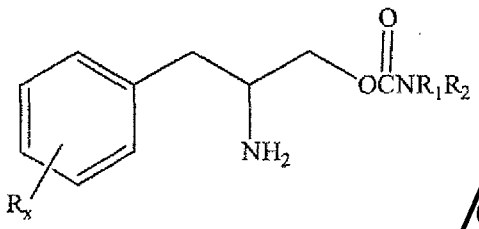
We claim:

1. A method of treating cataplexy in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or ester thereof;
wherein R is a member selected from the group consisting of hydrogen, lower alkyl of 1 to 8 carbon atoms, halogen selected from F, Cl, Br and I, alkoxy containing 1 to 3 carbon atoms, nitro, hydroxy, trifluoromethyl, and thioalkoxy containing 1 to 3 carbon atoms;
x is an integer of 0 to 3, with the proviso that R may be the same or different when x is 2 or 3;
R_1 and R_2 are independently selected from the group consisting of hydrogen, lower alkyl of 1 to 8 carbon atoms, aryl, arylalkyl, cycloalkyl of 3 to 7 carbon atoms; or
R_1 and R_2 can be joined to form a 5 to 7-membered heterocycle substituted with a member selected from the group consisting of hydrogen, alkyl, and aryl groups, wherein the heterocycle can comprise 1 to 2 nitrogen atoms and 0 to 1 oxygen atom, wherein the nitrogen atoms are not directly connected with each other or with the oxygen atom.

2. The method of claim 1, wherein x = 0.

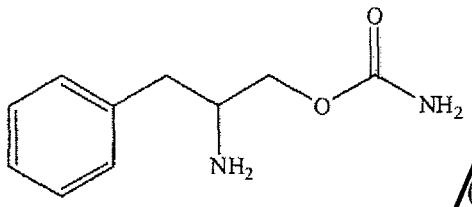
3. The method of claim 1, wherein R_1 and R_2 are hydrogen and x = 0.

4. The method of any one of claims 1-3, wherein the compound of Formula I is an enantiomer of Formula I substantially free of other enantiomers or an enantiomeric mixture wherein one enantiomer of Formula I predominates.

5. The method of claim 4, wherein the enantiomer of Formula I predominates to the extent of about 90% or greater.

6. The method of claim 4, wherein the enantiomer of Formula I predominates to the extent of about 98% or greater.

7. The method of claim 4, wherein the enantiomer of Formula I is an enantiomer of Formula Ia:



(Ia)

or a pharmaceutically acceptable salt or ester thereof.

8. The method of claim 7, wherein the enantiomer of Formula Ia is the (R) or (D) enantiomer.

9. The method of claim 7, wherein the enantiomer of Formula Ia is the (S) or (L) enantiomer.

10. The method of claim 7, wherein the enantiomer of Formula Ia predominates to the extent of about 90% or greater.

11. The method of claim 7, wherein the enantiomer of Formula Ia predominates to the extent of about 98% or greater.

12. The method of claim 4, wherein the enantiomer of Formula I substantially free of other enantiomers is the compound of Formula Ib or an enantiomeric mixture wherein the compound of Formula Ib predominates:

or a pharmaceutically acceptable salt or ester thereof.

13. The method of claim 12, wherein the compound of Formula Ib predominates to the extent of about 90% or greater.

14. The method of claim 12, wherein the compound of Formula Ib predominates to the extent of about 98% or greater.

15. The method of any one of claims 1-14, wherein the cataplexy is associated with narcolepsy.

16. The method of any one of claims 1-14, wherein the cataplexy is secondary to a condition that lowers hypocretin levels in the subject.

17. The method of claim 16, wherein the condition is selected from the group consisting of brain tumor, astrocytomas, glioblastoma, glioma, subependynoma, craniopharyngioma, arterio-venous malformations, ischemic events, multiple sclerosis, head injury, brain surgery, paraneoplastic syndromes, Neimann-Pick type C disease, and encephalitis.

18. The method of any one of claims 1-17, wherein the therapeutically effective amount of the compound of Formula I is from about 0.01 mg/kg/dose to about 150 mg/kg/dose.

19. The method of any one of claims 1-17, wherein the therapeutically effective amount of the compound of Formula I is from about 1 mg/day to about 7000 mg/day.

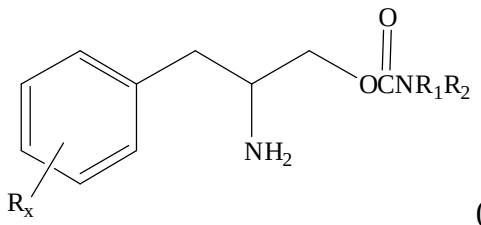
20. The method of any one of claims 1-19, wherein the compound of Formula I is administered orally.

21. The method of any one of claims 1-20, wherein the compound of Formula I is administered in the form of a capsule or tablet.

22. The method of any one of claims 1-20, wherein the compound of Formula I is administered in the form of a capsule at a dose of about 150 mg to about 300 mg without any excipients.

CLAIMS

1. A composition for treating cataplexy comprising a therapeutically effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt or ester thereof;

wherein R is a member selected from the group consisting of hydrogen, lower alkyl of 1 to 8 carbon atoms, halogen selected from F, Cl, Br and I, alkoxy containing 1 to 3 carbon atoms, nitro, hydroxy, trifluoromethyl, and thioalkoxy containing 1 to 3 carbon atoms;

x is an integer of 0 to 3, with the proviso that R may be the same or different when x is 2 or 3;

R_1 and R_2 are independently selected from the group consisting of hydrogen, lower alkyl of 1 to 8 carbon atoms, aryl, arylalkyl, cycloalkyl of 3 to 7 carbon atoms; or

R_1 and R_2 can be joined to form a 5 to 7-membered heterocycle substituted with a member selected from the group consisting of hydrogen, alkyl, and aryl groups, wherein the heterocycle can comprise 1 to 2 nitrogen atoms and 0 to 1 oxygen atom, wherein the nitrogen atoms are not directly connected with each other or with the oxygen atom.

2. The composition of claim 1, wherein x = 0.

3. The composition of claim 1, wherein R_1 and R_2 are hydrogen and x = 0.

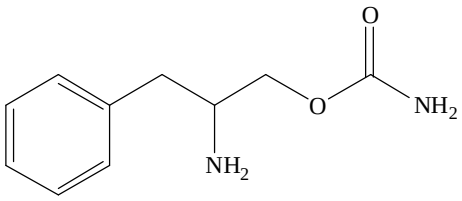
4. The composition of any one of claims 1-3, wherein the compound of Formula I is an enantiomer of Formula I substantially free of other enantiomers or an enantiomeric mixture wherein one enantiomer of Formula I predominates.

5. The composition of claim 4, wherein the enantiomer of Formula I predominates to the extent of about 90% or greater.

6. The composition of claim 4, wherein the enantiomer of Formula I predominates to the extent of about 98% or greater.

7. The composition of claim 4, wherein the enantiomer of Formula I is an enantiomer of

Formula Ia:



(Ia)

or a pharmaceutically acceptable salt or ester thereof.

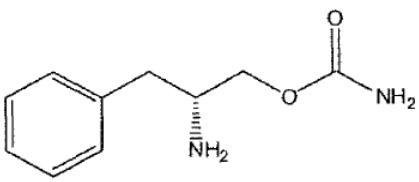
8. The composition of claim 7, wherein the enantiomer of Formula Ia is the (R) or (D) enantiomer.

9. The composition of claim 7, wherein the enantiomer of Formula Ia is the (S) or (L) enantiomer.

10. The composition of claim 7, wherein the enantiomer of Formula Ia predominates to the extent of about 90% or greater.

11. The composition of claim 7, wherein the enantiomer of Formula Ia predominates to the extent of about 98% or greater.

12. The composition of claim 4, wherein the enantiomer of Formula I substantially free of other enantiomers is the compound of Formula Ib or an enantiomeric mixture wherein the compound of Formula Ib predominates:



(Ib)

or a pharmaceutically acceptable salt or ester thereof.

13. The composition of claim 12, wherein the compound of Formula Ib predominates to the extent of about 90% or greater.

14. The composition of claim 12, wherein the compound of Formula Ib predominates to the extent of about 98% or greater.

15. The composition of any one of claims 1-14, wherein the cataplexy is associated with narcolepsy.

16. The composition of any one of claims 1-14, wherein the cataplexy is secondary to a condition that lowers hypocretin levels in the subject.

17. The composition of claim 16, wherein the condition is selected from the group consisting of brain tumor, astrocytomas, glioblastoma, glioma, subependynoma, craniopharyngioma, arterio-venous malformations, ischemic events, multiple sclerosis, head injury, brain surgery, paraneoplastic syndromes, Neimann-Pick type C disease, and encephalitis.

18. The composition of any one of claims 1-17, wherein the therapeutically effective amount of the compound of Formula I is from about 0.01 mg/kg/dose to about 150 mg/kg/dose.

19. The composition of any one of claims 1-17, wherein the therapeutically effective amount of the compound of Formula I is from about 1 mg/day to about 7000 mg/day.

20. The composition of any one of claims 1-19, wherein the composition is administered orally.

21. The composition of any one of claims 1-20, wherein the composition is in the form of a capsule or tablet.

22. The composition of any one of claims 1-20, wherein the composition is administered in the form of a capsule at a dose of about 150 mg to about 300 mg without any excipients.