight of the composition and a propellant or a mixture of propellants at 0-20 % by weight of the composition. The lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component and a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils at 40-60 % by weight of the lipophilic component. The medium to high viscosity oil or oil mixture has a viscosity above 50 cP at room temperature (20°C) and comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

Thus, in this aspect of the embodiments the composition consists of at least a lipophilic component. The composition may optionally also include surfactant(s), pharmaceutically active agent(s) and/or propellant(s).

15

In an embodiment, the composition consists of the lipophilic component comprising a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component (and thereby of the composition) and a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils at 40-60 % by weight of the lipophilic component (and thereby of the composition). In this embodiment, the composition thereby solely consists of the lipophilic component and does not comprise any additional components or ingredients.

In another embodiment, the composition consists of the lipophilic component and a surfactant or a mixture of surfactants up to an amount of no more than 5 % by the weight of the composition.

25

In a further embodiment, the composition consists of the lipophilic component and a pharmaceutically active agent or a mixture of pharmaceutically active agents up to an amount of no more than 5 % by weight of the composition.

In yet another embodiment, the composition consists of the lipophilic component and a propellant or a mixture of propellants up to an amount of no more than 20 % by weight of the composition.

In still another embodiment, the composition consists of the lipophilic component, a surfactant or a mixture of surfactants up to an amount of no more than 5 % by the weight of the composition, and a

pharmaceutically active agent or a mixture of pharmaceutically active agents up to an amount of no more than 5 % by weight of the composition.

In a further embodiment, the composition consists of the lipophilic component, a surfactant or a mixture
5 of surfactants up to an amount of no more than 5 % by the weight of the composition, and a propellant
or a mixture of propellants up to an amount of no more than 20 % by weight of the composition.

In another embodiment, the composition consists of the lipophilic component, a pharmaceutically active
agent or a mixture of pharmaceutically active agents up to an amount of no more than 5 % by weight of
10 the composition, and a propellant or a mixture of propellants up to an amount of no more than 20 % by
weight of the composition.

In a further embodiment, the composition consists of the lipophilic component, a surfactant or a mixture
of surfactants up to an amount of no more than 5 % by the weight of the composition, a pharmaceutically
15 active agent or a mixture of pharmaceutically active agents up to an amount of no more than 5 % by
weight of the composition, and a propellant or a mixture of propellants up to an amount of no more than
20 % by weight of the composition.

In a particular embodiment, the composition consists of the lipophilic component at 90-100 % by weight
20 of the composition, the surfactant or the mixture of surfactants at 0-5 % by weight of the composition, the
pharmaceutically active agent or the mixture of pharmaceutically active agents at 0-5 % by weight of the
composition, and the propellant or the mixture of propellants at 0-10 % by weight of the composition.

The lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by
25 weight of the lipophilic component. According to the embodiments, the medium to high viscosity
vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°). In a particular
embodiment, the medium to high viscosity vegetable oil or oil mixture has a viscosity within an interval of
50 to 100 cP at room temperature (20°), preferably within an interval of 60 to 90 cP at room temperature
(20°).

30

The medium to high viscosity vegetable oil or oil mixture comprises mono- and/or polyunsaturated fats
at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture. Hence, the medium
to high viscosity vegetable oil or oil mixture comprises a total amount of unsaturated fats of at least 40 %
by weight of the medium to high viscosity vegetable oil or oil mixture. The unsaturated fats of the medium

to high viscosity vegetable oil or oil mixture could be monounsaturated fats, polyunsaturated fats or a mixture of mono- and polyunsaturated fats.

In a particular embodiment, the medium to high viscosity vegetable oil or oil mixture comprises the mono-
5 and/or polyunsaturated fats at at least 50 % by weight, preferably at at least 60 % by weight, of the medium to high viscosity vegetable oil or oil mixture.

In an embodiment, the mono- and/or polyunsaturated fats are selected from a group consisting of palmitoleic acid ((9Z)-hexadec-9-enoic acid), oleic acid ((9Z)-octadec-9-enoic acid), linoleic acid
10 ((9Z,12Z)-9,12-octadecadienoic acid), linolenic acid ((9Z,12Z,15Z)-9,12,15-octadecatrienoic acid, α -linolenic acid and/or all-*cis*-6,9,12-octadecatrienoic acid, χ -linolenic acid), eicosenoic acid ((9Z)-9-icosenoic acid, gadoleic acid or 9-eicosenoic acid; (Z)-eicos-11-enoic acid, gondoic acid or 11-eicosenoic acid; and/or (13Z)-13-eicosenoic acid, paullinic acid or 13-eicosenoic acid).

15 In an embodiment, the medium to high viscosity vegetable oil or oil mixture comprises at least one antioxidant. In a particular embodiment, the at least one antioxidant is selected from a group consisting of vitamin E, vitamin K and carotenoids.

Vitamin E may be in the form of a tocopherol, a mixture of tocopherols, a tocotrienol, a mixture of
20 tocotrienols, or a mixture of at least one tocopherol and at least one tocotrienol. Examples of tocopherols include α -tocopherol, β -tocopherol, χ -tocopherol, δ -tocopherol and ε -tocopherol. Examples of tocotrienols include α -tocotrienol, β -tocotrienol, χ -tocotrienol, δ -tocotrienol and ε -tocotrienol.

Vitamin K comprises 2-methyl-1,4-naphthoquinone (3-) derivatives and includes the two natural vitamins
25 vitamin K₁ (also known as phyloquinone, phytomenadione, or phytonadione) and vitamin K₂ (also known as menaquinones or MK-n, wherein M stands for menaquinone, K stands for vitamin K, and n represents the number of isoprenoid side chain residues, for instance n=4, 7, 8 or 9).

Carotenoids are organic pigments that are found in the chloroplasts and chromoplasts of plants and some
30 other photosynthetic organisms, including some bacteria and some fungi. Carotenoids are generally classified as xanthophylls or carotenes. Non-limiting examples of suitable carotenoids include β -carotene, α -carotene, and β -cryptoxanthin. Further non-limiting examples of carotenoids include lycopersene, phytofluene, hexahydrolycopene, torulene, α -zeacarotene, alloxanthin, cynthiaxanthin,

pectenoxanthin, cryptomonaxanthin, crustaxanthin, gazaniaxanthin, OH-chlorobactene, lodoxanthin, lutein, lycoxanthin, rhodopsin, rhodopinol, saproxanthin, zeaxanthin, oscillaxanthin, phleixanthophyll, rhodovibrin, spheroidene, diadinoxanthin, luteoxanthin, mutatoxanthin, citroxanthin, zeaxanthin furanoxide, neochrome, foliachrome, trollichrome, vaucheriaxanthin, rhodopinal, warmingone, 5 torularhodinaldehyde, torularhodin, torularhodin methyl ester, astacene, astaxanthin, canthaxanthin, capsanthin, capsorubin, cryptocapsin, 2,2'-diketospirilloxanthin, flexixanthin, 3-OH-canthaxanthin, hydroxyspheriodenone, okenone, pectenolone, phoeniconone, phoenicopterone, rubixanthone, siphonaxanthin, astacein, fucoxanthin, isofucoxanthin, physalien, zeaxanthin, siphonein, apocarotenoids, apo-2-lycopenal, apo-6'-lycopenal, azafrinaldehyde, bixin, citranaxanthin, crocetin, 10 crocetinsemialdehyde, crocin, hopkinsiaxanthin, methyl apo-6'-lycopenoate, paracentrone, syntaxanthin, actinioerythrin, β -Carotenone, peridinin, pyrrhoxanthin, semi- α -carotenone, semi- β -carotenone, triphasiaxanthin, eschscholtzanthin, eschscholtzanthone, rhodoxanthin, tangeraxanthin, nonaprenoxanthin, decaprenoxanthin, 2-[4-hydroxy-3-(hydroxymethyl)-2-butenyl]-2'-(3-methyl-2-butenyl)-b,b-carotene, 2'-(4-hydroxy-3-methyl-2-butenyl)-2-(3-methyl-2-butenyl)-3',4'-didehydro-1',2'- 15 dihydro-b,y-caroten-1'-ol and bacterioruberin. A particular carotenoid of the embodiments is β -carotene.

The medium to high viscosity vegetable oil or oil mixture is preferably selected from a group consisting of sesame oil, olive oil, almond oil, apricot kernel oil, avocado oil, evening primrose oil, grapeseed oil, hazelnut oil, jojoba oil, pumpkiness oil, roship oil, safflower oil, walnut oil, wheatgerm oil, sunflower oil 20 and a mixture thereof. In a preferred embodiment, the medium to high viscosity vegetable oil is selected from a group consisting of sesame oil, almond oil, olive oil, sunflower oil and a mixture thereof.

In a particular embodiment, the medium to high viscosity vegetable oil is sesame oil. In such a particular embodiment, the lipophilic component of the composition comprises sesame oil at 40-60 % by weight of 25 the lipophilic component and the low viscous triglyceride or the mixture of low viscous triglycerides and/or the low viscous mineral oil or the mixture of low viscous mineral oils at 40-60 % by weight of the lipophilic component.

Sesame oil typically comprises about 39.7 % by weight of monounsaturated fats and about 41.7 % by 30 weight of polyunsaturated fats, i.e. unsaturated fats above 80 % by weight. The monounsaturated fats of sesame oil include palmitoleic acid, typically up to 0.5 %; oleic acid, typically within 35 to 50 %; and eicosenoic acid, typically up to 1 %. The polyunsaturated fats of sesame oil include linoleic acid, typically 35 to 50 %; and linolenic acid, typically up to 1 %. Sesame oil comprises several antioxidants including sesmin, sesamol, sesamolin, γ -tocopherol (vitamin E) and vitamin K.

Almond oil typically comprises about 62 % monounsaturated oleic acid, 29 % linoleic acid (a polyunsaturated fatty acid) and 9 % saturated fatty acid. Almond oil comprises antioxidants including vitamin E.

- 5 Olive oil typically comprises more than 85 % by weight of unsaturated fatty acids, including oleic acid at 70 % (monounsaturated), palmitoleic acid at 0.3-3.5 % (monounsaturated), linoleic acid at 15 % (polyunsaturated) and α -linolenic acid at 0.5 % (polyunsaturated). Saturated fatty acids include palmitic acid at 13 % and stearic acid at 1.5 %. Olive oil comprises high levels of antioxidants, including polyphenols and vitamin E.

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Sunflower oil typically comprises oleic oil (monounsaturated) at 30 % by weight, linoleic acid (polyunsaturated) at 59 % by weight, palmitic and stearic acid (saturated) at 5 % and 6 % by weight, respectively. Sunflower oil comprises antioxidants, including vitamin E.

- 15 The lipophilic component comprises, in an embodiment, a low viscous triglyceride or a mixture of low viscous triglycerides in addition to the medium to high viscosity vegetable oil or oil mixture, such as sesame oil. In another embodiment, the lipophilic component comprises a low viscous mineral oil or a mixture of low viscous mineral oils in addition to the medium to high viscosity vegetable oil or oil mixture, such as sesame oil. In a further variant, low viscous triglyceride(s) and low viscous mineral oil(s) are
20 present in the lipophilic component in addition to the medium to high viscosity vegetable oil or oil mixture, such as sesame oil. However, it is typically sufficient to include only one of low viscous triglyceride(s) and low viscous mineral oil(s) in the lipophilic component in order to obtain the desired characteristics of the composition.

- 25 The low viscous triglyceride is preferably a triglyceride having a viscosity no higher than 40 cP at room temperature (20°C), preferably having a viscosity no higher than 35 cP at room temperature (20°).

The low viscous triglyceride is preferably selected among medium-chain triglycerides (MCTs) containing 6–12 carbon fatty acid esters of glycerol.

30

In a preferred embodiment, the low viscous triglyceride is selected from a group consisting of capric triglyceride and caprylic triglyceride. Correspondingly, the mixture of low viscous triglycerides is preferably a mixture of capric triglyceride and caprylic triglyceride.

Capric triglyceride is a capric acid ester of glycerol. Capric acid, also referred to as decanoic acid, $\text{CH}_3(\text{CH}_2)_8\text{COOH}$, is a C10 medium-chain fatty acid. Caprylic triglyceride is a caprylic acid ester of glycerol. Caprylic acid, also referred to as octanoic acid, $\text{CH}_3(\text{CH}_2)_6\text{COOH}$, is a C8 medium-chain fatty acid.

5

The mixture of capric and caprylic triglycerides is preferably a mixture of capric triglyceride at 20-50 % by weight of the mixture and caprylic triglyceride at 50-80 % by weight of the mixture. In a particular embodiment, the mixture is preferably a mixture of capric triglyceride at 25-40 % by weight of the mixture and caprylic triglyceride at 60-75 % by weight of the mixture.

10

In an embodiment, the lipophilic component of the composition consists of the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, and the low viscous triglyceride or the mixture of low viscous triglycerides. In such a case, the lipophilic component preferably consists of the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at X % by weight of the lipophilic component
15 and the low viscous triglyceride or the mixture of low viscous triglycerides at 100-X % by weight of the lipophilic component, wherein $X \in 40-60$ % by weight of the lipophilic component.

In a preferred embodiment, the lipophilic component consists of the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at X % by weight of the lipophilic component and a mixture of capric
20 and caprylic triglycerides at 100-X % by weight of the lipophilic component. In an embodiment, $X \in 40-60$ % by weight of the lipophilic component, preferably $X \in 45-55$ % by weight of the lipophilic component, more preferably $X = 50$ % by weight of the lipophilic component.

Thus, preferred variants of lipophilic components include:

25 the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 40 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 60 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 41 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 59 % by weight of the
30 lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 42 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 58 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 43 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 57 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 44 % by weight
5 of the lipophilic component and a mixture of capric and caprylic triglycerides at 56 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 45 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 55 % by weight of the lipophilic component;

10 the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 46 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 54 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 47 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 53 % by weight of the
15 lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 48 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 52 % by weight of the lipophilic component;

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 49 % by weight
20 of the lipophilic component and a mixture of capric and caprylic triglycerides at 51 % by weight of the lipophilic component; and

the medium to high viscosity vegetable oil or oil mixture, such as sesame oil, at 50 % by weight of the lipophilic component and a mixture of capric and caprylic triglycerides at 50 % by weight of the lipophilic component.

25

The low viscous mineral is preferably a mineral oil having a viscosity no higher than 40 cP at room temperature (20°C), preferably having a viscosity no higher than 35 cP at room temperature (20°).

In an embodiment, the low mineral oil is liquid paraffin, liquid petroleum or variants or mixtures thereof.

30

A currently preferred example of liquid paraffin is so-called medicinal liquid paraffin, also known as paraffinum liquidum. Medicinal liquid paraffin is a very highly refined mineral oil traditionally used in cosmetics and for medical purposes. Also variants of medicinal liquid paraffin having slightly different

alkane blends and that are pharmaceutically acceptable could be used as low viscous mineral oil according to the embodiments.

Non-limiting examples of liquid petroleum that can be used according to the embodiments include
5 petroleum jelly, also referred to as petrolatum.

The surfactant, if present, is preferably a non-ionic surfactant or a mixture of non-ionic surfactants. However, also ionic surfactants, including zwitterionic surfactants, formulated to be non-irritating could be used according to the embodiments.

10

The surfactant, preferably non-ionic surfactant, is preferably selected from a group consisting of a glycerol monooleate, a sorbitan laurate or a mixture thereof.

Non-irritating as used herein is preferably measured by ISO 10993-10: 2002 Standard, "Biological
15 Evaluation of Medical Devices, Part 10-Test for Irritation and Sensitization", pp. 6-10, 21.

The propellant, if present, could be selected among currently used propellants for nasal sprays and aerosols. Non-limiting examples include hydrofluoralkane (HFA), such as HFA 134a (1,1,1,2-tetrafluoroethane) or HFA 227 (1,1,1,2,3,3,3-heptafluoropropane); mixtures of volatile hydrocarbons,
20 such as propane, n-butane and isobutene; dimethyl ether (DME); methyl ethyl ether; chlorofluorocarbons (CFC), or compressed gases, such as nitrogen, carbon dioxide or air.

The propellant or the mixture of propellants is typically optional in the composition. Hence, the composition could be delivered by non-propellant solutions, including manual pump sprays.

25

The composition of the embodiments is preferably an intranasal composition formulated for intranasal administration.

Preferred uses of the composition of the embodiments other than intranasal administration include
30 administration to the mouth and/or throat, topical administration to the skin, vaginal administration, anal administration or mucosal administration to various mucous membranes.

The composition of the embodiments may optionally comprise a pharmaceutically active agent or a mixture of pharmaceutically active agents. Any such pharmaceutically active agent preferably suitable

for intranasal administration can be used according to the embodiments. The at least one pharmaceutically active agent could be intended for local administration in the nose. Alternatively, or in addition, the pharmaceutically active agent could be intended for systemic administration by being taken up by the mucous membrane in the nose and entering the systemic circulation of the patient.

5

Non-limiting examples of pharmaceutically acceptable agents that can be used according to the embodiments include anti-inflammatory agents, anti-allergenic agents, anti-viral agents, anti-bacterial agents, anti-irritant agents, constricting agents, decongestant agents, anesthetic agents, analgesic agents or mixtures thereof.

10

Examples of anti-inflammatory agents include non-steroidal anti-inflammatory drugs (NSAIDs) including salicylates, such as aspirin, diflunisal, salsalate, choline magnesium trisalicylate; propionic acid derivatives, such as ibuprofen, dexibuprofen, naproxen, fenoprofen, ketoprofen, dexketoprofen, flurbiprofen, oxaprozin, loxoprofen; acetic acid derivatives, such as indomethacin, tolmetin, sulindac, etodolac, ketorolac, diclofenac, aceclofenac, nabumetone; enolic acid derivatives, such as piroxicam, meloxicam, tenoxicam, droxicam, lornoxicam, isoxicam; anthranilic acid derivatives, such as mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid; selective COX-2 inhibitors, such as celecoxib, rofecoxib, valdecoxib, parecoxib, lumiracoxib, etoricoxib, firocoxib; sulfonanilides, such as nimesulfide; licofelone; corticosteroids.

20

Examples of anti-allergenic agents include antihistamines, such as acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, cetirizine, chlorpromazine, cimetidine, cyclizine, chlorpheniramine, chlorodiphenhydramine, clemastine, cyproheptadine, desloratadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, emramine, famotidine, fexofenadine, hydroxyzine, lafutidine, levocetirizine, loratadine, meclizine, mirtazapine, nizatidine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, pyrilamine, quetiapine, ranitidine, roxatidine, rupatadine, tripeleminamine, triprolidine; glucocorticoids, such as cortisol (hydrocortisone), cortisone, prednisone, prednisolone, methylprednisolone, dexamethasone, betamethasone, triamcinolone, beclomethasone, fludrocortisone acetate, deoxycorticosterone acetate, aldosterone; epinephrine (adrenaline); theophylline; cromolyn sodium; anti-leukotrienes, such as montelukast, zafirlukast; anti-cholinergics; mast cell stabilizers.

Examples of anti-viral agents include amantadine; rimantadine; pleconaril; acyclovir; zidovudine; lamivudine; rifampicin; zanamivir and oseltamivir.

Examples of anti-bacterial agents (sometimes also referred to as anti-septic agents) include bactericides, such as Daquin's solution, sodium benzenesulfochloramide, iodopovidone, urea perhydrate solutions, peracetic acid solutions, sorbic acid, benzoic acid, lactic acid, salicylic acid, hexachlorophene, triclosan, dibromol, benzalkonium, chlorhexidine, octenidine solutions, beta-lactam antibiotics, vancomycin, daptomycin, fluoroquinolones, metronidazole, nitrofurantoin, co-trimoxazole, telithromycin, aminoglycosidic antibiotics; and bacteriostatic agents, such as tetracyclines, sulfonamides, spectinomycin, trimethoprim, chloramphenicol, macrolides, lincosamides, clindamycin, ethambutol, nitrofurantoin, novobiocin, tigecycline, oxazolidinone.

Example of anti-irritant agents include allantoin, menthol, Aloe Vera.

Examples of constricting agents include vasoconstrictors, such as amphetamines, antihistamines, caffeine, methylphenidate, mephedrone, oxymetazoline, phenylephrine, propylhexedrine, pseudoephedrine, tetrahydrozoline hydrochloride.

Examples of decongestant agents include ephedrine, levo-methamphetamine, naphazoline, oxymetazoline, phenylephrine, phenylpropanolamine, propylhexedrine, synephrine, tetrahydrozoline, xylometazoline, pseudoephedrine, tramazoline.

Examples of anesthetic agents include local anesthetic agents in particular ester local anesthetics, such as procaine benzocaine, chlorprocaine, cyclomethycaine, dimethocaine/larocaine, piperocaine, propoxycaine, procaine/novocaine, proparacaine, tetracaine/amethocaine; and amide anesthetics, such as lidocaine articaine, bupivacaine, cinchocaine/dibucaine, etidocaine, levobupivacaine, lidocaine/lignocaine, mepivacaine, prilocaine, ropivacaine, trimecaine.

Examples of analgesic agents include paracetamol; NSAIDs; COX-2 inhibitors; opioids, such as morphine, codeine, oxycodone, hydrocodone, dihydromorphine, pethidine, buprenorphine tramadol, tapentadol; flupirtine; tricyclic antidepressants, such as amitriptyline; nefopam; carbamazepine; gabapentin; pregabalin.

Another example of pharmaceutically active agent is eucalyptus and in particular eucalyptus oil that can be used to relieve the symptoms of influenza and colds. Eucalyptus oil has antibacterial effects on pathogenic bacteria in the respiratory tract. Inhaled eucalyptus oil vapor is a decongestant and treatment for bronchitis. Eucalyptus oil can also control airway mucus hypersecretion and asthma via anti-inflammatory cytokine inhibition. Eucalyptus oil has also anti-inflammatory and analgesic qualities.

In a particular embodiment, the pharmaceutically active agent is selected from a group consisting of a corticosteroid, oxymetazoline, phenylephrine, xylometazoline, naphazoline, eucalyptus, menthol, Aloe Vera, acrivastine, azelastin or a mixture thereof.

10

Non-limiting examples of compositions of the embodiments include a composition based on sunflower oil, preferably comprising sunflower oil at about 40 % by weight of the composition, a mixture of capric and caprylic triglycerides at about 60 % by weight of the composition and oxymetazoline at about 0.05 % by weight of the composition.

15

Another example composition is based on olive oil and comprises olive oil at about 40 % by weight of the composition, a mixture of capric and caprylic triglycerides at about 55 % by weight of the composition, glycerol monooleate at about 5 % by weight of the composition and corticosteroid at about 0.025 % by weight of the composition.

20

Other variants of these example compositions are possible by replacing the respective pharmaceutically active substance (oxymetazoline or corticosteroid) by another pharmaceutically active agent.

Another aspect of the embodiments relates to a composition comprising a lipophilic component at 90-99.9 % by weight of the composition. The composition also comprises a surfactant or a mixture of surfactant at 0.1-5 % by weight of the composition. The lipophilic component comprises, in this aspect, a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component and a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C) and comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

In an embodiment, the medium to high viscosity vegetable oil or oil mixture comprises at least one antioxidant. The at least one antioxidant can be selected among the previously discussed embodiments.

The medium to high viscosity vegetable oil or oil mixture, mono- and/or polyunsaturated fats and antioxidants and preferred ranges can advantageously be selected among the previously discussed embodiments. An example of a medium to high viscosity vegetable oil or oil mixture that can be used in
5 this aspect is sesame oil.

The composition is preferably an intranasal composition suitable for intranasal administration.

The previously described preferred mixtures of capric and caprylic triglycerides can advantageously be
10 used also in the composition of the present aspect.

The surfactant or mixture of surfactants can be selected among the previously described embodiments.

In an embodiment, the composition comprises the surfactant or the mixture of surfactants at Y % by
15 weight of the composition and the lipophilic component at 100 – Y % by weight of the composition. In such an embodiment, $Y \in 0.1 - 5$ % by weight of the composition.

In a particular embodiment, the surfactant or the mixture of surfactants is present in the composition according to this aspect at an amount of 0.1-1 % by weight of the composition, preferably at 0.25-0.75 %
20 by weight of the composition, such as at about 0.5 % by weight of the composition.

In an embodiment of this aspect, the composition may comprise other constituents than the lipophilic component and the surfactant(s), including other constituents than pharmaceutically active agent(s) and propellant(s).
25

A further aspect of the embodiments relates to a composition according to any previously described aspects or embodiments for use in treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject.

30 A related aspect defines use of a composition according to any previously described aspects or embodiments for the manufacture of a medicament for treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject.

Another related aspect defines a method of treating, preventing and/or relieving a nasal medical condition in a human subject. The method comprises intranasally administering a composition according to any previously described aspects or embodiments to the human subject.

5 In this aspects, the composition is preferably an intranasal composition.

Yet another aspect of the embodiments relates to a composition comprising a lipophilic component at 80-100 % by weight of the composition for use in treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject. In this aspect, the lipophilic component comprises a medium
10 to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component and a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C) and comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

15

A related aspect defines use of a composition comprising a lipophilic component at 80-100 % by weight of the composition for the manufacture of a medicament for treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject. In this related aspect, the lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the
20 lipophilic component and a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C) and comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

25 In a preferred embodiment of these aspects, the composition comprises the lipophilic component at 90-100 % by weight to the composition.

Another related aspect defines a method of treating, preventing and/or relieving a nasal medical condition in a human subject. The method comprises intranasally administering a composition comprising a
30 lipophilic component at 90-100 % by weight of the composition to the human subject. In this another related aspect, the lipophilic component comprises a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of the lipophilic component and a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of the lipophilic component. The medium to high viscosity vegetable oil

or oil mixture has a viscosity above 50 cP at room temperature (20°C) and comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

In these aspects embodiment, the medium to high viscosity vegetable oil or oil mixture optionally
5 comprises at least one antioxidant. The at least one antioxidant can be selected among the previously discussed embodiments.

In these aspects, the medium to high viscosity vegetable oil or oil mixture is preferably sesame oil.

10 In these aspects, the composition is preferably an intranasal composition.

The nasal medical condition mentioned above is preferably selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis and nasal swelling.

15

The compositions of the embodiments comprising at least one pharmaceutically acceptable agent may also, or alternatively, be used for treating, preventing and/or relieving symptoms of other medical conditions, including non-nasal medical conditions, depending on the particular pharmaceutically acceptable agent(s) present in the composition. For instance, the composition could be applied for anti-
20 inflammatory use, pruritus relief, pain reduction, hormone management, either locally or systemically, etc.

A further aspect of the embodiments relates to a nasal spray delivery device. The nasal spray delivery device comprises a nozzle configured to be inserted into a nostril of a human subject. The nasal spray
25 delivery device also comprises a composition container in fluid connection with the nozzle. The composition container comprises a composition according to any previously described aspect or embodiment.

The composition can be delivered from the composition container through the nozzle according to various
30 mechanisms. In an embodiment, the nasal spray delivery device operates as a manually operated pump and thereby comprises a pump mechanism actuated by the user to deliver the composition as a spray or aerosol. The composition container, or a separate propellant container of the nasal spray delivery device, may comprise a propellant for efficient delivery of the composition in the form of a spray or aerosol.

Hence, the nasal spray delivery device may be used for administering a composition according to the embodiments to a human subject, such as for the purpose of treating, preventing and/or relieving symptoms of a nasal medical condition.

- 5 Yet another aspect of the embodiments relates to use of a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils as an additive to a composition comprising a medium to high viscosity vegetable oil or oil mixture to improve spray characteristics during administration of the composition as a spray or aerosol. The medium to high viscosity vegetable oil or oil mixture has a viscosity above 50 cP at room temperature (20°C) and
10 comprises mono- and/or polyunsaturated fats at at least 40 % by weight of the medium to high viscosity vegetable oil or oil mixture.

In an embodiment, the medium to high viscosity vegetable oil or oil mixture comprises at least one antioxidant. The at least one antioxidant can be selected among the previously discussed embodiments.

15

In an embodiment, the composition comprises the medium to high viscosity vegetable oil at a concentration of 40-60 % by weight of the lipophilic component.

In an embodiment, the medium to high viscosity vegetable oil or oil mixture is sesame oil.

20

In a particular embodiment, improve spray characteristics means improve adsorption onto skin or mucous membrane during administration of the composition as a spray or aerosol.

In another particular embodiment, improve spray characteristics means increase spray area of the spray
25 or aerosol when administered to skin or mucous membrane.

In a further particular embodiment, improve spray characteristics means improve adsorption onto skin or mucous membrane as mentioned above and increase spray area as mentioned above.

30

EXPERIMENTS

Properties of nasal sprays of the embodiments were compared to reference nasal sprays based on pure medium to high viscosity vegetable oils using a sample canister in the form of a precompressed spray pump.

EXPERIMENT 1

In the present experiment a first test nasal spray of the embodiments containing, in addition to sesame oil and low viscous triglycerides, a surfactant was tested and compared to a reference nasal spray consisting solely of sesame oil.

5

The reference nasal spray consisted of 100 % by weight of pure sesame oil (winterized refined sesame oil (Pharmacopoea Europaea (Ph Eur)), Textron Tecnica, S.L, Spain). The test nasal spray of the embodiments consisted of 49.75 % by weight of pure sesame oil (winterized refined sesame oil (Ph Eur), Textron Tecnica, S.L., Spain), 49.75 % by weight of capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden) and 0.50 % by weight of glycerol monooleate (Cithrol™ GMO HP (Ph Eur), CRODA).

Organoleptic evaluation

Table 1 below lists the results of organoleptic evaluation of spray delivered products. Briefly, the organoleptic evaluation involved the following procedure:

- 1) Shake the sample canister for 3-5 s.
- 2) Spray 1 s for the sample canister to pre-adjust the spray.
- 3) Keep the sample canister about 15 cm from the arm.
- 4) Spray 1 s with the sample canister on the inside of the arm. Move the spray gradually down from the elbow to hand, or in the opposite direction.
 - a. Note if the spray comes out as a fine mist or as a non-even spray containing many individual droplet of different sizes.
 - b. Note the appearance of the spray on the arm. Is it evenly distributed or non-evenly distributed with clumps.
- 5) Use the hand to gently rub in the sprayed sample on the arm.
 - a. Note if the spray feels greasy, non-greasy or watery.
 - b. Note if the spray goes in quickly into the skin.
- 6) Wait 1 minute and feel on the sprayed sample on the arm.
 - a. Does it feel sticky or not.
 - b. Does it feel smooth and soft, or does it have a rough feeling.

Table 1 – Organoleptic evaluation of nasal sprays

Nasal spray	Adsorption onto skin	Feeling	Stickiness	Easiness to smear out on skin
Reference	Difficult	Soft	Non-sticky	Easy
Test	Easy	Soft	Non-sticky	Easy

The test nasal spray is similar to the reference nasal spray but adsorbs significantly better onto the skin. Hence, the addition of low viscous triglycerides does not negatively affect the soft feeling, non-stickiness and easiness to smear out of pure sesame oil. However, the addition of the low viscous triglycerides improved the adsorption onto the skin of the composition.

Spray pattern testing on paper

Spray pattern testing was conducted according to a spray patterning testing of spray delivered products. Briefly, the spray patterning testing involved:

- 1) Place the sample canister in 25°C water bath for 30 minutes.
- 2) Shake the sample canister for 4 s.
- 3) Actuate the pump and spray 5 times on a red A4 paper at 5 cm distance from the paper.
- 4) Measure the diameter (circular spray pattern) or the width and height (elliptical spray pattern).
- 5) Note if the spray is evenly distributed or if the spray is concentrated to the center alternatively to the edges.

A circular spray pattern form was obtained in the testing. Samples of the test and reference nasal sprays were each actuated once on a paper. The actuation was done at a vertical position spraying onto the paper from below at a 5 cm distance from the paper.

Fig. 1 illustrates the average spray pattern diameter for the test and reference nasal sprays. The test nasal spray achieved a significantly larger average spray pattern diameter (78 mm) as compared to the reference nasal spray (24 mm). Fig. 2 illustrate papers showing the spray patterns of the reference nasal spray (Fig. 2A) and the test nasal spray (Fig. 2B).

Vertical flow testing

A test subject had his arm in a vertical position. A nasal spray was actuated one time, at the top of the arm. The delivered product was followed down the length of the arm and the distance and time was recorded.

Table 2 – results of vertical flow analysis on inside of arm

Nasal spray	Amount added on skin (g)	Flow distance (cm)	Flow rate (cm/s)
Reference	0.08	13.5	0.45
Reference	0.08	13.9	0.46
Reference	0.09	12.5	0.42
Reference	0.07	13.5	0.45
Test	0.08	7.6	0.25
Test	0.07	8.0	0.27
Test	0.08	6.7	0.22
Test	0.08	7.5	0.25

Fig. 3 illustrates a relative comparison of flow rates for the test nasal spray and the reference nasal spray.

- 5 Fig. 4 illustrates vertical flow of reference nasal spray (Fig. 4A) and test nasal spray (Fig. 4B) on intact skin. A test subject had the arm in vertical position. Two labels marked in black indicated a distance of 11 cm. The nasal spray was actuated at the top of the arm and the delivered nasal spray was followed by distance and time down the length of the arm.

10 *Spray pattern testing on paper cone*

A red paper was cut into circles with 9 cm diameter. Each circle was cut towards the middle and mounted into a cone with the following dimensions: 7.5 cm width and 4.5 cm height. The nasal spray was pre-actuated two times and then placed on a table facing upwards. The cone was placed 1 cm above and the spray was actuated once into the cone.

15

Fig. 5 illustrates the results following actuation of reference nasal spray (Fig. 5A) and test nasal spray (Fig. 5B). In the case of reference nasal spray, the product gave a spray pattern with a central jet of sesame oil resulting in a central oil droplet on the paper. This droplet was thick and was quickly running off the paper. On the contrary, the test nasal spray resulted in a spray mist that targeted the center of the cone in a wider pattern but also with smaller droplets with a non-running product.

20

EXPERIMENT 2

In the present experiment a second test nasal spray of the embodiments containing sesame oil and low viscous triglycerides was tested and compared to a reference nasal spray consisting solely of sesame oil.

25 oil.

The reference nasal spray consisted of 100 % by weight of pure sesame oil (winterized refined sesame oil (Pharmacopoea Europaea (Ph Eur)), Textron Tecnica, S.L, Spain). The test nasal spray of the embodiments consisted of 50 % by weight of pure sesame oil (winterized refined sesame oil (Ph Eur), Textron Tecnica, S.L., Spain) and 50 % by weight of capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden). Hence, the test nasal spray lacked any surfactant in this experiment.

Organoleptic evaluation

- 10 Table 3 below lists the results of organoleptic evaluation of spray delivered products conducted as previously described for Experiment 1.

Table 3 – Organoleptic evaluation of nasal sprays

Nasal spray	Adsorption onto skin	Feeling	Stickiness	Easiness to smear out on skin
Reference	Difficult	Soft	Non-sticky	Easy
Test	Easy	Soft	Non-sticky	Easy

- 15 The test nasal spray is similar to the reference nasal spray but adsorbs better onto the skin, which is a significant advantage. Hence, the addition of low viscous triglycerides does not negatively affect the soft feeling, non-stickiness and easiness to smear out of pure sesame oil. However, the addition of the low viscous triglycerides improved the adsorption onto the skin of the composition. The same positive results are, thus, obtained for a test nasal spray lacking any surfactant (compare with Table 1).

20

Spray pattern testing on paper

Spray pattern testing was conducted according to the spray patterning testing of spray delivered products as previously described for Experiment 1. A circular spray pattern form was obtained for the reference nasal spray and an elliptical spray pattern form was obtained for the test nasal spray in the testing.

- 25 Samples of the test and reference nasal sprays were each actuated once on a paper. The actuation was done at a vertical position spraying onto the paper from below at a 5 cm distance from the paper.

The reference nasal spray resulted in an average spray pattern diameter of 20 mm (n=4). The test nasal spray resulted in an elliptical spray pattern with an average height of 86.25 mm and an average width of 42.50 mm (n=4). The test nasal spray achieved a significantly larger average spray pattern area as

30

compared to the reference nasal spray. Fig. 6 illustrate papers showing the spray patterns of the reference nasal spray (Fig. 6A) and the test nasal spray (Fig. 6B).

Vertical flow testing

- 5 A test subject had his arm in a vertical position. A nasal spray was actuated one time, at the top of the arm. The delivered product was followed down the length of the arm and the distance and time was recorded.

Table 4 – results of vertical flow analysis on inside of arm

Nasal spray	Amount added on skin (g)	Flow distance (cm)	Flow rate (cm/s)
Reference	0.08	13.0	0.43
Reference	0.08	14.2	0.47
Reference	0.08	14.0	0.47
Reference	0.08	13.2	0.44
Test	0.08	7.2	0.24
Test	0.09	8.0	0.27
Test	0.09	9.0	0.30
Test	0.08	8.0	0.27

10

Fig. 7 illustrates a relative comparison of flow rates for the test nasal spray and the reference nasal spray.

Fig. 8 illustrates vertical flow of reference nasal spray (Fig. 8A) and test nasal spray (Fig. 8B) on intact skin. A test subject had the arm in vertical position. Two labels marked in black indicated a distance of
 15 11 cm. The nasal spray was actuated at the top of the arm and the delivered nasal spray was followed by distance and time down the length of the arm.

Spray pattern testing on paper cone

A red paper was cut into circles with 9 cm diameter. Each circle was cut towards the middle and mounted
 20 into a cone with the following dimensions: 7.5 cm width and 4.5 cm height. The nasal spray was pre-actuated two times and then placed on a table facing upwards. The cone was placed 1 cm above and the spray was actuated once into the cone.

Fig. 9 illustrates the results following actuation of reference nasal spray (Fig. 9A) and test nasal spray
 25 (Fig. 9B). In the case of reference nasal spray, the product gave a spray pattern with a central jet of

sesame oil resulting in a central oil droplet on the paper. On the contrary, the test nasal spray resulted in a spray mist that targeted the center of the cone in a wider pattern but also with smaller droplets with a less running product.

5 EXPERIMENT 3

In the present experiment various test nasal sprays of the embodiments containing low viscous triglycerides, an optional surfactant and different medium to high viscosity vegetable oils were tested and compared to respective reference nasal sprays consisting solely of the vegetable oils.

10 The test nasal sprays of the embodiments consisted of:

- 1) 49.75 % by weight of pure sesame oil (winterized refined sesame oil (Ph Eur), Textron Tecnica, S.L., Spain), 49.75 % by weight of capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden) and 0.50 % by weight of glycerol monooleate (Cithrol™ GMO HP (Ph Eur), CRODA);
- 15 2) 55 % by weight Seatons Almond oil (Croda Europe Limited), 40 % by weight capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden) and 5 % by weight of glycerol monooleate (Cithrol™ GMO HP (Ph Eur), CRODA);
- 3) 40 % by weight Seatons Sunflower oil, 60 % by weight capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden); and
- 20 4) 40 % Super refined Olive oil (Croda Europe Limited), 55 % by weight capric and caprylic triglycerides (Radia 7101 (Ph Eur), Vendico Chemical AB, Sweden) and 5 % by weight of glycerol monooleate (Cithrol™ GMO HP (Ph Eur), CRODA).

The reference nasal sprays consisted of:

- 25 1) 100 % by weight of pure sesame oil (winterized refined sesame oil (Pharmacopoea Europaea (Ph Eur)), Textron Tecnica, S.L., Spain);
- 2) 100 % by weight of Seatons Almond oil (Croda Europe Limited);
- 3) 100 % by weight of Seatons Sunflower oil (Croda Europe Limited); and
- 4) 100 % by weight of Super refined Olive oil (Croda Europe Limited).

30

Spray pattern testing on paper

Spray pattern testing was conducted according to the spray patterning testing of spray delivered products as previously described for Experiment 1. A circular spray pattern form was obtained for the reference nasal sprays and an elliptical spray pattern form was obtained for the test nasal sprays in the testing.

Samples of the test and reference nasal sprays were each actuated once on a paper. The actuation was done at a vertical position spraying onto the paper from below at a 5 cm distance from the paper.

The test nasal sprays achieved significantly larger average spray pattern areas as compared to the reference nasal sprays. Fig. 6A and 6B illustrate papers showing the spray patterns of the reference sesame oil nasal spray (Fig. 6A) and the test sesame oil nasal spray (Fig. 6B). Fig. 10 illustrates the average diameter (reference samples) and average width and height (test nasal sprays) for all four tested oils (n=4).

10 The embodiments described above are to be understood as a few illustrative examples of the present invention. It will be understood by those skilled in the art that various modifications, combinations and changes may be made to the embodiments without departing from the scope of the present invention. In particular, different part solutions in the different embodiments can be combined in other configurations, where technically possible. The scope of the present invention is, however, defined by the appended
15 claims.

CLAIMS

1. A composition consisting of:
a lipophilic component comprising:
a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of said lipophilic
5 component, said medium to high viscosity vegetable oil or oil mixture having a viscosity above 50
centipoise (cP) at room temperature (20°C) and comprising mono- and/or polyunsaturated fats at at least
40 % by weight of said medium to high viscosity vegetable oil or oil mixture; and
a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous
mineral oil or a mixture of low viscous mineral oils at 40-60 % by weight of said lipophilic component;
10 a surfactant or a mixture of surfactants at 0-5 % by weight of said composition;
a pharmaceutically active agent or a mixture of pharmaceutically active agents at 0-5 % by weight
of said composition; and
a propellant or a mixture of propellants at 0-20 % by weight of said composition.
- 15 2. The composition according to claim 1, wherein said medium to high viscosity oil or oil mixture
comprises at least one antioxidant.
3. The composition according to claim 2, wherein said at least one antioxidant is selected from a
group consisting of vitamin E, vitamin K and carotenoids.
- 20 4. The composition according to any of the claims 1 to 3, wherein said medium to high viscosity
vegetable oil or oil mixture has a viscosity within an interval of 50 to 100 cP at room temperature (20°C),
preferably within an interval of 60 to 90 cP at room temperature (20°C).
- 25 5. The composition according to any of the claims 1 to 4, wherein said mono- and/or polyunsaturated
fats are selected from a group consisting of palmitoleic acid, oleic acid, linoleic acid, linolenic acid,
eicosenoic acid and erucic acid.
6. The composition according to any of the claims 1 to 5, wherein said medium to high viscosity
30 vegetable oil or oil mixture comprises said mono- and/or polyunsaturated fats at at least 50 % by weight,
preferably at at least 60 % by weight, of said medium to high viscosity vegetable oil or oil mixture.
7. The composition according to any of the claims 1 to 6, wherein said medium to high viscosity
vegetable oil or oil mixture is selected from a group consisting of sesame oil, olive oil, almond oil, apricot

kernel oil, avocado oil, evening primrose oil, grapeseed oil, hazelnut oil, jojoba oil, pumpkiness oil, roship oil, safflower oil, walnut oil, wheatgerm oil, sunflower oil and a mixture thereof.

8. The composition according to claim 7, wherein said medium to high viscosity vegetable oil is
5 sesame oil.

9. The composition according to any of the claims 1 to 8, wherein said composition is an intranasal composition formulated for intranasal administration.

10 10. The composition according to any of the claim 1 to 9, wherein said low viscous mineral oil is a liquid paraffin or liquid petroleum.

11. The composition according to any of the claims 1 to 10, wherein said lipophilic component consists of:

15 said medium to high viscosity vegetable oil or oil mixture at X % by weight of said lipophilic component, wherein $X \in 40-60$ % by weight of said lipophilic component; and
said low viscous triglyceride or said mixture of low viscous triglycerides at $100-X$ % by weight of said lipophilic component.

20 12. The composition according to any of the claims 1 to 11, wherein said low viscous triglyceride is a triglyceride having a viscosity no higher than 40 cP at room temperature (20°C), preferably a triglyceride having a viscosity no higher than 35 cP at room temperature.

13. The composition according to any of the claims 1 to 12, wherein said low viscous triglyceride or
25 said mixture of low viscous triglyceride is selected from a group consisting of capric triglyceride, caprylic triglyceride and a mixture of capric triglyceride and caprylic triglyceride.

14. The composition according to claim 13, wherein said mixture of low viscous triglyceride is a mixture of capric triglyceride at 20-50 % by weight of said mixture and caprylic triglyceride at 50-80 % by weight
30 of said mixture, preferably a mixture of capric triglyceride at 25-40 % by weight of said mixture and caprylic triglyceride at 60-75 % by weight of said mixture.

15. The composition according to any of the claims 1 to 14, wherein said composition consists of:
said lipophilic component at 90-100 % by weight of said composition;

said surfactant or said mixture of surfactants at 0-5 % by weight of said composition;
said pharmaceutically active agent or said mixture of pharmaceutically active agents at 0-5 % by weight of said composition; and
said propellant or said mixture of propellants at 0-10 % by weight of said composition.

5

16. The composition according to any of the claims 1 to 15, wherein said pharmaceutically active agent or said mixture of pharmaceutically active agents is selected from a group consisting of an anti-inflammatory agent, an anti-allergenic agent, an anti-viral agent, an anti-bacterial agent, an anti-irritant agent, a constricting agent, a decongestant agent, an anesthetic agent, an analgesic agent or a mixture thereof.

17. The composition according to claim 16, wherein said pharmaceutically active agent or said mixture of pharmaceutically active agents is selected from a group consisting of a corticosteroid, oxymetazoline, phenylephrine, xylometazoline, naphazoline, eucalyptus, menthol, Aloe Vera, acrivastine, azelastin or a mixture thereof.

18. The composition according to any of the claims 1 to 17, wherein said surfactant or said mixture of surfactants is a non-ionic surfactant or a mixture of non-ionic surfactants.

19. The composition according to claim 18, wherein said non-ionic surfactant or said mixture of non-ionic surfactants is selected from a group consisting of a glycerol monooleate, sorbitan laurate, or a mixture thereof.

20. A composition comprising:
a lipophilic component at 90-99.9 % by weight of said composition, said lipophilic component comprises:

a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of said lipophilic component, said medium to high viscosity vegetable oil or oil mixture having a viscosity above 50 centipoise (cP) at room temperature (20°C) and comprising mono- and/or polyunsaturated fats at at least 40 % by weight of said medium to high viscosity vegetable oil or oil mixture; and

a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of said lipophilic component; and

a surfactant or a mixture of surfactants at 0.1-5 % by weight of said composition.

21. The composition according to claim 20, wherein said medium to high viscosity vegetable oil is sesame oil.

22. A composition according to any of the claims 1 to 21 for use in treating, preventing and/or relieving
5 symptoms of a nasal medical condition in a human subject, wherein said nasal medical condition is selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling.

23. A composition comprising a lipophilic component at 80-100 % by weight of said composition,
10 preferably comprising said lipophilic component at 90-100 % by weight of said composition, said lipophilic component comprises:

a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of said lipophilic component, said medium to high viscosity vegetable oil or oil mixture having a viscosity above 50 centipoise (cP) at room temperature (20°C) and comprising mono- and/or polyunsaturated fats at at least
15 40 % by weight of said medium to high viscosity vegetable oil or oil mixture; and

a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of said lipophilic component, for use in treating, preventing and/or relieving symptoms of a nasal medical condition in a human subject, wherein said nasal medical condition is selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and
20 nasal swelling.

24. A method of treating, preventing and/or relieving a nasal medical condition selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling in a human subject, said method comprises intranasally
25 administering a composition according to any of the claims 1 to 21 to said human subject.

25. A method of treating, preventing and/or relieving a nasal medical condition selected from a group consisting of dry nasal mucous membrane, irritated nasal mucous membrane, sinus infection, rhinosinusitis, allergic rhinitis, and nasal swelling in a human subject, said method comprises intranasally
30 administering a composition comprising a lipophilic component at 80-100 % by weight of said composition to said human subject, preferably comprising said lipophilic component at 90-100 % by weight of said composition, said lipophilic component comprises:

a medium to high viscosity vegetable oil or oil mixture at 40-60 % by weight of said lipophilic component, said medium to high viscosity vegetable oil or oil mixture having a viscosity above 50

centipoise (cP) at room temperature (20°C) and comprising mono- and/or polyunsaturated fats at at least 40 % by weight of said medium to high viscosity vegetable oil or oil mixture; and

a mixture of capric triglyceride and caprylic triglyceride at 40-60 % by weight of said lipophilic component.

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26. A nasal spray delivery device comprising:

a nozzle configured to be inserted into a nostril of a human subject; and

a composition container in fluid connection with said nozzle and comprising a composition according to any of the claims 1 to 21.

10

27. Use of a low viscous triglyceride or a mixture of low viscous triglycerides and/or a low viscous mineral oil or a mixture of low viscous mineral oils as an additive to a composition comprising a medium to high viscosity vegetable oil or oil mixture having a viscosity above 50 centipoise (cP) at room temperature (20°C) and comprising mono- and/or polyunsaturated fats at at least 40 % by weight of said

15 medium to high viscosity vegetable oil or oil mixture, improve spray characteristics during administration of said composition as a spray or aerosol.

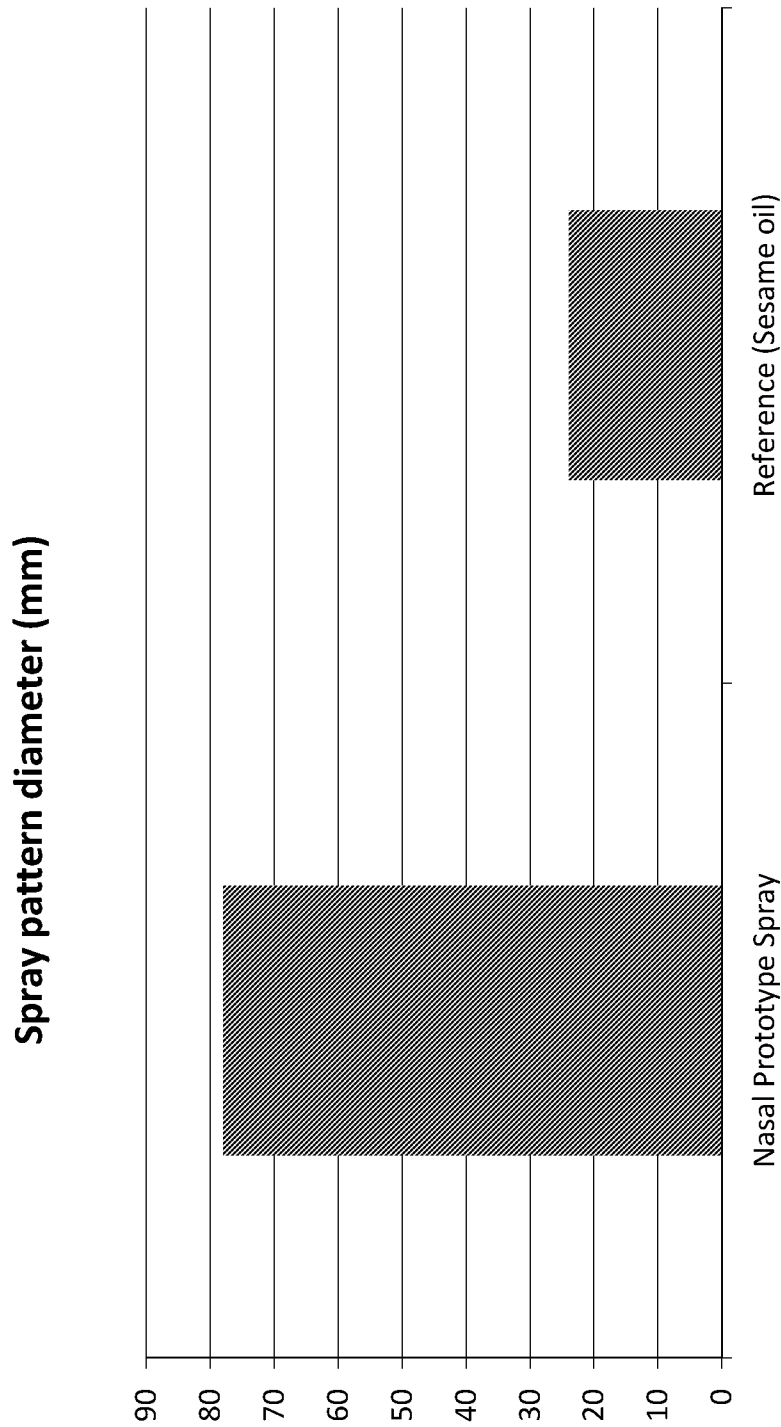


Fig. 1

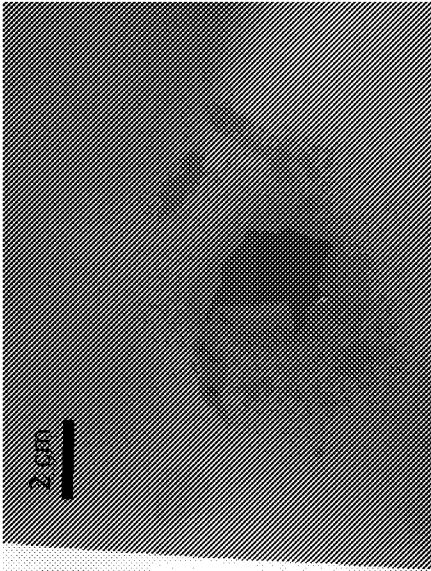


Fig. 2B

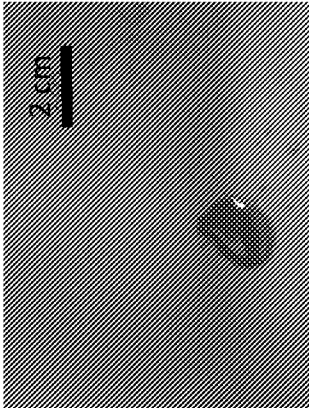


Fig. 2A

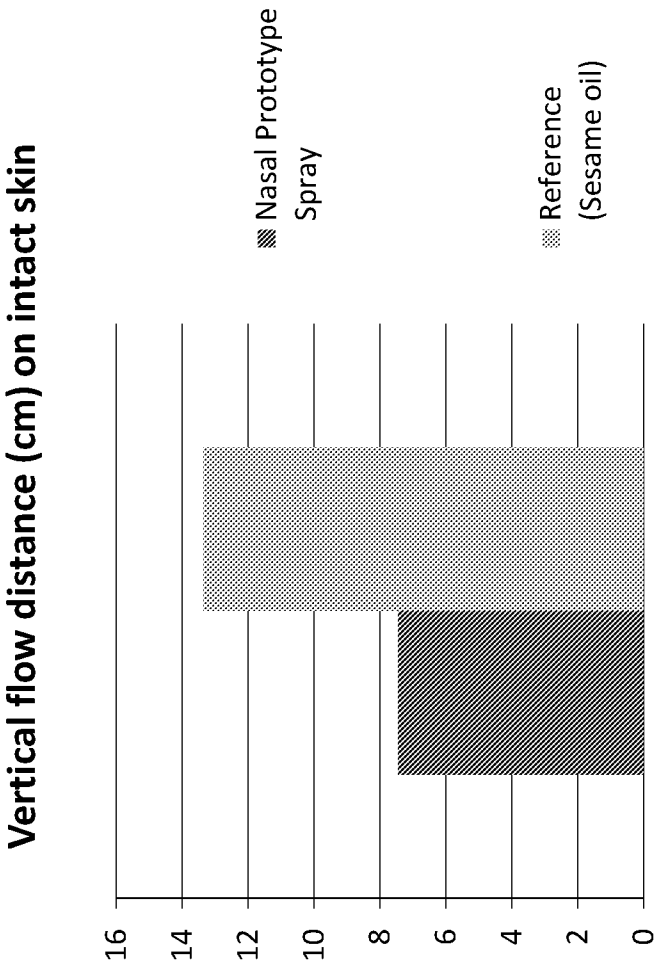


Fig. 3

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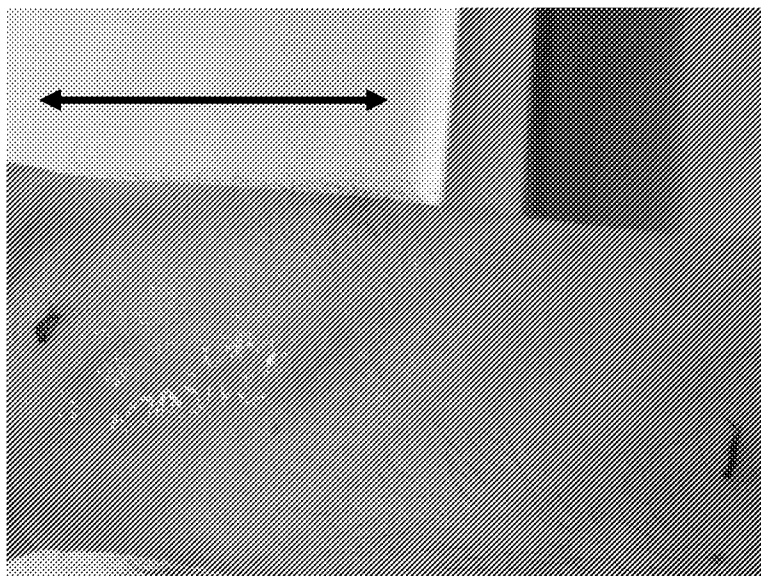


Fig. 4B

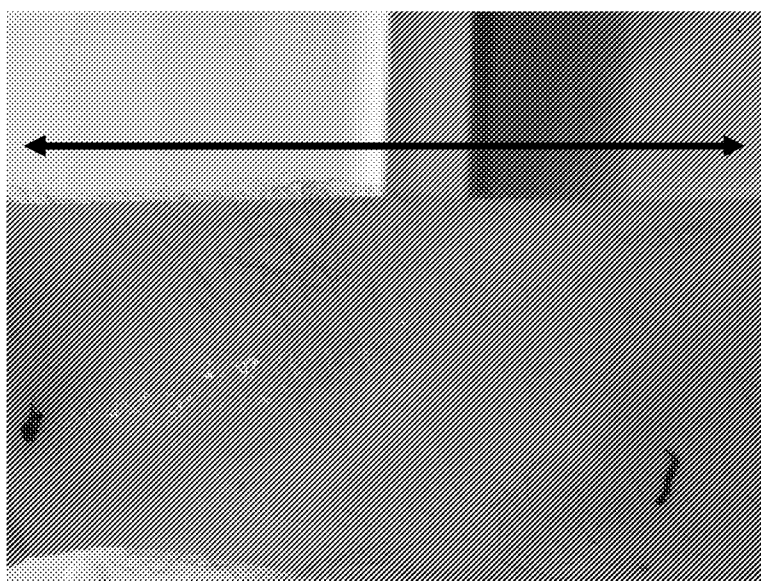


Fig. 4A

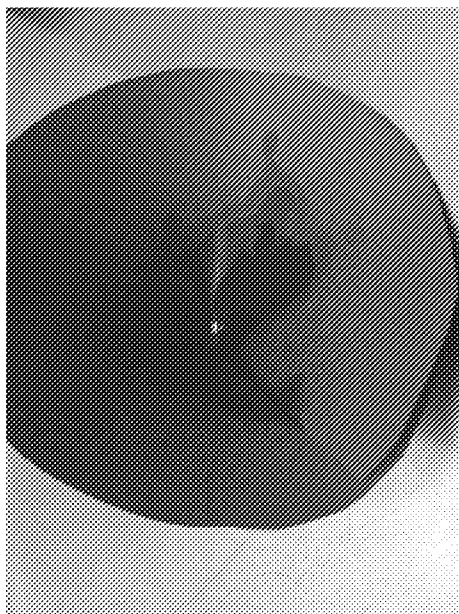


Fig. 5B

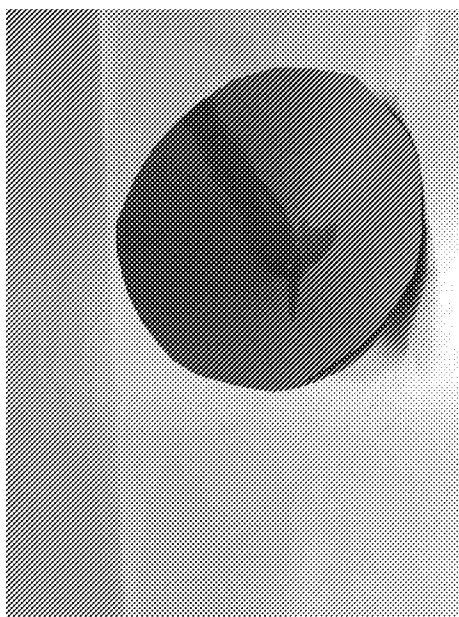


Fig. 5A

6/10

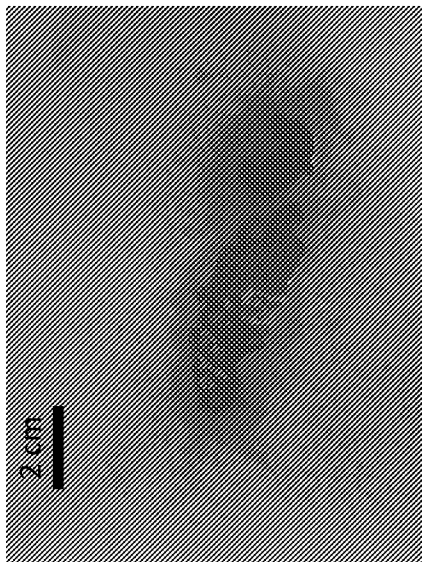


Fig. 6B

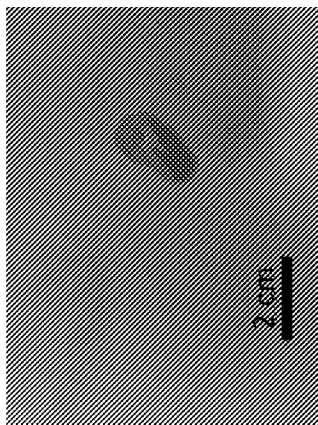


Fig. 6A

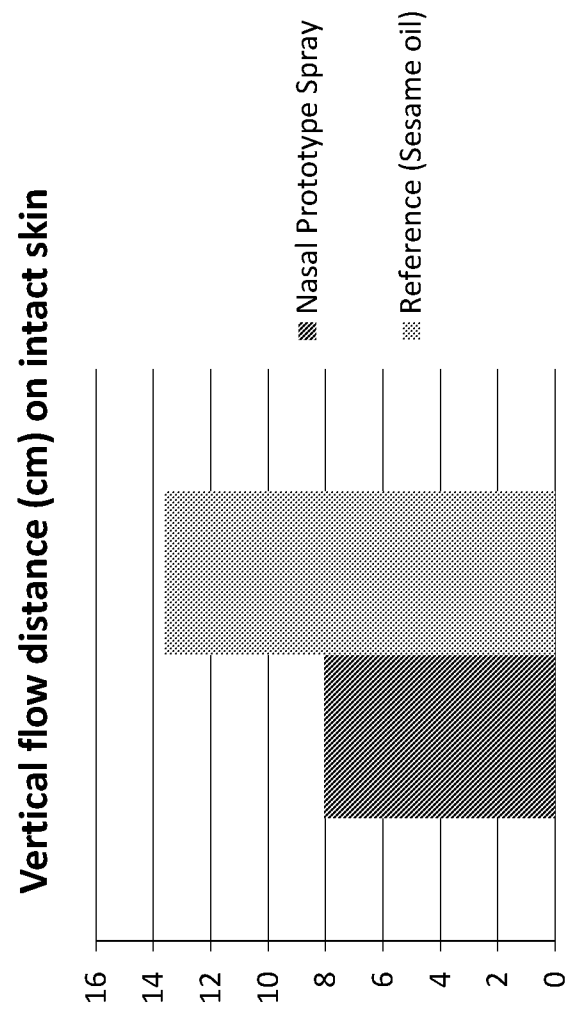


Fig. 7

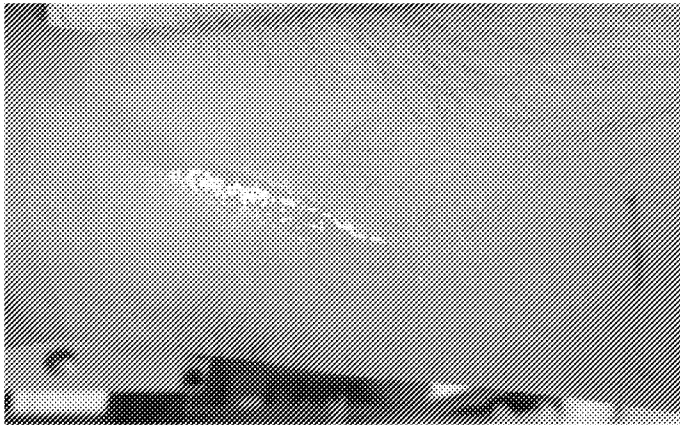


Fig. 8B

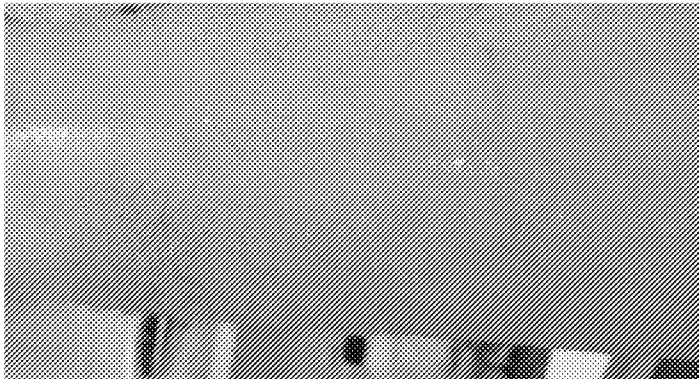


Fig. 8A

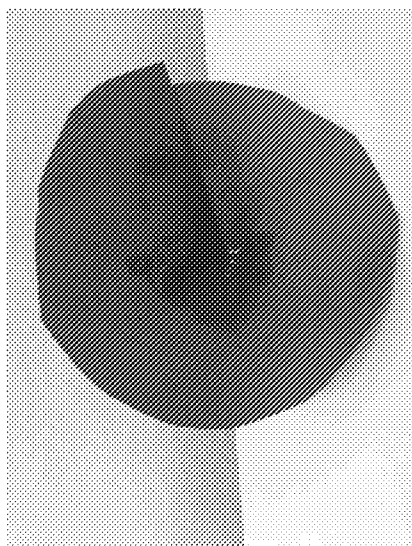


Fig. 9B

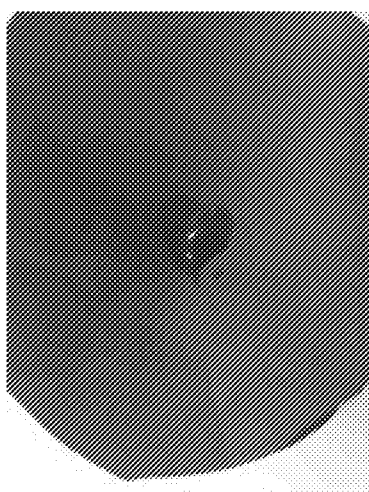
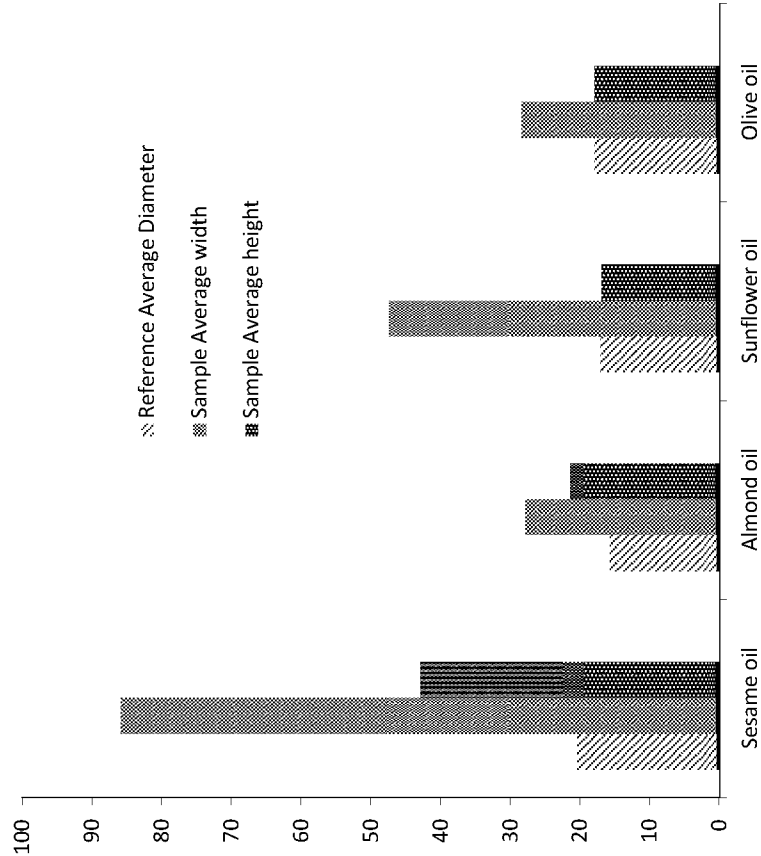


Fig. 9A

Fig. 10



INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2015/050525

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet

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)

IPC: A61K

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

SE, DK, FI, NO classes as above

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

EPO-Internal, PAJ, WPI data, CHEM ABS Data, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN103705427 (CENG N ET AL) 2014-04-09, abstract, retrieved from WPI dabase; abstract --	1-7, 10, 15
X	US 20080220107 A1 (PHARMACURE HEALTH CARE AB), 11 September 2008 (2008-09-11); abstract --	26
X	GB 2337528 A (ST GILES FOODS LTD), 24 November 1999 (1999-11-24); claims; table 2.1 --	1, 4-8, 11-15, 27
A	WO 2013065051 A1 (NAVEH PHARMA 1996 LTD), 10 May 2013 (2013-05-10); claims; Formulation 12, p 42 --	1-27



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&” document member of the same patent family

Date of the actual completion of the international search

03-09-2015

Date of mailing of the international search report

03-09-2015

Name and mailing address of the ISA/SE

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2015/050525

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JP2011213680 (IWAFUJI Y ET AL) 2011-10-27, abstract, retrieved from WPI database; abstract --	1-27
A	US 20130123720 A1 (LIND MARIANNE ET AL), 16 May 2013 (2013-05-16); claims; [0126] -- -----	1-27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2015/050525

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **24-25**
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 24-25 relate to a method for treatment of the human or animal body by .../...
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Continuation of: Box No. II

therapy, see PCT rule 39.1(iv). Nevertheless, a search has been made for these claims. The search has been directed to the technical content of the claims.

Continuation of: second sheet

International Patent Classification (IPC)

A61K 47/44 (2006.01)

A61K 9/12 (2006.01)

A61K 47/14 (2006.01)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SE2015/050525

US	20080220107	A1	11/09/2008	NONE		
GB	2337528	A	24/11/1999	NONE		
WO	2013065051	A1	10/05/2013	NONE		
US	20130123720	A1	16/05/2013	AU	2011264198	A1 29/11/2012
				CA	2800181	A1 15/12/2011
				CN	102939078	B 24/12/2014
				DK	2579852	T3 23/02/2015
				EP	2859886	A1 15/04/2015
				ES	2529506	T3 20/02/2015
				HK	1182321	A1 17/07/2015
				HR	P20150154	T1 10/04/2015
				JP	2013533859	A 29/08/2013
				KR	20130109096	A 07/10/2013
				MX	2012013591	A 01/02/2013
				NZ	603470	A 24/12/2014
				RU	2013100996	A 20/07/2014
				SG	185521	A1 28/12/2012
				WO	2011154004	A1 15/12/2011