

administered in a fasted state, however, and the bioavailability of semaglutide from this product is only about 1%.

Efforts have been made to develop improved compositions and dosage forms. For example, WO2022049310 describes solid oral pharmaceutical compositions stated to provide improved bioavailability.

Nevertheless, there remains a need for new therapies providing greater bioavailability than currently available therapies. There also remains a need for new therapies with greater flexibility in administration, in particular with no requirements regarding administration in either a fed or fasted state.

BRIEF SUMMARY

The present disclosure provides compositions suitable for oral administration of proteins or peptides. The compositions are designed to provide greater bioavailability as compared to currently available therapies that are orally administered. The compositions also may be administered to a patient in either a fasted or a fed state.

According to an example of the present disclosure there is provided a solid oral pharmaceutical dosage form comprising:

- a) a core composition comprising a therapeutic protein or peptide;
- b) a capsule that contains the core composition and wherein the capsule has a body and a cap;
- c) a polymeric seal covering the transition between the capsule cap and body; and
- d) an enteric coating that coats the polymeric seal and capsule.

According to a preferred example, the dosage form releases: none of the therapeutic peptide or protein in fluid having $\text{pH} \leq 4.5$ and releases the majority of the peptide or protein in fluid having $\text{pH} \geq 6.0$.

According to another preferred example, the dosage form releases: none of the therapeutic peptide or protein for up to 2 hours in fluid having pH between 4.5 and 6.0; and the majority of the peptide or protein in fluid having $\text{pH} \geq 6.0$.

According to a preferred example, the dosage form releases: none of the therapeutic peptide or protein for up to 2 hours in fluid having pH between 4.5 and 6.0; and the majority of the peptide or protein in fluid having $\text{pH} \geq 6.8$.

According to another preferred example, the enteric coating comprises a co-polymer comprising at least one polymer selected from the group consisting of methyl acrylate, methyl methacrylate, methacrylic acid and ethyl acrylate.

According to another preferred example, the enteric coating comprises
5 poly[methacrylic acid, ethyl acrylate] wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.

According to another preferred example, the enteric coating comprises poly[methyl acrylate, methyl methacrylate, methacrylic acid] in a ratio of about 7:3:1.

According to another preferred example, the therapeutic peptide or protein is an
10 analog of peptide tyrosine-tyrosine (PYY) or has agonistic activity at one or more of the glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1), glucagon (GCG), amylin and/or calcitonin receptors.

According to another preferred example, the core composition further comprises a permeation enhancer is selected from the group consisting of sodium N-[8-(2-
15 hydroxybenzoyl) amino] caprylate (SNAC), salcaprozate sodium, sodium caprate (C10), or 8-(N-2-hydroxy-5-chlorobenzoyl)-amino-caprylic acid (5-CNAC).

According to another preferred example, the relative bioavailability of the therapeutic peptide or protein following oral administration of the dosage form is greater than 1% of what would be achieved through subcutaneous administration.

According to another preferred example, the bioavailability of the therapeutic peptide
20 or protein on oral administration of the dosage form is not negatively impacted if administered with food.

According to an aspect of the present disclosure there is provided a solid oral pharmaceutical dosage form comprising:

- 25 a) a core composition comprising a therapeutic protein or peptide and C10;
 b) a capsule that contains the core composition and wherein the capsule has a body and a cap;
 c) a polymeric seal covering the transition between the capsule cap and body;
 and
30 d) an enteric coating that coats the polymeric seal and capsule, wherein the coating comprises one or more co-polymers selected from the group consisting of:

- i) poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.; and
- ii) poly[methyl acrylate, methyl methacrylate, methacrylic acid], wherein the methyl acrylate, methyl methacrylate and methacrylic acid are present in a ratio of about 7:3:1.

5

In another example, there is provided a solid pharmaceutical dosage form for oral administration comprising: (a) a core composition comprising: (i) 5-25 mg of tirzepatide; and (ii) about 280 mg C10; (b) a capsule that contains the core composition and that has a body and a cap; (c) a polymeric seal over the transition between the capsule cap and body comprising: (i) about 17% HPMC; (ii) about 58% ethanol; and (iii) about 25% water; and (d) a coating that coats the polymeric seal and capsule and that comprises: (i) about 12.9% poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.; (ii) about 51.6% poly[methyl acrylate, methyl methacrylate, methacrylic acid], wherein the methyl acrylate, methyl methacrylate and methacrylic acid are present in a ratio of about 7:3:1; (iii) about 2.9% TEC; and (iv) about 32.6% water; and wherein the coating level is about 10 mg/cm².

10

15

In another example, there is provided a solid pharmaceutical dosage form for oral administration comprising: (a) a core composition comprising: (i) 1-25 mg of a therapeutic peptide or protein; (ii) about 280 mg C10; (iii) about 66 mg MCC; (b) a capsule that contains the core composition and that has a body and a cap; (c) a polymeric seal over the transition between the capsule cap and body comprising: (i) about 17% HPMC; (ii) about 58% ethanol; and (iii) about 25% water; and (d) a coating that coats the polymeric seal and capsule and that comprises: (i) about 12.9% poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.; (ii) about 51.6% poly[methyl acrylate, methyl methacrylate, methacrylic acid], wherein the methyl acrylate, methyl methacrylate and methacrylic acid are present in a ratio of about 7:3:1; (iii) about 2.9% TEC; and (iv) about 32.6% water; and wherein the coating level is about 10 mg/cm².

20

25

In another example, there is provided a solid pharmaceutical dosage form for oral administration comprising: (a) a core composition comprising: (i) 1-25 mg of a therapeutic peptide or protein; (ii) about 280 mg C10; (iii) about 66 mg MCC; (b) a capsule that contains the core composition and that has a body and a cap; (c) a polymeric

30

seal over the transition between the capsule cap and body comprising: (i) about 17% HPMC; (ii) about 58% ethanol; and (iii) about 25% water; and (d) a coating that coats the polymeric seal and capsule and that comprises: (i) about 64.5% poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.; (ii) about 2.9% TEC; and (iii) about 32.6% water; and wherein the coating level is about 7 mg/cm².

According to another example of the present disclosure there is provided a method of treating a disease or condition in a patient in need thereof comprising administering a dosage form as described herein.

10 According to another aspect of the present disclosure there is provided the dosage form as disclosed herein for use in treating a disease or condition.

According to another example of the present disclosure there is provided a dosage form of the present disclosure for use in the treatment of a disease or condition in a patient.

15 According to a preferred example, the dosage form may be administered with or without food. According to a preferred example, the disease or condition is selected from the group consisting of type 2 diabetes mellitus (T2DM), obesity, cardiovascular disease (CVD), non-alcoholic steatohepatitis (NASH), fatty liver disease (FLD), dyslipidemia, metabolic syndrome, cognitive decline, Parkinson's syndrome and Alzheimer's disease.

20 According to another aspect of the present disclosure there is provided use of the dosage form as disclosed herein in the manufacture of a medicament for treating a disease of condition, wherein the disease or condition is selected from the group consisting of type 2 diabetes mellitus (T2DM), obesity, cardiovascular disease (CVD), non-alcoholic steatohepatitis (NASH), fatty liver disease (FLD), dyslipidemia, metabolic syndrome, 25 cognitive decline, Parkinson's syndrome and Alzheimer's disease.

According to another example of the present disclosure there is provided a process for preparing a dosage form as described herein, comprising:

- a) blending all components comprised in the core composition in a suitable blender;
- 30 b) weighing an amount of the blend formed in step (a) to be the core composition;

-5a-

- c) compressing the blend weighed in step (b) using a capsule slug mold;
- d) placing the slug formed in step (c) into the capsule;
- e) covering the transition between the capsule cap and body with the polymeric seal; and
- f) coating the capsule with the enteric coating.

WE CLAIM:

1. A solid oral pharmaceutical dosage form comprising:

- a) a core composition comprising a therapeutic protein or peptide and C10;
- b) a capsule that contains the core composition and wherein the capsule has a
5 body and a cap;
- c) a polymeric seal covering the transition between the capsule cap and body;
and
- d) an enteric coating that coats the polymeric seal and capsule, wherein the
coating comprises one or more co-polymers selected from the group
10 consisting of:
 - i) poly[methacrylic acid, ethyl acrylate], wherein the methacrylic
acid and ethyl acrylate are present in a ratio of about 1:1.; and
 - ii) poly[methyl acrylate, methyl methacrylate, methacrylic acid],
wherein the methyl acrylate, methyl methacrylate and
15 methacrylic acid are present in a ratio of about 7:3:1.

2. The dosage form of claim 1, wherein:

the core composition comprises: (i) 5-25 mg of tirzepatide; and (ii) about 280
mg C10;

the polymeric seal comprises: (i) about 17% HPMC; (ii) about 58% ethanol;
20 and (iii) about 25% water; and

the enteric coating comprises: (i) about 12.9% poly[methacrylic acid, ethyl
acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of
about 1:1.; (ii) about 51.6% poly[methyl acrylate, methyl methacrylate, methacrylic
acid], wherein the methyl acrylate, methyl methacrylate and methacrylic acid are
25 present in a ratio of about 7:3:1; (iii) about 2.9% TEC; and (iv) about 32.6% water;
and

wherein the coating level is about 10 mg/cm².

3. The dosage form of claim 1 wherein:

the core composition comprises: (i) 1-25 mg of a therapeutic peptide or
30 protein; (ii) about 280 mg C10; and (iii) about 66 mg MCC;

the polymeric seal comprises: (i) about 17% HPMC; (ii) about 58% ethanol;
and (iii) about 25% water; and

the enteric coating comprises: (i) about 12.9% poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1; (ii) about 51.6% poly[methyl acrylate, methyl methacrylate, methacrylic acid], wherein the methyl acrylate, methyl methacrylate and methacrylic acid are present in a ratio of about 7:3:1; (iii) about 2.9% TEC; and (iv) about 32.6% water; and wherein the coating level is about 10 mg/cm².

4. The dosage form of claim 1 wherein:

the core composition comprises: (i) 1-25 mg of a therapeutic peptide or protein; (ii) about 280 mg C10; and (iii) about 66 mg MCC;

the polymeric seal comprises: (i) about 17% HPMC; (ii) about 58% ethanol; and (iii) about 25% water; and

the enteric coating comprises: (i) about 64.5% poly[methacrylic acid, ethyl acrylate], wherein the methacrylic acid and ethyl acrylate are present in a ratio of about 1:1.; (ii) about 2.9% TEC; and (iii) about 32.6% water;

and wherein the coating level is about 7 mg/cm².

5. The dosage form of any of claims 1-4 wherein the relative bioavailability of the therapeutic peptide or protein following oral administration is greater than 1% of what would be achieved through subcutaneous administration.

6. The dosage form of any of claims 1-5 for use in treating a disease or condition.

7. Use of the dosage form of any of claims 1-5 in the manufacture of a medicament for treating a disease or condition, wherein the disease or condition is selected from the group consisting of type 2 diabetes mellitus (T2DM), obesity, cardiovascular disease (CVD), non-alcoholic steatohepatitis (NASH), fatty liver disease (FLD), dyslipidemia, metabolic syndrome, cognitive decline, Parkinson's syndrome and Alzheimer's disease.

8. The use of claim 7 wherein the disease or condition is T2DM.

9. The use of claim 7 wherein the disease or condition is obesity.

10. The use of any of claims 7-9, wherein the dosage form is to be administered once daily, twice daily, alternate days, every third day, every fourth day, every fifth day, every sixth day or once weekly.

11. The use of claim 10, wherein the dosage form is to be administered once daily.