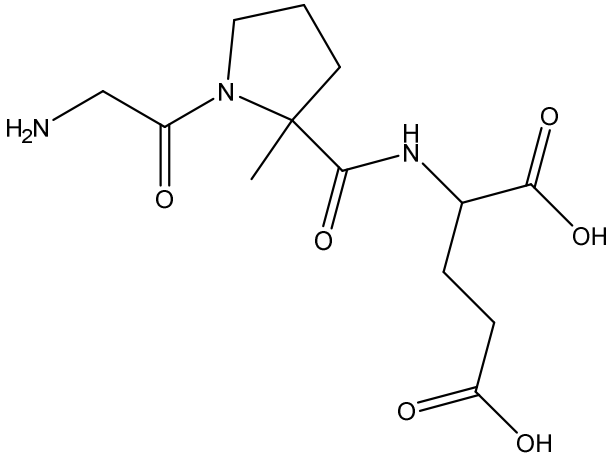
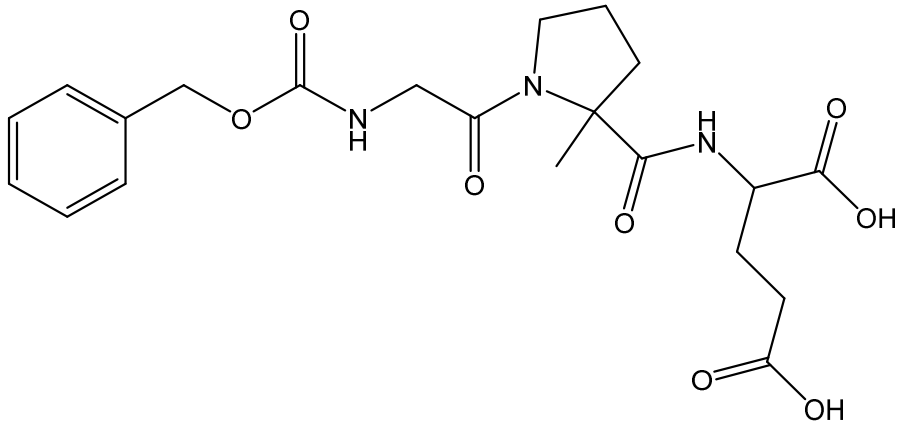
What is Claimed is:

1. A composition comprising a compound of Formula (I)



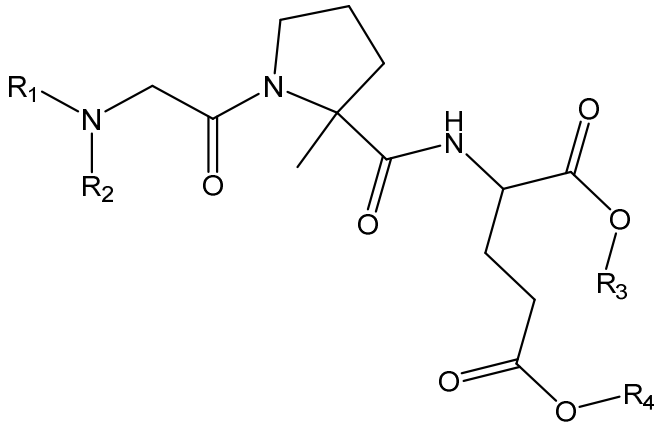
(I),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, and a compound of Formula (II):



(II),

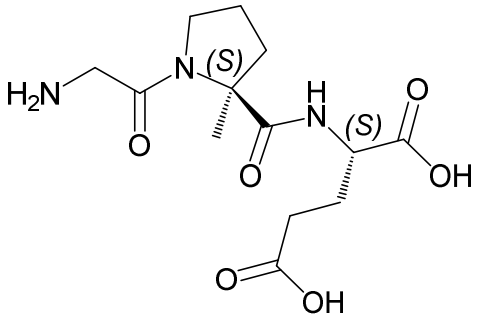
or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, and/or a compound of Formula (III):



(III),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, wherein R_1, R_2, R_3 and R_4 independently are selected from the group consisting of hydrogen and C_{1-4} alkyl, provided at least one of R_1, R_2, R_3 and R_4 is C_{1-4} alkyl.

2. The composition according to Claim 1, wherein the compound according to Formula (I) is a compound of Formula (Ia).



(Ia) (trofinetide),

or a hydrate, or pharmaceutically acceptable salt thereof.

3. The composition according to Claim 1 or 2, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent or present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%; and the compound of Formula (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent or present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, provided that at least one of the compounds of Formula (II) or (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present; and/or~~.~~

~~4. The composition according to any one of Claims 1 to 3,~~

wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount of between about 0.001±0.0002 wt% and about 0.3±0.06 wt%; and/or~~.~~

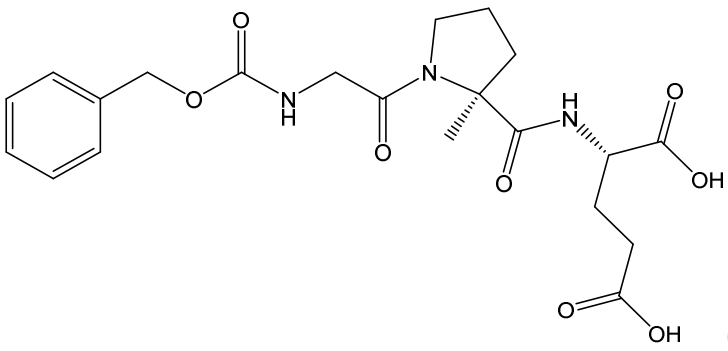
~~5. The composition according to any one of Claims 1 to 4,~~ wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 0.1±0.02 wt%; and/or~~.~~

~~6. The composition according to Claim 1 or 2,~~ wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount

between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%; and/or

wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent.~~.~~

~~7~~4. The composition according to any one of Claims 1 to ~~6~~3, wherein the compound according to Formula (II) is a compound of Formula (IIa):



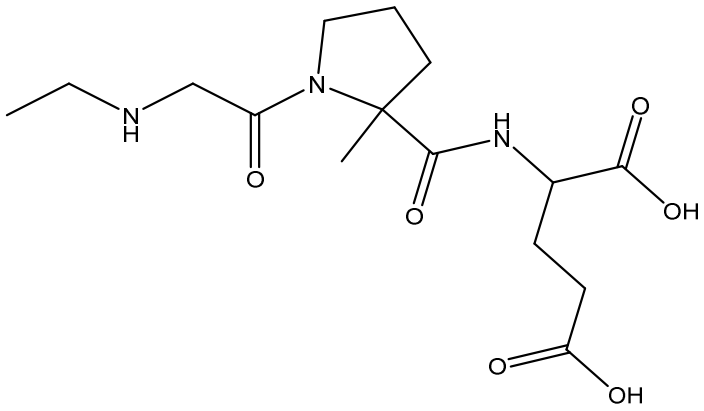
(IIa) (Z-Gly-MePro-Glu-OH),

or a hydrate, or pharmaceutically acceptable salt thereof.

~~8. The composition according to any one of Claims 1 to 7, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent.~~

~~9~~5. The composition according to any one of Claims 1 to ~~8~~4, wherein the compound of Formula (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2.0±0.4 wt%.

~~10~~6. The composition according to any one of Claims 1 to ~~9~~5, wherein said composition comprising the compound of Formula (III), wherein the compound of Formula (III) is a compound of Formula (IX),

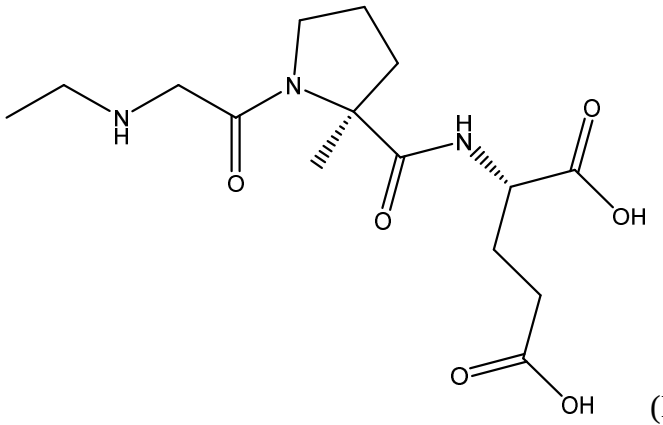


(IX),

or hydrate, or pharmaceutically acceptable salt thereof; and/or

.

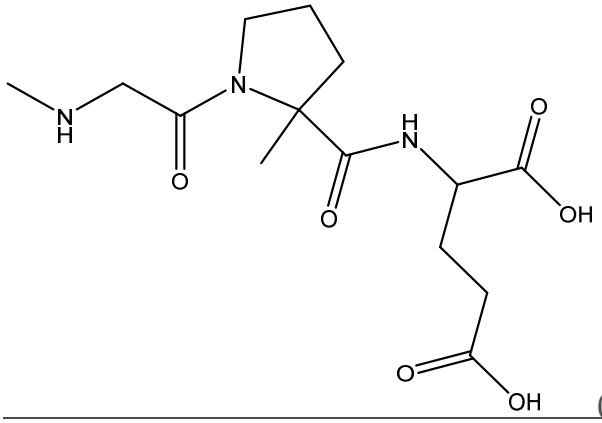
11. The composition according to any one of Claims 1 to 10, comprising the compound of Formula (III), wherein the compound according to Formula (III) is a compound of Formula (IIIa):



(IIIa) (Et-Gly-MePro-Glu-OH),

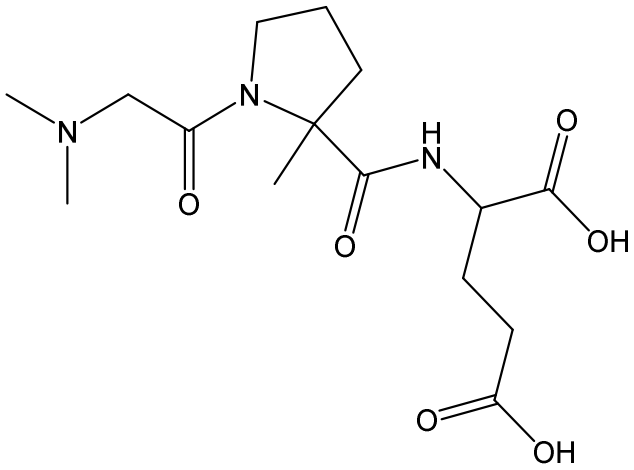
or hydrate, or pharmaceutically acceptable salt thereof; and/or.

12. The composition according to Claim 11, wherein the compound of Formula (IIIa), or hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2.0±0.4 wt%; and/or the compound according to Formula (III) is a compound of Formula (IV):



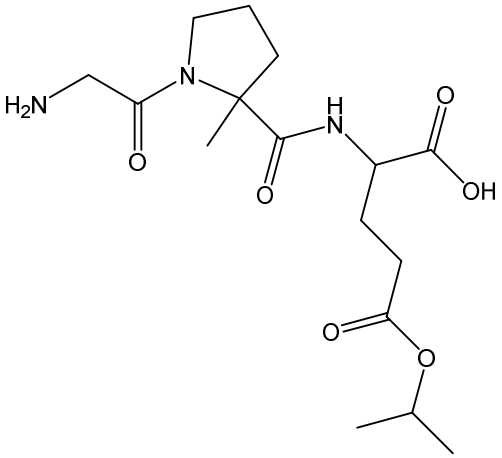
(IV) (Me-Gly-MePro-Glu), or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof~~.~~; and/or

the compound of Formula (III) is a compound of Formula (V):



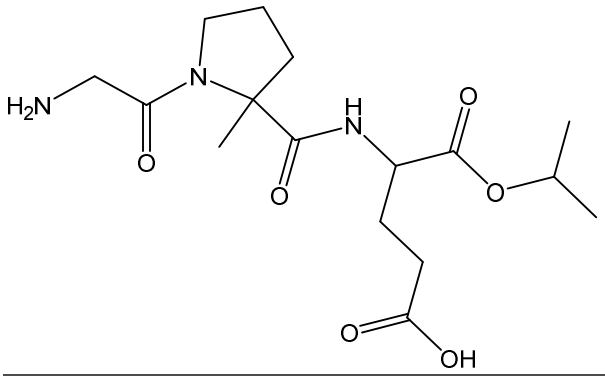
(V) (Me_2-Gly-MePro-Glu), or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof; and/or

wherein the compound of Formula (III) is a compound of Formula (VI):



(VI) (Gly-MePro-Glu(OiPr)-OH), or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof; and/or

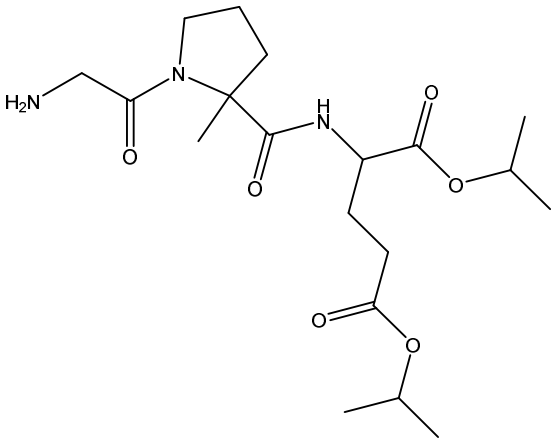
~~wherein~~ the compound of Formula (III) is a compound of Formula (VII):



(VII) (Gly-MePro-Glu-OiPr),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof; and/or

~~wherein~~ the compound of Formula (III) is a compound of Formula (VIII):



(VIII) (Gly-MePro-Glu-$(OiPr)_2$),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.

~~13~~7. The composition according to Claims ~~11 to 12~~6, wherein

~~wherein~~ the compound of Formula (IIIa), or hydrate, or pharmaceutically acceptable salt thereof is present in an amount between about 0.001±0.0002 wt% and about 2.0±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%~~.~~; and/or

the compound of Formula (IV), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%; and/or

wherein the compound of Formula (V), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%; and/or

the compound of Formula (VI), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%; and /or

the compound of Formula (VII) or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%; and/or

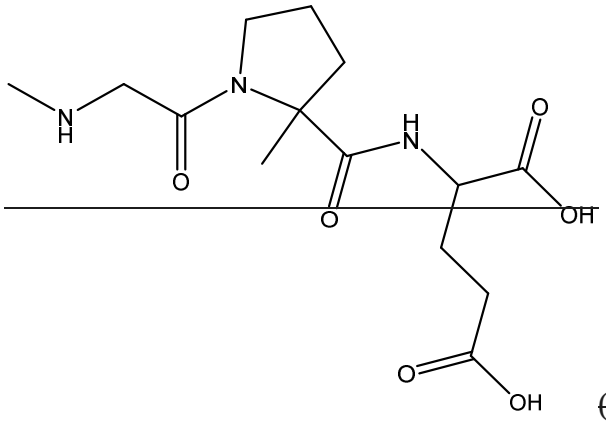
the compound of Formula (VIII) or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

148. The composition according to any one of Claims 1 to 13 7 comprising between about 97 wt% and about 100 wt% of the compound of Formula (I) or Formula (Ia), alternatively between about 98 wt% and about 100 wt%, or between about 99 wt% and about 100 wt% on an anhydrous basis, or.

comprising at least 90 wt%, such as at least 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, and 97 wt%, of the compound of Formula (I) or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, on an anhydrous basis, or

comprising at least 90 wt%, such as at least 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, and 97 wt%, of the compound of Formula (Ia) or a hydrate, or pharmaceutically acceptable salt thereof, on an anhydrous basis.

~~15. The composition according to any one of Claims 1 to 9, wherein the compound according to Formula (III) is a compound of Formula (IV):~~

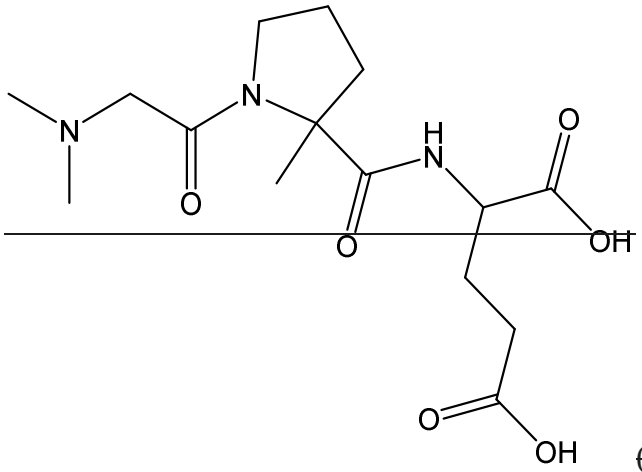


~~(IV) (Me-Gly-MePro-Glu),~~

~~or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.~~

~~16. The composition according to Claim 15, wherein the compound of Formula (IV), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.~~

~~17. The composition according to any one of Claims 1-9, and 15-16, wherein the compound of Formula (III) is a compound of Formula (V):~~

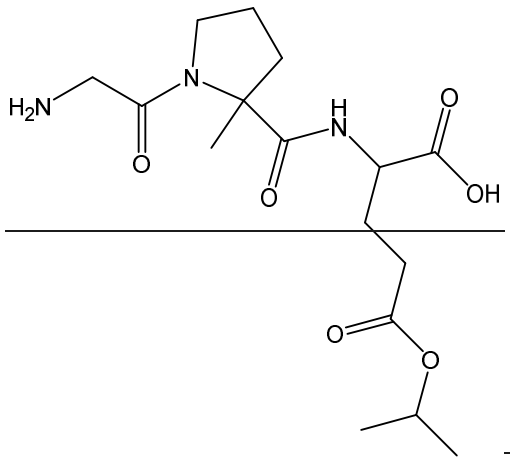


(V) (Me_2-Gly-MePro-Glu),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.

18. The composition according to Claim 17, wherein the compound of Formula (V), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

19. The composition according to any one of Claims 1-9, wherein the compound of Formula (III) is a compound of Formula (VI):

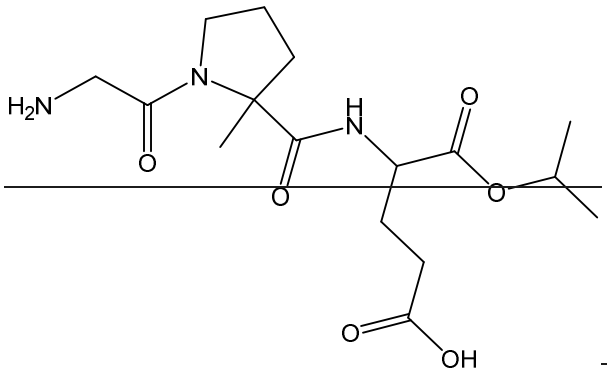


(VI) (Gly-MePro-Glu(OiPr)-OH),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.

20. The composition according to Claim 19, wherein the compound of Formula (VI), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

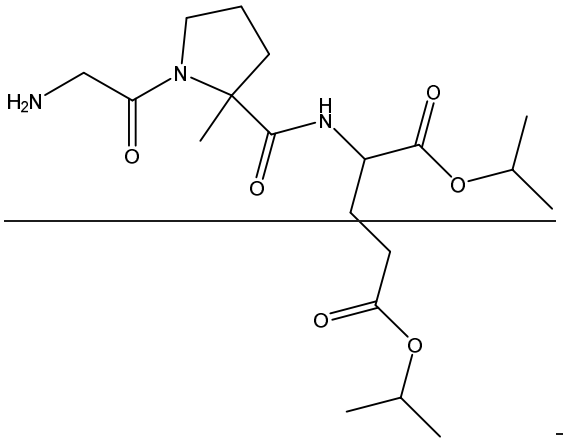
21. The composition according to any one of Claims 1-9, or 19-20, wherein the compound of Formula (III) is a compound of Formula (VII):



(VII) (Gly-MePro-Glu-OiPr), or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.

22. The composition according to Claim 21, wherein the compound of Formula (VII) or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

23. The composition according to any one of Claims 1-9, and 19-22, wherein the compound of Formula (III) is a compound of Formula (VIII):

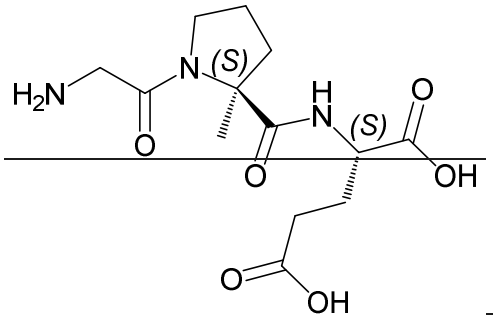


(VIII) (Gly-MePro-Glu-(OiPr)$_2$),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof.

24. The composition according to Claim 23, wherein the compound of Formula (VIII) or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

25. A composition comprising a compound of Formula (Ia),



(Ia) (trofinetide),

said composition obtained by:

a) coupling H-MePro-OH and Z-Gly-OH in the presence of an activating reagent, silylating agent and a solvent, or

b) coupling Z-Gly-OH and Suc-OH and then coupling the obtained Z-Gly-OSu and H-MePro-OH in the absence or presence of an activating reagent, a solvent and in the absence or presence of a silylating agent;

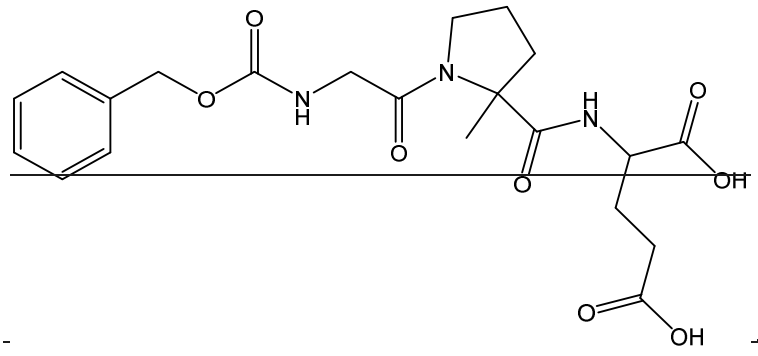
c) coupling the obtained Z-Gly-MePro-OH and H-Glu-OH in the presence of an activating reagent, silylating agent and a solvent;

d) obtaining Z-Gly-MePro-Glu-OH; and

e) deprotecting Z-Gly-MePro-Glu-OH, to obtain a composition comprising the compound of Formula (Ia).

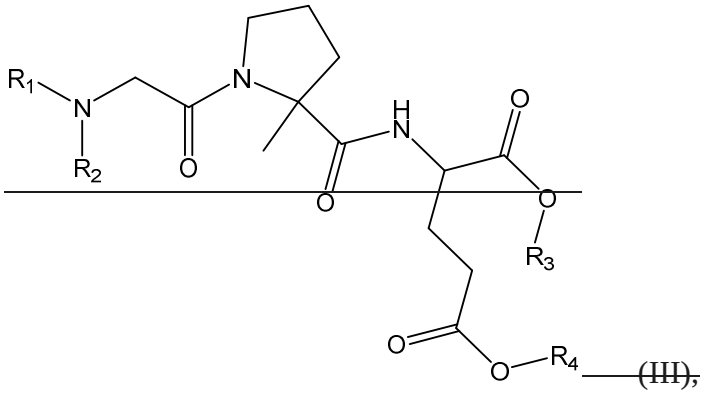
26. The composition according to Claim 25, wherein the obtained composition is dissolved or suspended in a solvent.

27. The composition according to either of Claims 25 or 26, wherein said composition additionally comprises a compound of Formula (II):



(II),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof; and optionally comprising a compound of Formula (III):



(III),

or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, wherein R_1, R_2, R_3 and R_4 independently are selected from the group consisting of hydrogen and C_{1-4} alkyl, provided at least one of R_1, R_2, R_3 and R_4 is C_{1-4} alkyl.

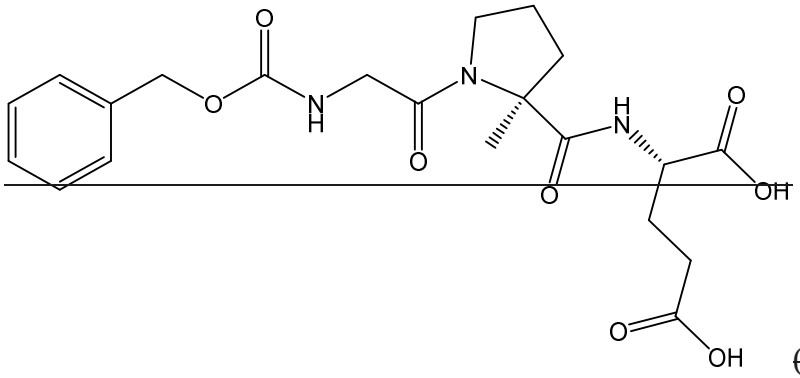
28. The composition according to Claim 26 or 27, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent or present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%; and the compound of Formula (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent or present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, provided that at least one of the compounds of Formula (II) or (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present.

29. The composition according to any one of Claims 26 to 28, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount of between about 0.001±0.0002 wt% and about 0.3±0.06 wt%.

30. The composition according to any one of Claims 26 to 29, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 0.1±0.02 wt%.

31. The composition according to Claim 26 or 27, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2±0.4 wt%, or between about 0.001±0.0002 wt% and about 1.5±0.3 wt%, or between about 0.001±0.0002 wt% and about 1±0.2 wt%, or between about 0.001±0.0002 wt% and about 0.7±0.14 wt%, or between about 0.001±0.0002 wt% and about 0.5±0.1 wt%, or between about 0.001±0.0002 wt% and about 0.3±0.06 wt%, or between about 0.001±0.0002 wt% and about 0.2±0.04 wt%.

32. The composition according to any one of Claims 26 to 31, wherein the compound according to Formula (II) is a compound of Formula (IIa):



(IIa) (Z-Gly-MePro-Glu-OH), or a hydrate, or pharmaceutically acceptable salt thereof.

33. The composition according to any one of Claims 26 to 32, wherein the compound of Formula (II), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is absent.

34. The composition according to any one of Claims 26 to 33, wherein the compound of Formula (III), or stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, is present in an amount between about 0.001±0.0002 wt% and about 2.0±0.4 wt%.

35. The composition according to any one of Claims 25 to 34, where said silylating agent does not contain a cyano group.

36. The composition according to Claim 35, where said silylating agent is selected from the group consisting of N,O-bis(trimethylsilyl)acetamide, N,O-bis(trimethylsilyl)trifluoroacetamide, hexamethyldisilazane, N-methyl-N-(trimethylsilyl)acetamide, N. methyl-N-(trimethylsilyl)trifluoroacetamide, N-(trimethylsilyl)acetamide, N-(trimethylsilyl)diethylamine, N-(trimethylsilyl)dimethylamine, 1-(trimethylsilyl)imidazole, and 3-(trimethylsilyl)2-oxazolidone.

37. The composition according to any one of Claims 25 to 36 wherein said solvent in step a) is a polar organic solvent, or a polar aprotic organic solvent.

38. The composition according to any one of Claims 25 to 37 wherein said solvent in step b) is a polar organic solvent, or a polar aprotic organic solvent.

39. The composition according to any one of Claims 25 to 38 wherein said solvent in step c) is a polar organic solvent, or a polar aprotic organic solvent.

40. The composition according to any one of Claims 25 to 39 wherein the solvent is selected from the group consisting of alkyl acetates, chlorinated hydrocarbons, alkyl cyanides and amide type solvents, or mixture thereof.

41. The composition according to any one of Claims 25 to 40 wherein said activating reagent is selected from the group consisting of carbodiimides, acyl halides, phosphonium salts, uronium salts and guanidinium salts.

42. The composition according to any one of Claims 25 to 41, wherein deprotecting is achieved by hydrogenation.

43. The composition according to Claim 42, wherein hydrogenation is performed in the presence of a Pd/C catalyst.

44. The composition according to Claim 42, wherein hydrogenation is performed in the presence of a Pd/Si catalyst.

45. The composition according to any one of Claims 42 to 44, wherein hydrogenation is performed at a temperature from about 10-40 °C, or a temperature of about 20-30 °C, or a temperature of about 25 °C.

46. The composition according to any one of Claims 42 to 45, wherein hydrogenation is performed at about 0 to about 6 bars of pressure.

47. The composition according to any one of Claims 42 to 46, wherein the hydrogenation is performed using at least one solvent selected from the group consisting of water, ethyl acetate, isopropyl acetate, methanol, ethanol, isopropanol, or mixtures thereof.

489. A method of manufacturing a composition containing trofinetide comprising the steps:

a) coupling H-MePro-OH and Z-Gly-OH in the presence of an activating agent, silylating agent and a solvent; or

b) coupling Z-Gly-OH and Suc-OH and then coupling the obtained Z-Gly-OSu and H-MePro-OH in the absence or presence of an activating reagent, a solvent and in the absence or presence of a silylating agent;

c) coupling the obtained Z-Gly-MePro-OH and H-Glu-OH in the presence of an activating reagent, silylating agent and a solvent;

d) obtaining Z-Gly-MePro-Glu-OH; and

e) deprotecting Z-Gly-MePro-Glu-OH, thereby producing trofinetide, wherein trofinetide is dissolved or suspended in a solvent.

4910. The method of Claim 489, where said silylating agent does not contain a cyano group and/or.

50. The method of Claim 48 or 49, wherein said silylating agent is selected from the group consisting of N,O-bis(trimethylsilyl)acetamide, N,O-bis(trimethylsilyl)trifluoroacetamide, hexamethyldisilazane, N-methyl-N-(trimethylsilyl)acetamide (TMA), N.-methyl-N-(trimethylsilyl)trifluoroacetamide, N-(trimethylsilyl)acetamide, N-(trimethylsilyl)diethylamine, N-(trimethylsilyl)dimethylamine, 1-(trimethylsilyl)imidazole, and 3-(trimethylsilyl)2-oxazolidone.

5111. The method of any one of Claims 48 to 50 Claim 9 or Claim 10 wherein said solvent in step a) is a polar organic solvent, or a polar aprotic organic solvent, and/or.

52. The method of any one of Claims 48 to 51 wherein said solvent in step b) is a polar organic solvent, or a polar aprotic organic solvent, and/or.

53. The method of any one of Claims 48 to 52 wherein said solvent in step c) is a polar organic solvent, or a polar aprotic organic solvent, and/or .

54. The method of any one of Claims 48 to 53 wherein the solvent is selected from the group consisting of alkyl acetates, chlorinated hydrocarbons, alkyl cyanides and amide type solvents, or mixture thereof.

5512. The method of any one of Claims 48 9 to 54 11, wherein said activating reagent is selected from the group consisting of carbodiimides, acyl halides, phosphonium salts, uronium salts and guanidinium salts.

5613. The method of any one of Claims 48 to 559 to 12, wherein deprotecting is achieved by hydrogenation, and/or .

57. The method of Claim 56, wherein hydrogenation is performed in the presence of a Pd/C catalyst.

58. The method of Claim 56, wherein hydrogenation is performed in the presence of or a Pd/Si catalyst, and/or.

~~59. The method of any one of Claims 56 to 58, wherein~~ hydrogenation is performed at a temperature from about 10-40 °C, or a temperature of about 20-30 °C, or a temperature of about 25 °C, and/or ~~.~~

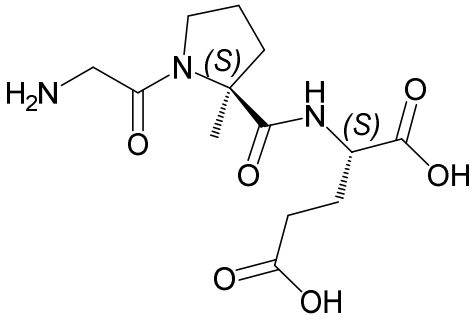
~~60. The method of any one of Claims 56 to 59, wherein~~ hydrogenation is performed at about 0 to about 6 bars of pressure, and/or ~~.~~

~~61. The method of any one of Claims 56 to 60, wherein the~~ hydrogenation is performed in at least one solvent selected from the group consisting of water, ethyl acetate, isopropyl acetate, methanol, ethanol, isopropanol, or mixtures thereof.

~~62. A product comprising a composition according to any one of Claims 1 to 47.~~

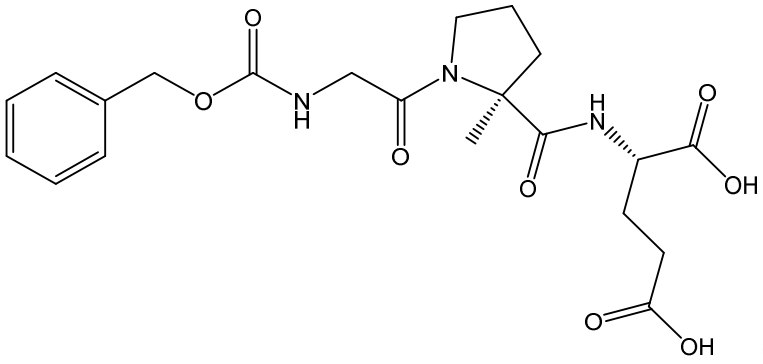
~~63. A product according to Claim 62 wherein the product is a kit.~~

~~64~~14. A kit containing a dosage form comprising a compound of Formula (Ia),



(Ia) (trofinetide),

a hydrate, or a pharmaceutically acceptable salt thereof, and a compound of Formula (IIa),



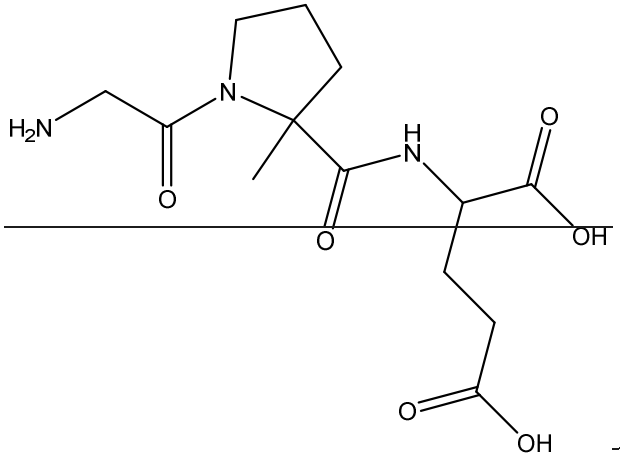
(IIa) (Z-Gly-MePro-Glu-OH),

or a hydrate, or pharmaceutically acceptable salt thereof, and instructions for administration to a subject in need thereof.

~~65~~15. The kit of Claim ~~64~~14, further comprising one or more compounds selected from the group consisting of Formula (III), Formula (IIIa), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), and Formula (IX).

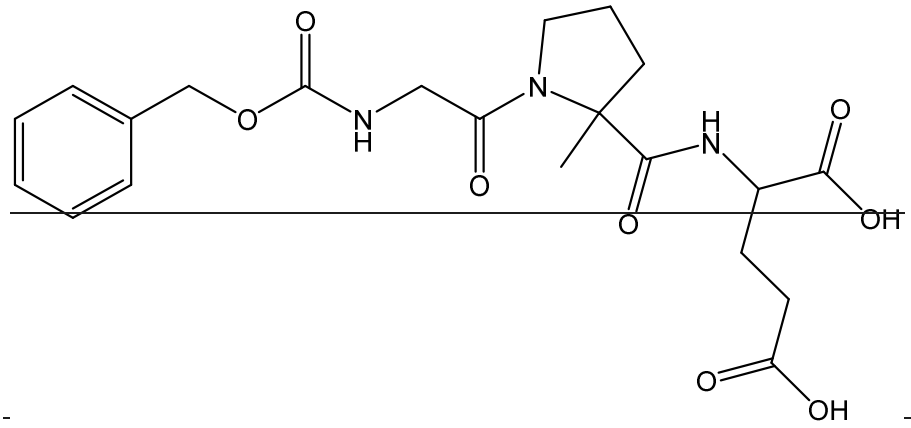
~~66. The composition according to any one of claims 1-47, comprising at least 90 wt%, such as at least 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, and 97 wt%, of the compound of Formula (I) or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, on an anhydrous basis.~~

~~67. The composition according to any one of claims 2-47, comprising at least 90 wt%, such as at least 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, and 97 wt%, of the compound of Formula (Ia) or a hydrate, or pharmaceutically acceptable salt thereof, on an anhydrous basis.~~
~~68. A composition comprising a compound of Formula (I)~~



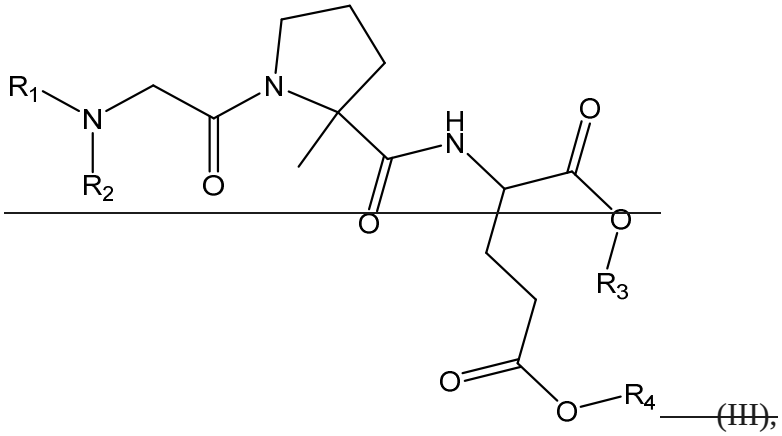
~~(I),~~

~~or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, and a compound of Formula (II):~~



~~(II),~~

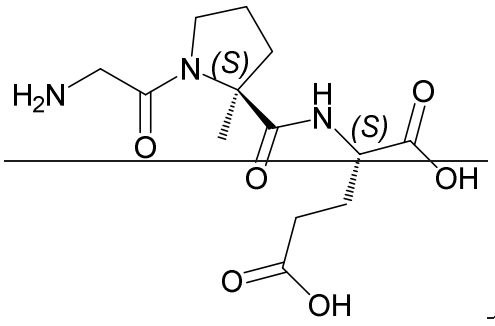
~~or a stereoisomer, a hydrate, or pharmaceutically acceptable salt thereof, and/or a compound of Formula (III):~~



(III),

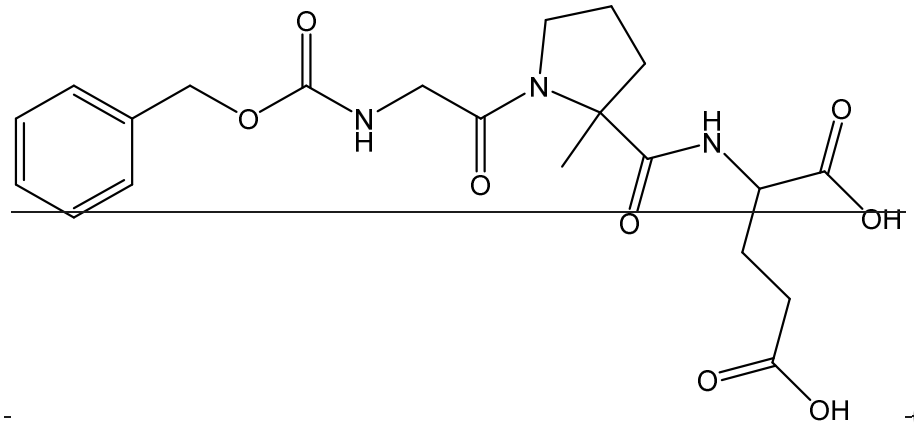
or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, wherein R_1, R_2, R_3 and R_4 independently are selected from the group consisting of hydrogen and C_{1-4} alkyl, provided that least one of R_1, R_2, R_3 and R_4 is C_{1-4} alkyl, and wherein the compositions comprises at least 90 wt%, such as 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, or 97 wt% of the compound of Formula (I) on an anhydrous basis.

69. A composition comprising a compound of Formula (Ia)



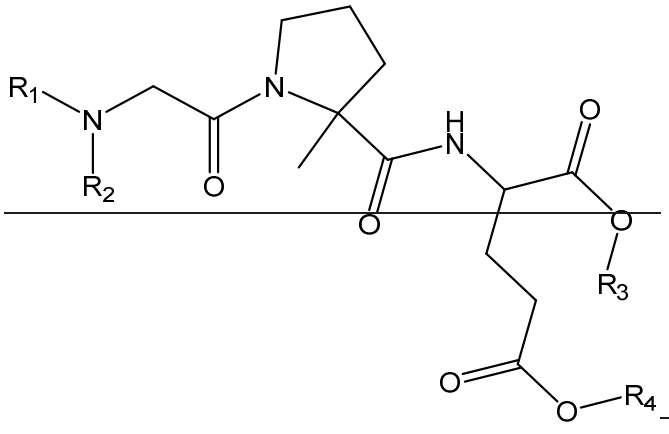
(Ia) (trofinetide),

or a hydrate, or pharmaceutically acceptable salt thereof, and a compound of Formula (II):



(II),

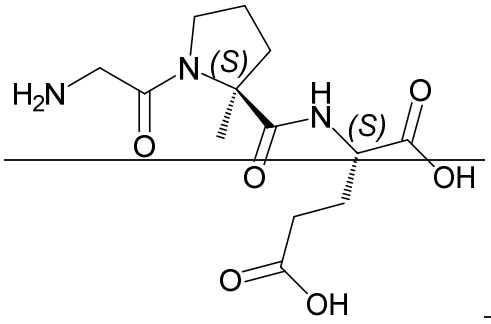
or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, and/or a compound of Formula (III):



(III),

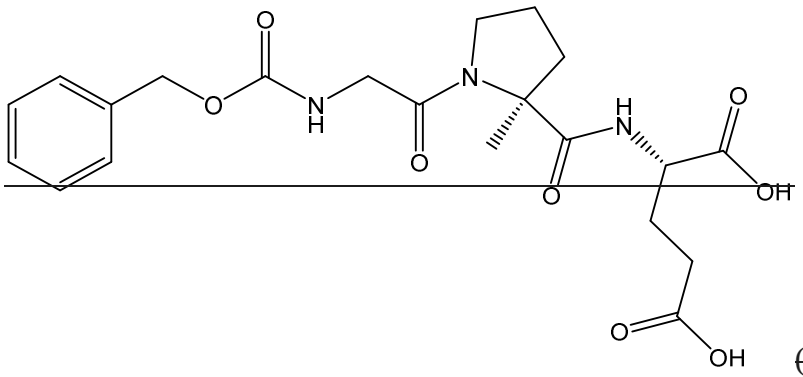
or a stereoisomer, hydrate, or pharmaceutically acceptable salt thereof, wherein R_1, R_2, R_3 and R_4 independently are selected from the group consisting of hydrogen and C_{1-4} alkyl, provided that least one of R_1, R_2, R_3 and R_4 is C_{1-4} alkyl, and wherein the composition comprises at least 90 wt% such as 91 wt%, 92 wt%, 93 wt%, 94 wt%, 95 wt%, 96 wt%, or 97w t% of the compound of Formula (Ia) on an anhydrous basis.

70. A product, including a kit containing a dosage form with instructions for use, comprising a compound of Formula (Ia)



(Ia) (trofinetide),

or a hydrate, or pharmaceutically acceptable salt thereof, and a compound of Formula (IIa)

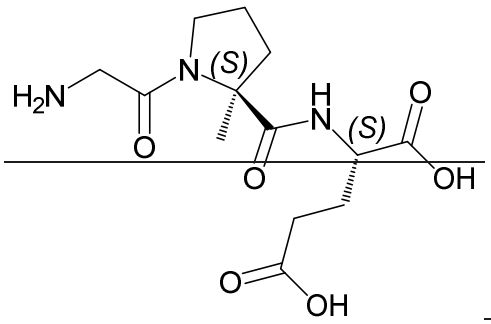


(IIa) (Z-Gly-MePro-Glu-OH),

or a hydrate, or pharmaceutically acceptable salt thereof, wherein the product comprises between 95 wt% to 105 wt%, such as 96 wt%, 97 wt%, 98 wt%, 99 wt%, 100 wt%, 101 wt%,

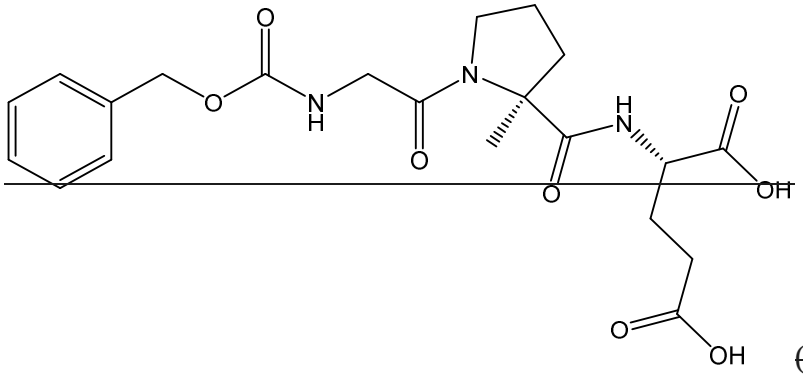
102 wt%, 103 wt%, or 104 wt% of the specified amount of the compound of Formula (Ia) in the product.

71. A product, including a kit containing a dosage form with instructions for use, comprising a compound of Formula (Ia)



(Ia) (trofinetide),

or a hydrate, or pharmaceutically acceptable salt thereof, and a compound of Formula (IIa)



(IIa) (Z-Gly-MePro-Glu-OH),

or a hydrate, or pharmaceutically acceptable salt thereof, and additionally comprising one or more compounds selected from the group consisting of Formula (III), Formula (IIIa), Formula (IV), Formula (V), Formula (VI), Formula (VII), Formula (VIII), and Formula (IX), wherein the composition comprises between 95 wt% and 105 wt%, such as 96 wt%, 97 wt%, 98 wt%, 99 wt%, 100 wt%, 101 wt%, 102 wt%, 103 wt%, or 104 wt% of the specified amount of the compound of Formula (Ia) in the product.