[0005] The present invention overcomes shortcomings in the art by providing methods and compositions for treating excessive sleepiness such that "normal" levels of wakefulness are achieved.

Summary

[0006] In one aspect, the present disclosure refers to a method of providing [*R*]-2-amino-3-phenylpropylcarbamate (APC) or a pharmaceutically acceptable salt thereof to a subject in need thereof according to a dose escalation regimen, said method comprising administering to the subject a daily dose of 75 mg APC for at least 3 days; and increasing the daily dose not more than once every 3 days until a maximum tolerated dose is achieved in the subject. The present disclosure relates to the development of methods for treating excessive sleepiness in a subject, *e.g.*, due to narcolepsy or obstructive sleep apnea, with the surprising outcome that "normal" levels of wakefulness are achieved based on standard objective and subjective sleepiness tests.

[0007] Accordingly, one example describes a method for treating excessive daytime sleepiness in a subject in need thereof, comprising administering to the subject (*R*)-2-amino-3-phenylpropyl carbamate or a pharmaceutically acceptable salt thereof in an amount sufficient to decrease the subject's score on the Epworth Sleepiness Scale (ESS) by 5 or more points, *e.g.*, by 10 or more points. In some examples, the method is effective to decrease the subject's score on the ESS to a "normal" level, *e.g.*, 10 or less.

[0008] Another example describes a method for treating excessive daytime sleepiness in a subject in need thereof, comprising administering to the subject (*R*)-2-amino-3-phenylpropyl carbamate or a pharmaceutically acceptable salt thereof in an amount sufficient to increase the subject's score on the maintenance of wakefulness test (MWT) by at least 5 minutes, *e.g.*, at least 10 minutes or 15 minutes.

[0009] A further example describes a method for treating excessive daytime sleepiness in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of (*R*)-2-amino-3-phenylpropyl carbamate or a pharmaceutically acceptable salt thereof no later than at least 12 hours before the bedtime of the subject.

[0010] The present invention is explained in greater detail in the drawings herein and the specification set forth below.

Brief Description of the Drawings

[0011] Fig. 1 shows the study design for treatment of excessive sleepiness in patients with obstructive sleep apnea.

[0012] Fig. 2 shows patient disposition through the three study phases.

What is Claimed is:

1. A method of providing [*R*]-2-amino-3-phenylpropylcarbamate (APC) or a pharmaceutically acceptable salt thereof to a subject in need thereof according to a dose escalation regimen, said method comprising administering to the subject a daily dose of 75 mg APC for at least 3 days; and increasing the daily dose not more than once every 3 days until a maximum tolerated dose is achieved in the subject.

2. The method of claim 1, wherein the daily dose is increased not more than once every 4, 5, 6, or 7 days.

3. The method of claim 1 or 2, wherein a first increase in the daily dose is an increase to a daily dose of 150 mg APC.

4. The method of any one of claims 1-3, wherein a second increase in the daily dose is an increase to a daily dose of 300 mg APC.

5. The method of any one of claims 1-4, further comprising decreasing the daily dose not more than once every 3 days if the subject exhibits signs that the previously provided daily dose exceeds the maximum tolerated dose.

6. The method of claim 5, wherein the daily dose is decreased not more than once every 4, 5, 6, or 7 days.

7. The method of claim 5 or 6, wherein the decrease in the daily dose is a decrease to a daily dose of 150 mg APC.

8. The method of claim 5 or 6, wherein the decrease in the daily dose is a decrease to a daily dose of 75 mg APC.

9. The method of claim 5 or 6, wherein the decrease in the daily dose is a decrease to a daily dose of 37.5 mg APC.

10. The method of any one of claims 1-9, wherein the APC is provided as a pharmaceutically acceptable salt of APC.

11. The method of claim 10, wherein the APC is provided as a hydrochloride salt.

12. The method of any one of claims 1-11, wherein the subject is provided APC or a pharmaceutically acceptable salt thereof for the treatment of excessive daytime sleepiness.

13. The method of claim 12, wherein the excessive daytime sleepiness is associated with narcolepsy.

14. The method of claim 12, wherein the excessive daytime sleepiness is associated with obstructive sleep apnea.

15. The method of any one of claims 1-14, wherein the oral daily dose is administered within 3 hours of the subject's awakening.

16. The method of any one of claims 1-15, wherein the oral daily dose is administered within 1 hour of the subject's awakening.

17. The method of any one of claims 1-16, wherein the daily dose is administered at least 10 hours in advance of the subject's bedtime.

18. The method any one of claims 1-17, wherein the daily dose is administered orally.

19. The method of any one of claims 1-18, comprising administering a pharmaceutical composition comprising the APC or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

20. The method of claim 19, wherein the pharmaceutical composition is a dosage form.

21. The method of claim 19, wherein the pharmaceutical composition is an immediate release oral dosage form.

22. The method of claim 20 or 21, wherein the composition is a tablet or a capsule.

23. The method of claim 22, wherein the composition is an immediate release compressed tablet, the tablet comprising:

APC or a pharmaceutically acceptable salt thereof in an amount of about 90-98% by weight of the tablet;

at least one binder in an amount of about 1-5% by weight of the tablet; and

at least one lubricant in an amount of about 0.1-2% by weight of the tablet;

wherein the tablet releases at least 85% of APC or a pharmaceutically acceptable salt thereof contained therein within a period of less than 15 minutes after administration of the tablet to the subject.

24. The method of any one of claims 20-23, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 300 mg.

25. The method of any one of claims 20-23, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 150 mg.

26. The method of any one of claims 20-23, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 75 mg.

27. The method of any one of claims 20-23, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 37.5 mg.

28. The method any one of claims 1-27, wherein the subject is a human.

29. The method of any one of claims 1-28, wherein the subject is an adult.

30. The method of any one of claims 1-28, wherein the subject is a juvenile.