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.

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

Summary

In one aspect, the present disclosure refers to an oil-in-water emulsion comprising
at least one glycopyrronium (GP) salt and an emulsifier system, wherein the emulsion comprises as the emulsifier system a combination of:
macrogol glycerol monostearate,
glycerol monostearate, and
a mixture of cetyl and stearyl alcohols with minimum 40.0 wt% stearyl alcohol.

In another aspect, the present disclosure refers to the oil-in-water emulsion as disclosed herein for use as a medicament.

In another aspect, the present disclosure refers to the use of the oil-in-water emulsion as disclosed herein in the manufacture of a medicament for treating a clinical disorder that is selected from the group consisting of primary and secondary hyperhidrosis, gustatory sweating associated with Frey's syndrome, gustatory sweating associated with diabetic autonomic neuropathy, and excessive sweating.

In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising the oil-in-water emulsion as disclosed herein and one or more pharmaceutically acceptable excipients.

In yet another aspect, the present disclosure refers to a cosmetic composition comprising the oil-in-water emulsion as disclosed herein and one or more pharmaceutically acceptable excipients.

In yet another aspect, the present disclosure refers to a non-therapeutic use of the oil-in-water emulsion as disclosed herein as a cosmetic, preferably for topical application on the skin of a mammal, in particular for reducing sweating in individuals who experience ordinary sweating and/or excessive sweating.

Detailed Description

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.

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 at least one macrogol glycerol fatty acid ester, at least one glycerol fatty acid ester, and at least one fatty alcohol. 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,

Claims

1. An oil-in-water emulsion comprising
at least one glycopyrronium (GP) salt and an emulsifier system,
wherein the emulsion comprises as the emulsifier system a combination of:
macrogol glycerol monostearate,
glycerol monostearate, and
a mixture of cetyl and stearyl alcohols with minimum 40.0 wt% stearyl alcohol.

2. The oil-in-water emulsion according to claim 1 comprising
a) a disperse/inner oil phase;
b) a continuous/outer water phase containing the glycopyrronium (GP) salt; and
c) the emulsifier system.

3. The oil-in-water emulsion according to claim 1 and/or claim 2, wherein the GP salt is selected from the group consisting of GP bromide, GP acetate, and GP tosylate.

4. The oil-in-water emulsion according to any one of claims 1 to 3, wherein the GP salt is 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.

5. The oil-in-water emulsion according to any one of claims 1 to 4, wherein the GP salt is contained 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.

6. The oil-in-water emulsion according to any one of claims 1 to 5 comprising as the emulsifier system a combination of
macrogol 20 glycerol monostearate,

glycerol monostearate 40-55, and
cetostearyl alcohol.

7. The oil-in-water emulsion according to any one of claims 1 to 6 comprising
an amount of 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 monostearate,
an amount of 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 monostearate, and
an amount of 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 the mixture of cetyl and stearyl alcohols,
based on the weight of the total emulsion, respectively.

8. The oil-in-water emulsion according to any one of claims 1 to 7, wherein the emulsifier system comprises
an amount of 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 monostearate,
an amount of 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 monostearate, and
an amount of 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 the mixture of cetyl and stearyl alcohols,
based on the weight of the emulsifier system.

9. The oil-in-water emulsion according to any one of claims 1 to 8 for use as a medicament.

10. Use of the oil-in-water emulsion according to any one of claims 1 to 8 in the manufacture of a medicament for treating a clinical disorder that is selected from the group consisting of primary and secondary hyperhidrosis, gustatory sweating

associated with Frey's syndrome, gustatory sweating associated with diabetic autonomic neuropathy, and excessive sweating.

11. The oil-in-water emulsion for use according to claim 9 and/or the use of claim 10, wherein the emulsion is to be topically applied onto the skin of a mammal, preferably 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.

12. Pharmaceutical composition comprising the oil-in-water emulsion according to any one of claims 1 to 8 and one or more pharmaceutically acceptable excipients.

13. Cosmetic composition comprising the oil-in-water emulsion according to any one of claims 1 to 8 and one or more cosmetically acceptable excipients.

14. Non-therapeutic use of the oil-in-water emulsion as defined in any one of claims 1 to 8 as a cosmetic, preferably for topical application on the skin of a mammal, in particular for reducing sweating in individuals who experience ordinary sweating and/or excessive sweating.