Increased water solubility of forskolin is achieved by complexing forskolin with cyclodextrins. WO2005025500A2 describes a method for complexing forskolin with cyclodextrin in an aqueous medium.

WO2017103840A1 describes water-soluble forskolin compositions by complexation with water-soluble polymers such as PVP, among others. After mixing forskolin with the polymer, a starch solution is added and the mixture is heated, then cooled and spray-dried.

WO2018127600A1 discloses a method for preparing forskolin-cyclodextrin complexes, which is based on a sintering process and allows an increased content of forskolin in the complex, as well as increased water solubility.

Another approach to increase the water solubility of forskolin is chemical derivatization. A forskolin derivative with higher water solubility compared to forskolin is 7-deacetyl forskolin, which shows a similar effect on adenylyl cyclase as forskolin (Laurenza A. et al, Molecular Pharmacology 1987, 32(1), 133-139, Pinto C. et al, Biochemical Pharmacology 2009, 78(1), 62-69). However, deacetylation of forskolin at position 7 can only increase water solubility to a limited extent (up to 1 mg/mL).

Therefore, there is a need for an improved water-soluble form of a forskolin derivative, which is characterized by both high water solubility and thus improved bioavailability, and high forskolin derivative content.

It is therefore an object of the present invention to provide a form of 7-deacetyl-forskolin having increased solubility in water and, at the same time, a high content of 7-deacetyl-forskolin.

SUMMARY

The object is solved by a complex of 7-deacetyl-forskolin (7-DAFSK) and polyvinylpyrrolidone (PVP), as described in the claims, aspects, examples and embodiments of the present disclosure.

The present disclosure discloses a complex of 7-deacetyl-forskolin (7-DAFSK) and polyvinylpyrrolidone (PVP).

In an aspect of the present disclosure, there is provided a complex of 7-deacetyl-forskolin (7-DAFSK) and polyvinylpyrrolidone (PVP), characterized in that PVP has an average molar mass relative to the weight average molar mass of from 2 to 25 kD, particularly preferably about 2.5 kD.

In another aspect of the present disclosure, there is provided a process for the preparation of a complex disclosed herein, characterized in that a mixture of 7-DAFSK

CLAIMS

1. Complex of 7-deacetyl-forskolin (7-DAFSK) and polyvinylpyrrolidone (PVP), characterized in that PVP has an average molar mass relative to the weight average molar mass of from 2 to 25 kD, particularly preferably about 2.5 kD.

~~2. Complex according to claim 1, characterized in that PVP has an average molar mass relative to the weight average molar mass of from 1 to 40 kD, preferably from 2 to 25 kD, particularly preferably about 2.5 kD.~~

~~3.~~2. Complex according to claim 1 ~~or 2~~, characterized in that 7-DAFSK is derived from synthetic forskolin.

~~4.~~3. Complex according to claim 1 or 2~~any one of claims 1 to 3~~, characterized in that the average mass fraction of 7-DAFSK in the total complex is in the range from 1 to 50% by weight, preferably 30% by weight, or higher.

~~5.~~4. Process for the preparation of a complex according to any one of claims 1 to 3~~4~~, characterized in that a mixture of 7-DAFSK and PVP is heated to a temperature which is above the glass transition temperature of the PVP used.

~~6.~~5. Process according to claim 4~~5~~, characterized in that a solvent, preferably water, ethanol, methanol, acetone, ethyl methyl ketone, dichloromethane and/or ethyl acetate, more preferably water, ethanol, methanol, propanol and/or dichloromethane, even more preferably water and/or ethanol, or a mixture thereof, is added to the mixture of 7-DAFSK and PVP.

~~7.~~6. Process according to claim 4~~5~~ or 5~~6~~, characterized in that the mixture is kept at a temperature above the glass transition temperature of the PVP used for at least 5 minutes.

~~8.~~7. Method according to any one of claims 4~~5~~ to 6~~7~~ comprising the steps of:

a) Preparation of a mixture of 7-DAFSK and PVP and addition of a solvent, preferably an alcohol, preferably ethanol, to the mixture,

b) Addition of water or an aqueous solution,

c) Heating the mixture above the glass transition temperature of the PVP for at least 5 minutes,

d) Cooling of the mixture and dissolving in water or an aqueous solution,

e) Removal of undissolved components, optionally by filtering.

~~9.~~8. Pharmaceutical composition comprising a complex according to any one of claims 1 to 3~~4~~.

~~10.~~9. Pharmaceutical composition according to claim ~~8~~9 for use as a medicament.

~~11.~~10. Pharmaceutical composition according to claim ~~8~~9, characterized in that the composition contains 7-DAFSK in a concentration of at least 25 mg/L, preferably at least 100 mg/mL, 250 mg/mL, 500 mg/mL, 1000 mg/mL, 2000 mg/mL, 3000 mg/mL or 4000 mg/mL, particularly preferably 4000 mg/mL.

~~12.~~11. Pharmaceutical composition according to claim ~~8~~9 or 10~~11~~ for intravenous, oral or inhalation administration.

~~13.~~12. Pharmaceutical composition of any one of claims ~~8~~9 to 11~~12~~ for use in the treatment of cardiovascular disease, bronchial asthma, obesity, glaucoma, pulmonary disease, joint inflammation, or osteoarthritis/arthritis.