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DESCRIPTION

[0001] The present invention relates to an oil-in-water emulsion comprising a glycopyrronium salt (GP salt) and an emulsifier system wherein the emulsifier system is a combination of macrogol glycerol monostearate, glycerol monostearate and a mixture of cetyl and glyceryl alcohols. Moreover, the present invention relates to such an emulsion for use as a medicament, in particular for treating and preventing diseases in conjunction with excessive sweating (hyperhidrosis). In addition, the present invention relates to the non-therapeutic (cosmetic) use of such an oil-in-water emulsion for topical application on the skin of a mammal in order to reduce sweating.

[0002] Excessive sweating or hyperhidrosis is a condition beyond what is physiologically required to maintain normal thermal regulation of the human body. Thus, hyperhidrosis is an extremely inconvenient condition negatively affecting daily life of a person suffering therefrom. Hyperhidrosis can be divided into focal and general primary hyperhidrosis. The focal is bilaterally symmetrical: hands, feet, axillae or groins. Focal hyperhidrosis from the face/head does occur but is often part of the general form. Generalized sweating usually involves both the head and trunk and in severe cases also extremities and groins/glutes. Whereas the majority of patients affected have the primary form which is hereditary, there is also a secondary form, often related to an underlying disease.

[0003] A variety of treatments have been proposed for treating excessive sweating/hyperhidrosis which include aluminum containing antiperspirants, surgical removal of sweat glands and systemic or local treatment with anticholinergic compounds. Any of these treatments, however, entail serious disadvantages. Aluminum containing antiperspirants, in particular upon continuous use, stain or discolor the textiles coming into contact with the antiperspirant. In addition, the increasing amount of aluminum in waste water recently has also been increasing environmental concerns. On the other hand, removal of the sweat glands means surgery that may be accompanied by at least inconvenient or even serious side effects.

[0004] As an alternative to the treatments mentioned above, glycopyrronium salts (also named glycopyrrolates) have been proposed for the treatment of excessive sweating and hyperhidrosis. WO 2006/069998 discloses the use of glycopyrronium bromide together with a large variety of other active ingredients for the treatment of excessive sweating. WO 2014/134510 relates to a specific glycopyrronium tosylate salt for the treatment of excessive sweating and hyperhidrosis. However, all of these known compositions basically suffer from at least one insufficiency selected from instability of the composition, inadequate cosmetic acceptance and skin care characteristics, systemic side effects and/or limited efficacy. WO 2012/103038, US 2015/196490 and US 2017/087088 disclose emulsions containing glycopyrrolate and a specific emulsifying agent for treating hyperhidrosis.

[0005] In view thereof there is still need in the prior art for new glycopyrronium salt containing compositions having improved properties.

[0006] Therefore, the object underlying the present invention is the provision of novel glycopyrronium salt containing compositions for the improved treatment of excessive sweating (hyperhidrosis) and in particular of primary hyperhidrosis.

[0007] This object is achieved by the provision of the oil-in-water emulsion of the present invention comprising, next to at least one glycopyrronium salt, the specific emulsifier system comprising the macrogol glycerol fatty acid ester, the glycerol fatty acid ester, and the mixture of fatty alcohols as defined in claim 1. In particular, it has surprisingly been found out that the oil-in-water emulsion according to the present invention is highly effective in the treatment of excessive sweating and in particular of hyperhidrosis. In fact, quite unexpectedly the present invention allows for an improved release of the glycopyrronium salt from the emulsion being considered as one of the reasons for the improved efficacy. Moreover, the inventive emulsion provides both for an increased stability (i.e. stable emulsion without phase separation over time) and for a cosmetic acceptance leading to a well-balanced conveniently applicable product with favorable skin care characteristics. Also surprisingly, despite of the increased release of the glycopyrronium salts, the emulsion is free of side effects typical for common glycopyrronium compositions (i.e. local and systemic side effects, such as skin irritation or even inflammation at application site, application site pain, dry mouth, dry skin, dry eye, blurred vision, mydriasis, constipation, urinary hesitation, urinary retention, and nasal dryness). In the prior art it was not possible to sufficiently fulfill these properties all together at the same time.

[0008] Therefore, the present invention relates to an oil-in-water emulsion (also named O/W emulsion) comprising one or more glycopyrronium salts (also named glycopyrrolate or GP) and a specific emulsifier system. The emulsion preferably contains a disperse (inner) oil phase and a continuous (outer) water phase containing the glycopyrronium (GP) salt. Namely, the glycopyrronium salt due to its hydrophilic property and its water solubility is mainly contained in the water phase itself and in particular at the interface of the water and oil phases of the emulsion.

[0009] The oil phase of the O/W emulsion of the present invention may be a typical oil phase of O/W emulsions known in the prior art. Preferred as the main (basic) oil ingredient of the oil phase, however, are linear or branched long chain fatty alcohols having 6 to 36 carbon atoms, preferably having 6 to 22 carbon atoms. More preferably according to the present invention the oil phase contains octyldodecanol because of its skin smoothening and moisturizing effects and stability against oxidation even under acidic conditions (e.g. pH 4). Octyldodecanol further improves the permeation behaviour of the O/W emulsion of the present invention. Thus, the oil phase containing octyldodecanol is preferred because it provides improved skin care (e.g. smoothening and moisturizing) effects corresponding to an improved cosmetic acceptance of the patient or user.

[0010] The water phase comprises mainly water as solvent and the GP salt as active ingredient for treating hyperhidrosis. The water phase may also comprise water soluble/miscible compounds (e.g. lower alcohols such as ethanol or isopropanol),

preservatives (such as benzyl alcohol or phenoxyethanol), pH adjusting agents or buffers (such as citric acid/citrate), as well as moisturizing agents (such as propylene glycol) and other typical hydrophilic pharmaceutical/cosmetic excipients.

[0011] The O/W emulsions of the present invention contain a smaller oil phase as compared to the water phase. Preferably the oil phase ranges from 10 to 25 %, and the water phase ranges from 65 to 80 wt.% of the total weight of the emulsion. Despite of the relatively small ratio of the oil phase the emulsion of the invention surprisingly provides both for better stability (no phase separation) and for improved skin care characteristics, as already mentioned above. At the same time it was unexpected that the release rate of GP salts from the larger water phase was increased. Actually, the opposite was expected, namely a decreased release rate due to the larger water phase and the high water solubility and hydrophilic properties of GP salts. This allows for further reducing the amount of GP salts leading to a better side effect profile without reducing efficacy.

[0012] The glycopyrronium (GP) salts that may be used according to the present invention are not particularly limited, and any GP salts may be used. GP salts chemically mean (2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium salts. These include the chloride, bromide, fluoride, iodide, nitrate, sulfate, sulfonate, and phosphate salts of GP. Also suitable are the acetate, propionate, glycolate, pyruvate, oxalate, succinate, fumarate, tartrate, citrate, benzoate, methanesulfonate, 4-methylbenzenesulfonate (tosylate), and salicylate salts of GP. The emulsion of the invention may contain one, two, three or more different GP salts. However, preferably it contains only one GP salt. Particularly preferred GP salts are GP bromide (GPB), GP acetate and GP tosylate.

[0013] The GP salt according to the present invention may be any (2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium salt and in particular a racemic mixture of the (3*R*)-3-[(2*S*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium and (3*S*)-3-[(2*R*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium salts. Preferably a racemic mixture of (3*R*)-3-[(2*S*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium bromide and (3*S*)-3-[(2*R*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium bromide or a racemic mixture of (3*R*)-3-[(2*S*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium tosylate and (3*S*)-3-[(2*R*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium tosylate is used.

[0014] The oil-in-water emulsion according to the present invention may contain the GP salt, and in particular the GP bromide (GPB), in an amount of 0.05 to 5 wt.%, preferably of 0.1 to 3 wt.%, more preferably of 0.2 to 2 wt.%, and even more preferably of 0.5 to 1.5 wt.%, based on the weight of the total emulsion. When the GP salt, and in particular GPB, is contained in an amount within these ranges a high efficacy in reducing excessive sweating may be achieved while at the same time potential undesirable side effects of GP salts can be avoided. Furthermore, surprisingly a stable emulsion can be obtained even with high amounts of GP salt (namely even with 2 to 5 wt.% and in particular with 2 to 3 wt.%). Overall, an amount of about 1.0 wt.% GP salt (in particular GPB or GP tosylate, most preferably GPB) is most preferred

especially from a cost, efficacy and side effect (safety) perspective.

[0015] The emulsifier system according to the present invention contains the macrogol glycerol fatty acid ester, the glycerol fatty acid ester, and the mixture of fatty alcohols as defined in claim 1. By using the specific emulsifier system in the O/W emulsion of the present invention the above mentioned effects (i.e. improved stability, increased release rate and efficacy, improved side effect profile and cosmetic acceptance/skin care characteristics) can be achieved.

[0016] With respect to the above described effects, the emulsifier system comprises a combination of macrogol glycerol monostearate, glycerol monostearate, and a mixture of cetyl alcohol and stearyl alcohol with minimum 40.0 wt% stearyl alcohol. More preferably, the emulsifier system comprises a combination of macrogol 20 glycerol monostearate, glycerol monostearate 40-55, and cetostearyl alcohol. Cetostearyl alcohol is a mixture of fatty acid alcohols, in particular a mixture of cetyl and stearyl alcohols. Most preferably the emulsifier system (essentially) consists of these indicated combinations.

[0017] The oil-in-water emulsion according to the present invention may contain the respective components of the emulsifier system in the following amounts: 4.0 to 10.0 wt.%, preferably of 5.0 to 9.0 wt.%, more preferably of 6.0 to 8.0 wt.%, and even more preferably of 6.5 to 7.5 wt.% of the macrogol glycerol fatty acid ester; 1.5 to 7.5 wt.%, preferably of 2.5 to 6.5 wt.%, more preferably of 3.5 to 5.5 wt.%, and even more preferably of 4.0 to 5.0 wt.% of glycerol fatty acid ester; 5.0 to 11.0 wt.%, preferably of 6.0 to 10.0 wt.%, more preferably of 7.0 to 9.0 wt.%, and even more preferably of 7.5 to 8.5 wt.% of fatty alcohol, based on the weight of the total emulsion, respectively. By applying these preferred ranges the stability, cosmetic acceptance and efficacy is further improved.

[0018] The emulsifier system of the oil-in-water emulsion according to the present invention may contain the respective components in the following ratios: 21 to 51 wt.%, preferably of 26 to 46 wt.%, more preferably of 31 to 41 wt.%, and even more preferably of 33 to 38 wt.% of macrogol glycerol fatty acid ester; 8 to 38 wt.%, preferably of 13 to 33 wt.%, more preferably of 18 to 28 wt.%, and even more preferably of 21 to 26 wt.% of glycerol fatty acid ester; 26 to 56 wt.%, preferably of 31 to 51 wt.%, more preferably of 36 to 46 wt.%, and even more preferably of 38 to 44 wt.% of fatty alcohol (or fatty alcohol mixture), based on the weight of the emulsifier system, respectively. By applying these preferred ratios the stability, cosmetic acceptance and efficacy is further improved.

[0019] The oil-in-water emulsion of the present invention can be used as a pharmaceutical composition/medicament, as a medical device or as a cosmetic composition, depending on the indication to be treated and the respective regulatory requirements.

[0020] The compositions in accordance with the present invention may contain cosmetically and pharmaceutically/dermatologically acceptable excipients known to the skilled person. These include, next to the ones already mentioned above, for example further solvents such

as organic solvents, gelling agents, buffers, detergents, emulsifiers, solubilizers, humectants, fillers, bioadhesives, emollients, preservatives, bactericides, surfactants, perfumes, thickeners, softening agents, moisturizing agents, oils, fats, waxes, water, alcohols, polyols, polymers, foam stabilizers, foaming agents, anti-foaming agents, hair coating agents or other suitable components of a pharmaceutical or cosmetic preparation.

[0021] Examples for bactericides are organic acids like formic acid, sorbic acid and benzoic acid. In addition esters of p-hydroxybenzoic acid, formaldehyde-releasing agents like DMDM hydantoin, imidazolidinylurea or methyl chlorisothiazolinone, methylisothiazolinone, dibromodicyanobutane, iodopropynyl butylcarbamate, phenoxyethanol or benzyl alcohol can be used as bactericides.

[0022] Further, pharmaceutically/dermatologically acceptable excipients according to the present invention may be inorganic or organic substances for topical administration. The pH value of the formulation can be stabilized using buffer systems consisting of polyacids and their salts. Examples for such polyacids are citric acid, tartaric acid and malic acid.

[0023] In the present invention, the emulsion is preferably a dermatological composition suitable to be applied topically on the skin of a mammal. The form of the composition is not particularly limited. In preferred embodiments, the compositions are in the form of lotions, creams, sprays, shampoos, foams, or saturated pads. Preferably they can be applied using a dispenser.

[0024] Clinical disorders/indications that may be treated with the emulsion of the invention generally are all indications associated with sweating, in particular excessive sweating. These include primary and secondary hyperhidrosis, gustatory sweating associated with Frey's syndrome, gustatory sweating associated with diabetic autonomic neuropathy, and excessive sweating in general. In particular, the following indications can be treated according to the present invention and are associated with dermatology, e.g. eccrine nevus, idiopathic unilateral focal hyperhidrosis, vascular deformities, pretibial myxedema; associated with gynaecology, e.g. postmenopausal hyperhidrosis; iatrogenic, such as associated with medicines, namely methadone or other opiates, cholinergics such as galantamine, SSRIs; associated with infection, e.g. brucellosis, HIV, chronic malaria, TBC, endocarditis; associated with surgery e.g. compensatory hyperhidrosis after sympathectomy; associated with medicines, such diabetes (hyperhidrosis due to neuropathy or hypoglycaemia), endocrine diseases (acromegaly, pheochromocytoma, hyperthyroidism, hypogonadism, insulinoma, heart failure, obesity); associated with neurology, e.g. central or peripheral lesion, Harlequin syndrome, Horner's syndrome, compensatory hyperhidrosis, Ross syndrome, Parkinson's disease, polyneuropathies; associated with oncology, such as carcinoid, lymphoma, with several malignancies; associated with orthopaedics, e.g. hyperhidrosis from amputation stump; associated with psychiatry, e.g. anxiety disorder, psychotropic drugs, social phobia.

[0025] Non-therapeutic (cosmetic) use of the oil-in-water emulsion of the present invention includes the topical application of the emulsion on the skin of a mammal in individuals who

experience inconvenient sweating (i.e. both including ordinary sweating and/or excessive sweating).

[0026] The emulsion or composition of the present invention preferably is applied topically on the skin of a mammal. Typical application sites include the face (e.g. forehead, chin, neck and scalp), armpit, underarms, palms of the hands, soles of the feet, backs of the knees, trunk, and groin.

[0027] The emulsion or composition of the present invention preferably is topically applied onto the skin of a mammal 1-4 times a day, more preferably 1-2 times a day, even more preferably 1 time per day prior to bedtime, most preferably 2-3 times per week.

[0028] The following examples show preferred embodiments of the invention.

Examples

[0029] The following examples have been prepared by combining the indicated ingredients using a conventional mixer (e.g. Becomix RW 320). All ingredients are commercially available. Macrogol 20 glycerol monostearate is also known as polyethylene glycol (PEG)-20 glyceryl stearate. Glycerol monostearate 40-55 is also known as glycerol monostearate 40-55% (Type II). Cetostearyl alcohol is a mixture of cetyl and stearyl alcohols.

Preparation Example 1:

Position	Substance	g/100 g
1	Macrogol 20 glycerol monostearate	7.00
2	Glycerol monostearate 40-55	4.50
3	Cetostearyl alcohol	8.00
4	Octyldodecanol	8.00
5	Benzyl alcohol	1.00
6	Glycopyrronium bromide	1.00
7	Citric acid, anhydrous	0.32
8	Sodium citrate	0.30
9	Propylene glycol	3.00
10	Purified water	66.88

Preparation Example 2:

Position	Substance	g/100 g
1	Macrogol 20 glycerol monostearate	7.00
2	Glycerol monostearate 40-55	4.50
3	Cetostearyl alcohol	8.00
4	Octyldodecanol	8.00

Position	Substance	g/100 g
5	Benzyl alcohol	1.00
6	Glycopyrronium bromide	0.50
7	Citric acid, anhydrous	0.32
8	Sodium citrate	0.30
9	Propylene glycol	3.00
10	Purified water	67.38

Preparation Example 3:

Position	Substance	g/100 g
1	Macrogol 20 glycerol monostearate	7.00
2	Glycerol monostearate 40-55	4.50
3	Cetostearyl alcohol	8.00
4	Octyldodecanol	8.00
5	Benzyl alcohol	1.00
6	Glycopyrronium bromide	2.00
7	Citric acid, anhydrous	0.32
8	Sodium citrate	0.30
9	Propylene glycol	3.00
10	Purified water	65.88

[0030] All Preparation Examples exhibited a good stability of the O/W emulsions over 18 months during stability testing (stability of emulsion in terms of phase separation and in terms of stability of active pharmaceutical ingredient (api)).

Example - Treatment of Hyperhidrosis

[0031] Preparation samples according to the present application were tested in a clinical trial assessing pharmacokinetics, local and systemic tolerability and local efficacy of ascending concentrations of glycopyrronium bromide (GPB) in a topical formulation in a placebo controlled, double blind study in subjects with axillary hyperhidrosis.

[0032] The above Preparation Examples 1 to 3 containing 0.5 to 2.0 wt.% GPB were assessed for their efficacy in treating hyperhidrosis. They were topically applied once daily for 14 days on the skin of patients suffering from hyperhidrosis.

[0033] Exemplary results of Preparation Example 1 are as follows: The sweat production after one application was reduced up to 80%. In addition, reduction of sweat production after 7 days

of treatment on day 8 was up to > 95%. In the four point HDSS (hyperhidrosis disease severity scale) a two-point improvement was observed for >70% of patients on day 8 following 7 days of treatment. Such a high efficacy of a composition containing only 1.0 wt.% of GPB is evidence for a surprisingly increased release rate of GPB from the O/W emulsion of the present invention. This is because GPB due to its hydrophilic property and significant solubility in water it was actually expected to provide for a reduced release rate from the continuous (outer) water phase of the O/W emulsion.

[0034] Apart from the efficacy the emulsion of the present invention showed local excellent tolerability and mainly a local effect. In addition, the cosmetic acceptance of the O/W emulsion was high. The emulsion provides improved skin care characteristics including smoothening and moisturizing effects.

REFERENCES CITED IN THE DESCRIPTION

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KRAV

1. En olie-i-vand-emulsion omfattende
mindst et glycopyrronium (GP)-salt og et emulgeringssystem,
5 hvor emulsionen omfatter som emulgeringssystemet en kombination af:
- macroglycerolmonostearat,
glycerolmonostearat, og
10 en blanding af cetyl- og stearylalkoholer med mindst 40,0 vægt-% stearylalkohol.
2. En olie-i-vand-emulsion ifølge krav 1, omfattende
- a) en dispergeret/indre oliefase;
b) en kontinuerlig/ydre vandfase indeholdende glycopyrronium (GP)-saltet; og
15 c) emulgeringssystemet.
3. En olie-i-vand-emulsion ifølge krav 1 og/eller krav 2, hvor GP-saltet er valgt fra gruppen bestående af GP-bromid, GP-acetat og GP-tosylat.
- 20 4. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 3, hvor GP-saltet er en racemisk blanding af (3*R*)-3-[(2*S*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium-bromid og (3*S*)-3-[(2*R*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidinium-bromid eller en racemisk blanding af (3*R*)-3-[(2*S*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-dimethylpyrrolidiniumtosylat og (3*S*)-3-[(2*R*)-(2-cyclopentyl-2-hydroxy-2-phenylacetyl)oxy]-1,1-
25 dimethylpyrrolidiniumtosylat.
5. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 4, hvor indholdet af GP-saltet er i en mængde på 0,05 til 5 vægt%, fortrinsvis fra 0,1 til 3 vægt%, mere foretrukket fra 0,2 til 2 vægt% og endnu mere fortrinsvis fra 0,5 til 1,5 vægt%, baseret på vægten af den samlede emulsion.
- 30 6. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 5 omfattende som emulgeringssystemet en kombination af
- macrogol 20 glycerolmonostearat,
35 glycerolmonostearat 40-55 og
cetostearylalkohol.

7. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 6, omfattende en mængde på 4,0 til 10,0 vægt%, fortrinsvis fra 5,0 til 9,0 vægt%, mere foretrukket på 6,0 til 8,0 vægt%, og endnu mere fortrinsvist på 6,5 til 7,5 vægt% af macrogolglycerolmonostearat,
- 5 en mængde på 1,5 til 7,5 vægt%, fortrinsvis på 2,5 til 6,5 vægt%, mere fortrinsvist på 3,5 til 5,5 vægt%, og endnu mere fortrinsvist på 4,0 til 5,0 vægt% glycerolmonostearat, og en mængde på 5,0 til 11,0 vægt%, fortrinsvis fra 6,0 til 10,0 vægt%, mere foretrukket på 7,0 til 9,0 vægt%, og endnu mere fortrinsvist på 7,5 til 8,5 vægt% af blandingen af cetyl- og stearylalkoholer, baseret på vægten af den totale emulsion.
- 10
8. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 7, hvor emulgeringssystemet omfatter en mængde på 21 til 51 vægt%, fortrinsvis fra 26 til 46 vægt%, mere foretrukket på 31 til 41 vægt%, og endnu mere fortrinsvist på 33 til 38 vægt% af macrogolglycerolmonostearat,
- 15 en mængde på 8 til 38 vægt%, fortrinsvist 13 til 33 vægt%, mere fortrinsvist fra 18 til 28 vægt% og endnu mere fortrinsvist på 21 til 26 vægt% glycerolmonostearat, og en mængde på 26 til 56 vægt%, fortrinsvis på 31 til 51 vægt%, mere fortrinsvist på 36 til 46 vægt%, og endnu mere fortrinsvist på 38 til 44 vægt% af blandingen af cetyl og stearylalkoholer, baseret på vægten af emulgeringssystemet.
- 20
9. En olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 8 til anvendelse som et medikament.
- 25
10. En olie-i-vand-emulsion til anvendelse ifølge krav 9, hvor den kliniske forstyrrelse, der skal behandles, er valgt fra gruppen bestående af primær og sekundær hyperhidrose, gustatorisk sved forbundet med Freys syndrom, gustatorisk sved forbundet med diabetisk autonom neuropati og overdreven svedtendens.
- 30
11. En olie-i-vand-emulsion til anvendelse ifølge et hvilket som helst af kravene 9 og/eller 10, hvor emulsionen påføres topisk på huden hos et pattedyr, fortrinsvis 1-4 gange om dagen, mere fortrinsvist 1-2 gange om dagen, endnu mere fortrinsvist 1 gang om dagen før sengetid, mest fortrinsvist 2-3 gange om ugen.
- 35
12. En farmaceutisk sammensætning omfattende en olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 8 og en eller flere farmaceutisk acceptable excipienser.

13. En kosmetisk sammensætning omfattende en olie-i-vand-emulsion ifølge et hvilket som helst af kravene 1 til 8 og en eller flere kosmetisk acceptable excipients.
14. En ikke-terapeutisk anvendelse af olie-i-vand-emulsionen som defineret i et hvilket som helst af kravene 1 til 8 som et kosmetisk middel, fortrinsvis til topisk påføring på huden hos et pattedyr, især til reduktion af sved hos personer, der oplever almindelig sved og/eller overdreven svedtendens.