CLAIMS

We claim:

1. A tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

2. The salt of claim 1, where the stoichiometric ratio of tris(hydroxymethyl)aminomethane to (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid in the salt is 1:1.

3. A solid composition comprising a tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

4. The solid composition of claim 3, where the stoichiometric ratio of tris(hydroxymethyl)aminomethane to (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid in the salt is 1:1.

5. The solid composition of claim 3 or 4, where the solid composition further comprises an evaporation residue.

6. The solid composition of claim 5, where the evaporation residue comprises at least a portion of the tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

7. The solid composition of claim 6, where the evaporation residue further comprises a binder.

8. The solid composition of claim 7, where the binder is selected from the group consisting of hydroxypropylmethyl cellulose acetate succinate (HPMCAS), polyvinylpyrrolidone (PVP), and hydroxypropylmethylcellulose (HPMC).

9. The solid composition of claim 8, where the binder is hydroxypropylmethyl cellulose acetate succinate (HPMCAS).

10. The solid composition of any one of claims 7 to 9, where the evaporation residue further comprises a water-soluble surfactant.

11. The solid composition of claim 10, where the water-soluble surfactant is selected from the group consisting of a polyoxyethylene sorbitan fatty acid ester, sodium lauryl sulfate, and vitamin E d-alpha tocopheryl polyethyleneglycol succinate (vitamin E TPGS).

12. The solid composition of claim 11, where the water-soluble surfactant is a polyoxyethylene sorbitan fatty acid ester.

13. The solid composition of any one of claims 6 to 12, where the solid composition further comprises a pharmaceutically acceptable basic excipient.

14. The solid composition of claim 13, where the pharmaceutically acceptable basic excipient is trisodium phosphate, potassium carbonate, sodium carbonate, sodium bicarbonate, potassium bicarbonate, or a mixture thereof.

15. The solid composition of claim 14, where the pharmaceutically acceptable basic excipient is a mixture of sodium carbonate and sodium bicarbonate.

16. A method of treating type 2 diabetes comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

17. A method of treating type 1 diabetes comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

18. A method of treating obesity comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

19. A method of lowering blood glucose comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

20. A method of slowing gastric emptying comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

21. A method of lowering an HbA1c level comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

22. A method of increasing glucose-dependent insulin secretion comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

23. A method of suppressing glucagon secretion comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

24. A method of treating an eating disorder comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

25. A method of modulating a human GLP1 receptor comprising administering to a subject a compound of claim 1 or 2 or a solid composition of any one of claims 3 to 15.

CLAIMS

We claim:

1. A tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

2. The salt of claim 1, where the stoichiometric ratio of tris(hydroxymethyl)aminomethane to (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid in the salt is 1:1.

3. A solid composition comprising a tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

4. The solid composition of claim 3, where the stoichiometric ratio of tris(hydroxymethyl)aminomethane to (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid in the salt is 1:1.

5. The solid composition of claim 3, where the solid composition further comprises an evaporation residue.

6. The solid composition of claim 5, where the evaporation residue comprises at least a portion of the tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid.

7. The solid composition of claim 6, where the evaporation residue further comprises a binder.

8. The solid composition of claim 7, where the binder is selected from the group consisting of hydroxypropylmethyl cellulose acetate succinate (HPMCAS), polyvinylpyrrolidone (PVP), and hydroxypropylmethylcellulose (HPMC).

9. The solid composition of claim 8, where the binder is hydroxypropylmethyl cellulose acetate succinate (HPMCAS).

10. The solid composition of claim 7, where the evaporation residue further comprises a water-soluble surfactant.

11. The solid composition of claim 10, where the water-soluble surfactant is selected from the group consisting of a polyoxyethylene sorbitan fatty acid ester, sodium lauryl sulfate, and vitamin E d-alpha tocopheryl polyethyleneglycol succinate (vitamin E TPGS).

12. The solid composition of claim 11, where the water-soluble surfactant is a polyoxyethylene sorbitan fatty acid ester.

13. The solid composition of claim 6, where the solid composition further comprises a pharmaceutically acceptable basic excipient.

14. The solid composition of claim 13, where the pharmaceutically acceptable basic excipient is trisodium phosphate, potassium carbonate, sodium carbonate, sodium bicarbonate, potassium bicarbonate, or a mixture thereof.

15. The solid composition of claim 14, where the pharmaceutically acceptable basic excipient is a mixture of sodium carbonate and sodium bicarbonate.

16. A method of making a solid composition comprising:

mixing a binder and a tris(hydroxymethyl)aminomethane salt of (S)-3-(4'-cyano-biphenyl-4-yl)-2-{[(3R,7S)-3-[4-(3,4-dichloro-benzyloxy)-phenyl]-1-methyl-2-oxo-6-((S)-1-phenyl-propyl)-2,3,5,6,7,8-hexahydro-1*H*-4-oxa-1,6-diaza-anthracene-7-carbonyl]-amino}-propionic acid in a solvent to form a solution or suspension; and

removing the solvent from the solution or suspension.

17. The method of claim 16, wherein the step of removing the solvent comprising spray drying the solution or suspension to form a powder.

18. The method of claim 16, wherein the step of removing the solvent comprises spraying the solution or suspension onto a solid powder.