skin is dependent on their ionic form, wherein non-ionized species generally have higher permeability coefficients in comparison to ionized species and further, cations generally have higher permeability coefficients than anions.

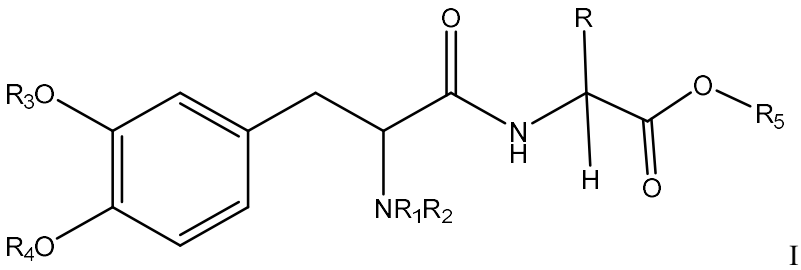
[0009] US 3,803,120, US 4,035,507, US 5,686,423 and US 2002/099013 disclose certain levodopa amino acid and levodopa peptide conjugates; however, details regarding formulations are not provided therein, and when provided, only solid oral formulations are contemplated. The theoretical option of preparing liquid compositions is briefly mentioned in US 3,803,120 (US '120, column 3, lines 49-53); however, no such compositions were prepared and moreover, it is erroneously disclosed that the conjugates are soluble (column 3, lines 65-66).

[0010] As detailed above, there is still a need to effective formulations, and particularly liquid formulations, for treating disorders such as Parkinson's disease.

SUMMARY

[0010a] In an aspect of the present disclosure, there is provided a liquid pharmaceutical composition comprising:

(a) 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 an amino acid side chain selected from the group consisting of arginine, lysine, aspartic acid, tyrosine, tryptophan, and lanthionine 1;

R_1 and R_2 are each H;

R_3 and R_4 are each independently selected from the group consisting of H, (C_1-C_3)alkyl, C_3-C_6cycloalkyl, phenyl, and-P(=O)(OR')$_2$;

R_5 is selected from the group consisting of H, (C_1- C_3)alkyl, C_3-C_6cycloalkyl and phenyl; R' is independently selected, for each occurrence, from the group consisting of H, (C_1-C_6)alkyl, (C_2-C_6)alkenyl, C_3-C_6cycloalkyl , phenyl, and heteroaryl bonded to the nitrogen through a ring carbon; and

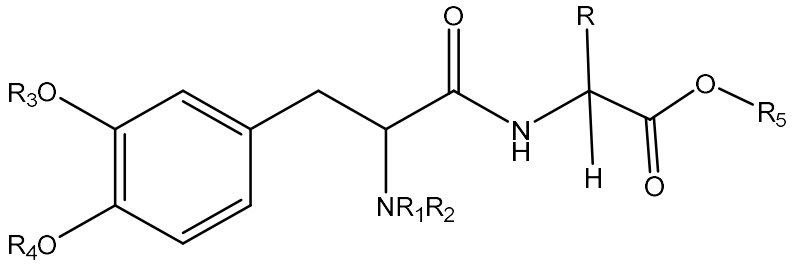
R" is independently selected, for each occurrence, from the group consisting of a (C_1-C_6)alkyl, (C_2-C_6)alkenyl, and (C_2-C_6)alkynyl; and

(b) carbidopa; and

(c) a pharmaceutically acceptable excipient.

[0010b] In another aspect of the present disclosure, there is provided a use of a liquid pharmaceutical composition in the manufacture of a medicament for treating neurodegenerative conditions and/or conditions characterized by reduced levels of dopamine in the brain, wherein the liquid pharmaceutical composition comprises:

(a) 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 an amino acid side chain selected from the group consisting of arginine, lysine, aspartic acid, tyrosine, tryptophan, and lanthionine 1;