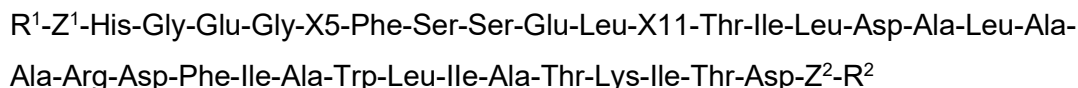


Claims:

Claim 1. A stable liquid pharmaceutical formulation, the formulation comprising a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:

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wherein:

R¹ is hydrogen;

10 X5 is Ser or Thr;

X11 is Ala or Ser;

R² is NH₂ or OH; and

Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

15 wherein the formulation comprises the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of 2 mg/mL to 30 mg/mL, histidine buffer at a concentration of about 15 mM, mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0;

20 wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C.

Claim 2. The formulation according to claim 1, wherein the total acetate concentration arising from the GLP2 analogue in the formulation is less than or equal to 11% acetate per mg GLP-2 analogue, and/or wherein formation of covalently linked oligomers of the GLP-2 analogue is inversely dependent on the concentration of the GLP-2 analogue in the formulation.

30 Claim 3. The formulation according to any one of claim 1 or 2, wherein the formulation

- a) is an aqueous formulation;
- b) is stable for at least 18 months when stored at 2-8°C;
- c)
-) is a ready-to-use formulation;
- 35 d) is free of reducing agent;

ef is stable at 2-8°C for at least 6 months, at least 12 months, at least 18 months or at least

24 months; and/or

f) is sterile.

Claim 4. The formulation according to any one of the preceding claims, wherein the

5 GLP-2 analogue in the formulation retains at least about 90% of its biological activity after 18 months of storage 2-8°C.

Claim 5. The formulation according to any one of the preceding claims, wherein the histidine buffer is L-histidine.

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Claim 6. The formulation according to any one of the preceding claims, wherein the mannitol is D-mannitol.

Claim 7. The formulation according to any one of the preceding claims, wherein the

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Claim 8. The formulation according to any one of the preceding claims, wherein the GLP-2 analogue is provided as an acetate salt, preferably wherein the GLP-2 analogue is ZP1848 or ZP1848-acetate, and/or preferably wherein the formulation consist of ZP1848-

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acetate at a concentration of about 20 mg/mL, histidine buffer at a concentration of about 15 mM, mannitol at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0.

Claim 9. An article of manufacture or a kit comprising a container holding the stable pharmaceutical formulation of any one of claims 1 to 8.

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Claim 10. A delivery device containing a liquid formulation comprising a GLP-2 analogue of any one of claims 1 to 8, optionally wherein the delivery device is pre-filled syringe, an injector device, an injector pen, an adjustable dose auto-injector, a disposable auto-injector, a wearable injector, an infusion pump.

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Claim 11. A formulation of the glucagon-like peptide 2 (GLP-2) analogue of any one of claims 1 to 8 for use in therapy, preferably wherein the GLP-2 analogue is to be administered once weekly or twice weekly.

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Claim 12. A formulation of the glucagon-like peptide 2 (GLP-2) analogue of any one of

claims 1 to 8 for use in treatment and/or prevention of a stomach and bowel-related disorder in a human patient, preferably wherein the GLP-2 analogue is to be administered once weekly or twice weekly.

- 5 Claim 13. The formulation of the glucagon-like peptide 2 (GLP-2) analogue for use according to claim 12, wherein the stomach and bowel-related disorder is ulcers, digestion disorders, malabsorption syndromes, short-gut syndrome, cul-de-sac syndrome, inflammatory bowel disease, celiac sprue (for example arising from gluten induced enteropathy or celiac disease), tropical sprue, hypogammaglobulinemic sprue, enteritis,
- 10 regional enteritis (Crohn's disease), ulcerative colitis, small intestine damage or short bowel syndrome (SBS), SBS-intestinal failure, being on the border between being a patient having SBS-intestinal insufficiency and SBS-intestinal failure, radiation enteritis, infectious or post-infectious enteritis, or small intestinal damage due to toxic or other chemotherapeutic agents.
- 15 Claim 14. The formulation of the glucagon-like peptide 2 (GLP-2) analogue for use according to claim 13, wherein the GLP-2 analogue is combined with one or more anti-cancer therapies, preferably wherein the one or more anti-cancer therapy comprises one or more chemotherapeutic agent(s) or radiation therapy.
- 20 Claim 15. The formulation of the glucagon-like peptide 2 (GLP-2) analogue for use according to claim 14, wherein the formulation is used in the treatment and/or prevention of a side effect of chemotherapy or radiation treatment, preferably wherein the side effect of chemotherapy is diarrhoea, abdominal cramping, vomiting or structural and functional damage of the intestinal epithelium resulting from chemotherapy treatment.
- 25 Claim 16. A process for producing a stable liquid pharmaceutical formulation comprising a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:
- 30
$$\text{R}^1\text{-Z}^1\text{-His-Gly-Glu-Gly-X5-Phe-Ser-Ser-Glu-Leu-X11-Thr-Ile-Leu-Asp-Ala-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Ala-Trp-Leu-Ile-Ala-Thr-Lys-Ile-Thr-Asp-Z}^2\text{-R}^2$$
- wherein:
- R¹ is hydrogen;
- X5 is Ser or Thr;
- X11 is Ala or Ser;
- 35 R² is NH₂ or OH;
- Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

wherein the total acetate concentration arising from the GLP2 analogue in the formulation is less than or equal to 11% acetate per mg GLP-2 analogue;

wherein the process comprising formulating (a) the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, (b) histidine buffer at a concentration of about 15 mM; (c) mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM; and (d) with arginine q.s. to provide a pH of about 7.0;

wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C, preferably wherein formation of covalently linked oligomers of the GLP-2 analogue is inversely dependent on the concentration of the GLP-2 analogue in the formulation.

Claim 17. The process according to claim 16, wherein the formulation is stable for at least 18 months when stored at 2-8°C, and/or wherein the formulation has a viscosity greater than 0.8 and lower than or equal to 2.0 mPa/sec measured at 25°C.

Claim 18. Use of a formulation comprising a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:

R^1 -Z¹-His-Gly-Glu-Gly-X₅-Phe-Ser-Ser-Glu-Leu-X₁₁-Thr-Ile-Leu-Asp-Ala-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Ala-Trp-Leu-Ile-Ala-Thr-Lys-Ile-Thr-Asp-Z²-R²

wherein:

R¹ is hydrogen;

X₅ is Ser or Thr;

X₁₁ is Ala or Ser;

R² is NH₂ or OH;

Z¹ is absent Z² is a peptide sequence of 1-6 amino acid units of Lys;

wherein the total acetate concentration arising from the GLP2 analogue in the formulation is less than or equal to 11% acetate per mg GLP-2 analogue;

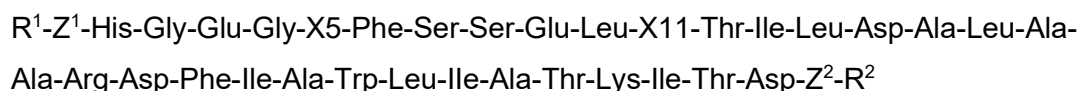
for providing an liquid pharmaceutical formulation which is stable for 24 months when stored at 2-8°C, wherein the formulation comprises the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, histidine buffer

at a concentration of about 15 mM, mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0;

wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C, preferably wherein formation of covalently linked oligomers of the GLP-2 analogue is inversely dependent on the concentration of the GLP-2 analogue in the formulation; and/or

wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C.

Claim 19. An *in vitro* method for modulating the viscosity of a stable liquid pharmaceutical formulation comprising a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:



wherein:

R¹ is hydrogen;

X5 is Ser or Thr;

X11 is Ala or Ser;

R² is NH₂ or OH;

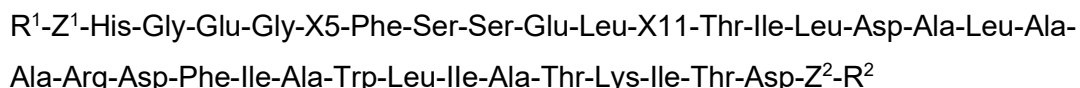
Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

wherein the method comprises formulating (a) the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, (b) histidine buffer at a concentration of about 15 mM; (c) mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM; and (d) with arginine q.s. to provide a pH of about 7.0;

wherein the total acetate concentration arising from the GLP2 analogue in the formulation is less than or equal to 11% acetate per mg GLP-2 analogue and wherein the formulation has a viscosity greater than 0.8 and lower than or equal to 2.0 mPa/sec measured at 25°C.

Claim 20. An *in vitro* method for reducing the formation of covalently bonded oligomeric products of a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue in a stable liquid pharmaceutical formulation comprising a GLP-2 analogue

represented by the formula:



wherein:

5 R¹ is hydrogen;

X5 is Ser or Thr;

X11 is Ala or Ser;

R² is NH₂ or OH;

Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

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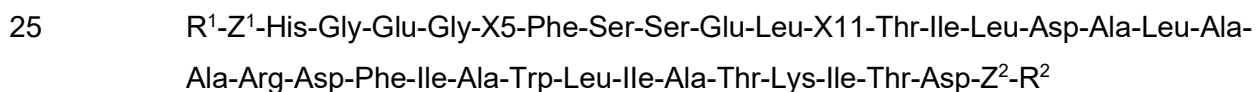
wherein the method comprises formulating (a) the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, (b) histidine buffer at a concentration of about 15 mM; (c) mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM; and (d) with arginine q.s. to provide a pH of about 7.0;

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wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C, preferably wherein formation of covalently linked oligomers of the GLP-2 analogue is inversely dependent on the concentration of the GLP-2 analogue in the formulation.

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Claim 21. Use of a formulation for reducing the formation of covalently bonded oligomeric products of a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:



wherein:

R¹ is hydrogen;

X5 is Ser or Thr; X11 is Ala or Ser; R² is NH₂ or OH;

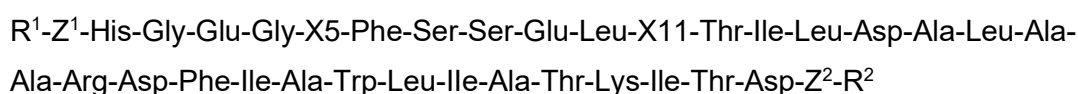
30 Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

in an liquid pharmaceutical formulation which is stable for 24 months when stored at 2-8°C, wherein the formulation comprises the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, histidine buffer at a concentration of about 15 mM, mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0;

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wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C, preferably wherein formation of covalently linked oligomers of the GLP-2 analogue is inversely dependent on the concentration of the GLP-2 analogue in the formulation.

Claim 22. Use of a formulation for modulating the viscosity of a liquid pharmaceutical formulation comprising a pharmaceutically acceptable acetate salt of a glucagon-like peptide 2 (GLP-2) analogue, wherein the GLP-2 analogue is represented by the formula:



wherein:

R¹ is hydrogen; X5 is Ser or Thr;

X11 is Ala or Ser

R² is NH₂ or OH;

Z¹ is absent and Z² is a peptide sequence of 1-6 amino acid units of Lys;

in an liquid pharmaceutical formulation which is stable for 24 months when stored at 2-8°C, wherein the formulation comprises the pharmaceutically acceptable acetate salt of the GLP-2 analogue at a concentration of about 2 mg/mL to about 30 mg/mL, histidine buffer at a concentration of about 15 mM, mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0;

wherein the total acetate concentration arising from the GLP2 analogue in the formulation is less than or equal to 11% acetate per mg GLP-2 analogue and the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C.

Claim 23. A solid composition comprising an acetate salt of a glucagon-like peptide 2 (GLP-2) analogue having the formula:



where x is selected from any one of from 1.0 to 8.0 from 4.0 to 6.0, from 2.0 to 7.0, from 3.0

to 6.0, from 4.0 to 6.0, and from 4.0 to 8.0.

Claim 24. A stable aqueous pharmaceutical formulation, the formulation comprising

(a) the solid composition of claim 23 at a concentration of 2 mg/mL to 30 mg/mL;

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(b) a buffer selected from the group consisting of a histidine buffer, mesylate buffer, lysine buffer, and Bis-Tris buffer, the buffer being present at a concentration of 5 mM to 50 mM;

(c) a non-ionic tonicity modifier selected from the group consisting of mannitol, sucrose, glycerol, sorbitol and trehalose at a concentration of 90 mM to 360 mM; and

10

(d) arginine q.s. to provide a formulation having a pH of 6.6 to 7.4;

wherein the formulation contains 5% or less of the GLP-2 analogue in the form of covalently bonded oligomeric products and wherein the formulation has a viscosity between 0.8 and 2.0 mPa/sec measured at 25°C.

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Claim 25. The formulation of claim 24, wherein the formulation is stable for at least 18 months when stored at 2-8°C, and/or wherein the GLP-2 analogue in the formulation retains at least about 90% of its biological activity after 18 months of storage 2-8°C.

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Claim 26. The formulation of claim 24 or claim 25, wherein the formulation comprises the GLP-2 analogue at a concentration of about 20 mg/mL, histidine buffer at a concentration of about 15 mM, mannitol as a non-ionic tonicity modifier at a concentration of about 230 mM, and arginine q.s. to provide a pH of about 7.0.

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