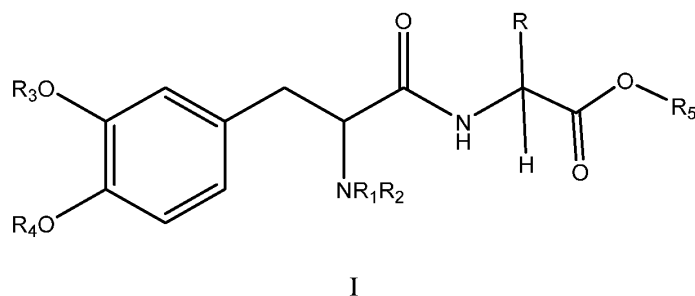


CLAIMS

1. A liquid pharmaceutical composition comprising:

a levodopa amino acid conjugate (LDAA) of the general formula (I):



an enantiomer, diastereomer, racemate, ion, zwitterion, pharmaceutically acceptable salt thereof, or any combination thereof, wherein:

R is an amino acid side chain;

R₁ and R₂ are each independently selected from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, C₃-C₆cycloalkyl, phenyl, -O-C(=O)-R', -C(=O)-OR', -C(=O)-R', -C(=S)-R', -O-C(=O)-NR'R', -O-C(=S)-NR'R', and -O-C(=O)-R'';

R₃ and R₄ are each independently selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl, phenyl, and -P(=O)(OR')₂;

R₅ is selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl and phenyl;

R' is independently selected, for each occurrence, from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, C₃-C₆cycloalkyl, phenyl, and heteroaryl bonded to the nitrogen through a ring carbon; and

R'' is independently selected, for each occurrence, from the group consisting of a (C₁-C₆)alkyl, (C₂-C₆)alkenyl, and (C₂-C₆)alkynyl; and

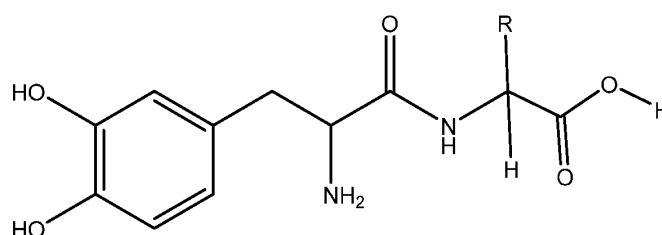
a pharmaceutically acceptable excipient.

2. The liquid pharmaceutical composition according to claim 1, wherein R is an amino acid side chain selected from the group consisting of arginine, histidine, lysine, aspartic acid, glutamic acid,

serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, tryptophan, and lanthionine side chains.

3. The liquid pharmaceutical composition according to claim 1 or 2, wherein R is an amino acid side chain selected from the group consisting of arginine, tyrosine, lysine, tryptophan, aspartic acid, or lanthionine 1.

4. The liquid pharmaceutical composition according to any one of claims 1-3, wherein the LDAA is represented by:



5. The liquid pharmaceutical composition according to any one of claims 1-4 comprising one LDAA conjugate, or a mixture of two or more different LDAA conjugates, each represented by Formula I, or an enantiomer, diastereomer, racemate, ion, zwitterion, pharmaceutically acceptable salt thereof, or any combination thereof.

6. The liquid pharmaceutical composition of any one of claims 1-5, comprising between about 10 to about 45 % w/v of one or more of the LDAA conjugate represented by Formula I.

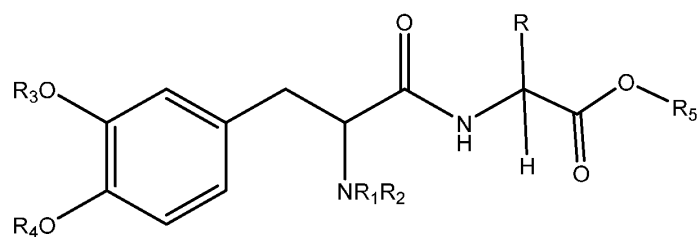
7. The liquid pharmaceutical composition according to any one of claims 1-6, wherein the liquid pharmaceutical composition has a pH in the range of between about 5 to about 10 at about 25°C.

8. The liquid pharmaceutical composition according to any one of claims 1-7, further comprising a decarboxylase inhibitor.

9. The liquid pharmaceutical composition according to claim 8, wherein the decarboxylase inhibitor is carbidopa.

10. The liquid pharmaceutical composition according to any one of claims 1-9, further comprising a base.

11. The liquid pharmaceutical composition according to claim 10, wherein the base is selected from the group consisting of arginine, NaOH, tris(hydroxymethyl)aminomethane (TRIS), and any combination thereof.
12. The liquid pharmaceutical composition according to any one of claims 10-11, wherein said liquid pharmaceutical composition comprises between about 0.1% to about 30% w/v of the base.
13. The liquid pharmaceutical composition according to any one of claims 8-12, wherein said liquid pharmaceutical composition comprises between about 0.25 to about 1.5 % w/v of the decarboxylase inhibitor.
14. The liquid pharmaceutical composition according to any one of claims 1-13, further comprising an antioxidant or a combination of two or more antioxidants.
15. The liquid pharmaceutical composition according to claim 14, wherein the antioxidant is each independently selected from the group consisting of ascorbic acid or a salt thereof, a cysteine, a bisulfite or a salt thereof, glutathione, a tyrosinase inhibitor, a Cu^{2+} chelator, and any combination thereof.
16. The liquid pharmaceutical composition according to claim 14 or 15, wherein said liquid pharmaceutical composition comprises between about 0.05 to about 1.5 % w/v of the antioxidant or the combination of antioxidants.
17. The liquid pharmaceutical composition according to any one of claims 1-16, further comprising at least one of: a catechol-O-methyltransferase (COMT) inhibitor, a monoamine oxidase (MAO) inhibitor, a surfactant, a buffer, an acid, a solvent, and any combination thereof.
18. The liquid pharmaceutical composition according to claim 17, wherein the buffer is TRIS.
19. The liquid pharmaceutical composition according to any one of claims 17-18, wherein said liquid pharmaceutical composition comprises between about 5.0 to about 40.0 % w/v of the buffer.
20. A method of treating neurodegenerative conditions and/or conditions characterized by reduced levels of dopamine in the brain, wherein the method comprises administering an effective amount of a liquid pharmaceutical composition to a patient in need thereof, wherein the liquid pharmaceutical composition comprises a levodopa amino acid conjugate (LDAA) of the general formula (I):



I

an enantiomer, diastereomer, racemate, ion, zwitterion, pharmaceutically acceptable salt thereof, or any combination thereof, wherein

R is an amino acid side chain;

R₁ and R₂ are each independently selected from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, C₃-C₆cycloalkyl, phenyl, -O-C(=O)-R', -C(=O)-OR', -C(=O)-R', -C(=S)-R', -O-C(=O)-NR'R', -O-C(=S)-NR'R', and -O-C(=O)-R'';

R₃ and R₄ are each independently selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl, phenyl, and -P(=O)(OR')₂;

R₅ is selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl and phenyl;

R' is independently selected, for each occurrence, from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, C₃-C₆cycloalkyl, phenyl, and heteroaryl bonded to the nitrogen through a ring carbon; and

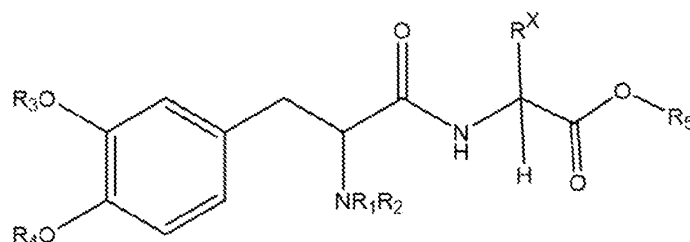
R'' is independently selected, for each occurrence, from the group consisting of a (C₁-C₆)alkyl, (C₂-C₆)alkenyl, and (C₂-C₆)alkynyl; and

a pharmaceutically acceptable excipient.

21. The method according to claim 20, wherein the neurodegenerative condition is Parkinson's disease.

22. The method according to claim 20 or claim 21, wherein the liquid pharmaceutical composition is administered concomitantly to the patient with an additional active ingredient.

23. The method according to claim 22, wherein the additional active ingredient is selected from the group consisting of a decarboxylase inhibitor, a COMT inhibitor, a MAO inhibitor, and any combination thereof.
24. The method according to any one of claims 20-23, wherein the liquid pharmaceutical composition is administered substantially continuously to the patient.
25. The method according to any one of claims 20-24, wherein the liquid pharmaceutical composition is administered subcutaneously.
26. A levodopa amino acid conjugate (LDAA) of the general formula (III):



III

an enantiomer, diastereomer, racemate, ion, zwitterion, pharmaceutically acceptable salt thereof, or any combination thereof, wherein

R^X is an amino acid side chain; or an O-phosphorylated amino acid side chain thereof;

R_1 and R_2 are each independently selected from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, C₃-C₆cycloalkyl, phenyl, -O-C(=O)-R', -C(=O)-OR', -C(=O)-R', -C(=S)-R', -O-C(=O)-NR'R', -O-C(=S)-NR'R', and -O-C(=O)-R'';

R_3 and R_4 are each independently selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl, phenyl, and -P(=O)(OR')₂;

R_5 is selected from the group consisting of H, (C₁-C₃)alkyl, C₃-C₆cycloalkyl and phenyl;

R' is independently selected, in each occurrence, from the group consisting of H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, C₃-C₆cycloalkyl, phenyl, and heteroaryl bonded to the nitrogen through a ring carbon; and

R" is independently selected, in each occurrence, from the group consisting of a (C₁-C₆)alkyl, (C₂-C₆)alkenyl, and (C₂-C₆)alkynyl.

27. The levodopa amino acid conjugate (LDAA) according to claim 26, wherein the amino acid side chain in R^x is selected from the group consisting of arginine, histidine, lysine, aspartic acid, glutamic acid, serine, threonine, asparagine, glutamine, cysteine, selenocysteine, glycine, proline, alanine, valine, isoleucine, leucine, methionine, phenylalanine, tyrosine, tryptophan, ornithine, lanthionine and 3,4-dihydroxyphenylalanine side chain.

28. The levodopa amino acid conjugate (LDAA) according to any one of claims 25 to 27, wherein the amino acid side chain in R^x is selected from the group consisting of arginine, lysine, serine, glycine, alanine, valine, phenylalanine, tyrosine, ornithine, and 3,4-dihydroxyphenylalanine.

29. The levodopa amino acid conjugate (LDAA) according to any one of claims 25 to 28, wherein each one of R₁, R₂ and R₅ are H; R₃, and R₄ independently is H or -P(=O)(OR')₂; and R' is H.

30. The levodopa amino acid conjugate (LDAA) selected from the group consisting of:

(2S)-2-amino-3-(3-hydroxy-4-phosphonooxyphenyl)propionamide,

2-[[(2S)-2-amino-3-(3-hydroxy-4-phosphonooxyphenyl)propanoyl]amino]ethanesulfonic acid,

(2S)-2-amino-6-[[(2S)-2-amino-3-(3-hydroxy-4-phosphonooxyphenyl)propanoyl]amino]hexanoic acid, and

(2S)-2-amino-5-[[(2S)-2-amino-3-(3-hydroxy-4-phosphonooxyphenyl)propanoyl]amino]pentanoic acid.

31. A method of treating Parkinson's disease in a patient in need thereof, comprising subcutaneously administering to the patient an effective amount of a compound of claim 30.