Summary

In one aspect of the present disclosure, there is provided a powder composition comprising glucagon (SEQ ID NO: 1), a phospholipid, and ß-cyclodextrin, wherein the ratio of glucagon to phospholipid to ß-cyclodextrin is 1:1:8 by weight.

In another aspect of the present disclosure, there is provided a powder composition consisting of glucagon (SEQ ID NO: 1), dodecylphosphocholine, and ß-cyclodextrin, wherein the ratio of glucagon to dodecylphosphocholine to ß-cyclodextrin is 1:1:8 by weight.

In a further aspect of the present disclosure, there is provided a nasal applicator for a powder formulation, said applicator including a powder formulation reservoir, and a powder formulation contained within the reservoir, wherein the powder formulation is a composition disclosed herein.

In another aspect of the present disclosure, there is provided a method for preparing a powder formulation disclosed herein, wherein at least a portion of the powder is present in a phase characterized by an XRPD mesopeak as determined by x-ray powder diffraction, said method comprising the steps of

a. forming a first solution of the glucagon (SEQ ID NO. 1) and the phospholipid in an aqueous carrier, wherein the phospholipid is present in a concentration greater than or equal to the critical micelle concentration;

b. adding the ß-cyclodextrin to the first mixture to form a second mixture;

c. drying the second mixture to form a solid formulation; and

d. processing the solid formulation to produce a uniform powder, said uniform powder including at least a portion of the powder in a phase characterized by an XRPD mesopeak.

In a further aspect of the present disclosure, there is provided a method for preparing a powder formulation disclosed herein, said method comprising the steps of

a. forming a first solution of the glucagon (SEQ ID NO. 1) and the phospholipid in an aqueous carrier, wherein the phospholipid is present in a concentration greater than or equal to the critical micelle concentration;

b. adding the ß-cyclodextrin to the first mixture to form a second mixture;

c. drying the second mixture to form a solid formulation; and

d. processing the solid formulation to produce a uniform powder.

In another aspect of the present disclosure, there is provided a use of a powder composition disclosed herein, in the manufacture of a medicament for treating hypoglycemia in an individual suffering from hypoglycemia, wherein the medicament is to be administered in a therapeutically effective amount as a powder to the nasal mucosa of the individual.

In a further aspect of the present disclosure, there is provided a powder composition disclosed herein for use in treating hypoglycemia.

The present disclosure also relates to a powder formulation of glucagon or a glucagon analog is provided. This powder composition comprises glucagon or a glucagon analog, a cyclodextrin, and a phospholipid surfactant, and is formulated such that at least a portion of the powder is present in a phase characterized by an XRPD mesopeak as determined by x-ray powder diffraction. In further specific embodiments, the powder composition consists of:

(a) 5 to 15 wt% glucagon or glucagon analog;

(b) 5 to 51 wt% of phospholipid surfactant;

(c) 44 to 90 wt% of cyclodextrin and

(d) optionally, up to 10 wt% of a low molecular weight organic acid, or a pharmaceutically acceptable water soluble salt of ester thereof.

A nasal applicator for a powder formulation is also provided. The applicator includes a powder formulation reservoir, and a powder formulation in accordance with the present disclosure contained within the reservoir

There is also provided a method for making the powder formulation of the present disclosure is provided. This method comprises the steps of :

(a) forming a first mixture of the glucagon and the surfactant in an aqueous carrier, wherein the surfactant is present at a concentration greater than or equal to the critical micelle concentration;

(b) adding the cyclodextrin to the first mixture to form a second mixture;

(c) drying the second mixture to form a solid formulation; and

(d) processing the solid formulation to produce a uniform powder, said uniform powder including at least a portion of the powder in a phase characterized by an XRPD mesopeak. In specific embodiments, the drying of the second mixture may be carried out by freeze drying or spray drying the second mixture.

WE CLAIM:

1. A powder composition comprising glucagon (SEQ ID NO: 1), a phospholipid, and ß-cyclodextrin, wherein the ratio of glucagon to phospholipid to ß-cyclodextrin is 1:1:8 by weight.
2. The powder composition of claim 1, wherein the phospholipid is at least one member selected from the group consisting of dodecylphosphocholine, didecylphosphatidylcholine, lysolauroylphosphatidylcholine, dioctanoylphosphatidylcholine, dilauroylphosphatidylglycerol or mixtures thereof.
3. The powder composition of claim 2, wherein the phospholipid is dodecylphosphocholine.
4. The powder composition of claim 2, wherein the phospholipid is didecylphosphatidylcholine.
5. The powder composition of claim 2, wherein the phospholipid is lysolauroylphosphatidylcholine.
6. The powder composition of claim 2, wherein the phospholipid is dioctanoylphosphatidylcholine.
7. The powder composition of claim 2, wherein the phospholipid is dilauroylphosphatidylglycerol.
8. A powder composition consisting of glucagon (SEQ ID NO: 1), dodecylphosphocholine, and ß-cyclodextrin, wherein the ratio of glucagon to dodecylphosphocholine to ß-cyclodextrin is 1:1:8 by weight.
9. The powder composition according to claim 1, further comprising sodium citrate or citric acid.
10. The powder composition according to claim 9, wherein the amount of sodium citrate or citric acid is up to 10 percent by weight of the overall weight of the composition.
11. The powder composition according to claim 1, further comprising water.
12. The powder composition according to claim 11 wherein the water content of the composition is below 5 percent by weight of the overall weight of the composition

13. A nasal applicator for a powder formulation, said applicator including a powder formulation reservoir, and a powder formulation contained within the reservoir, wherein the powder formulation is a composition in accordance with claim 1.

14. A method for preparing a powder formulation of claim 1, wherein at least a portion of the powder is present in a phase characterized by an XRPD mesopeak as determined by x-ray powder diffraction, said method comprising the steps of

    a. forming a first solution of the glucagon (SEQ ID NO. 1) and the phospholipid in an aqueous carrier, wherein the phospholipid is present in a concentration greater than or equal to the critical micelle concentration;

    b. adding the ß-cyclodextrin to the first mixture to form a second mixture;

    c. drying the second mixture to form a solid formulation; and

    d. processing the solid formulation to produce a uniform powder, said uniform powder including at least a portion of the powder in a phase characterized by an XRPD mesopeak.

15. A method for preparing a powder formulation of claim 1, said method comprising the steps of

    a. forming a first solution of the glucagon (SEQ ID NO. 1) and the phospholipid in an aqueous carrier, wherein the phospholipid is present in a concentration greater than or equal to the critical micelle concentration;

    b. adding the ß-cyclodextrin to the first mixture to form a second mixture;

    c. drying the second mixture to form a solid formulation; and

    d. processing the solid formulation to produce a uniform powder.

16. The method of claim 14, wherein the drying of the second mixture is carried out by freeze drying or spray drying the second mixture.

17. The method of claim 15, wherein the drying of the second mixture is carried out by freeze drying or spray drying the second mixture.

18. Use of a powder composition according to claim 1, in the manufacture of a medicament for treating hypoglycemia in an individual suffering from hypoglycemia, wherein the medicament is to be administered in a therapeutically effective amount as a powder to the nasal mucosa of the individual.

19. The use of claim 18, wherein the powder formulation is to be administered to only one nostril of the individual.

20. A powder composition according to claim 1 for use in treating hypoglycemia.