[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 the use of [R]-2-amino-3-phenylpropylcarbamate (APC) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating excessive daytime sleepiness in a subject, wherein the medicament is to be administered according to a dose escalation regimen, said regimen comprising the subject to be administered a once-daily dose of 75 mg APC for at least 3 days; followed by a once-daily dose of 150 mg, wherein the once-daily dose of 150 mg is the maximum dose in the dosing regimen, and wherein the amount is a) sufficient to decrease the subject's score on the Epworth Sleepiness Scale (ESS) to 10 points or less; or b) sufficient to increase the subject's score on the maintenance of wakefulness test (MWT) by at least 10 minutes. In one example, there is disclosed 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. Use of [*R*]-2-amino-3-phenylpropylcarbamate (APC) or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating excessive daytime sleepiness in a subject, wherein the medicament is to be administered according to a dose escalation regimen, said regimen comprising the subject to be administered a once-daily dose of 75 mg APC for at least 3 days; followed by a once-daily dose of 150 mg, wherein the once-daily dose of 150 mg is the maximum dose in the dosing regimen, and wherein the amount is a) sufficient to decrease the subject's score on the Epworth Sleepiness Scale (ESS) to 10 points or less; or b) sufficient to increase the subject's score on the maintenance of wakefulness test (MWT) by at least 10 minutes.

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

3. The use of claim 1 or 2, wherein the dosing regimen comprises a once-daily dose of 75 mg for 3 days followed by a once-daily dose of 150 mg.

4. The use of any one of claims 1-3, further comprising a decrease in 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.

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

6. The use of claim 4 or 5, wherein the decrease in the daily dose is a decrease to a daily dose of 75 mg APC.

7. The use of any one of claims 1-6, wherein the APC is provided as a pharmaceutically acceptable salt of APC.

8. The use of claim 7, wherein the APC is provided as a hydrochloride salt.

9. The use of claim 1, wherein the excessive daytime sleepiness is associated with narcolepsy.

10. The use of claim 1, wherein the excessive daytime sleepiness is associated with obstructive sleep apnea.

11. The use of any one of claims 1-10, wherein the oral daily dose is to be administered within 3 hours of the subject's awakening.

12. The use of any one of claims 1-11, wherein the oral daily dose is to be administered within 1 hour of the subject's awakening.

13. The use of any one of claims 1-12, wherein the daily dose is to be administered at least 10 hours in advance of the subject's bedtime.

14. The use any one of claims 1-13, wherein the daily dose is to be administered orally.

15. The use of any one of claims 1-14, wherein the medicament is a pharmaceutical composition comprising the APC or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

16. The use of claim 15, wherein the pharmaceutical composition is a dosage form.

17. The use of claim 15, wherein the pharmaceutical composition is an immediate release oral dosage form.

18. The use of claim 16 or 17, wherein the composition is a tablet or a capsule.

19. The use of claim 18, wherein the composition is an immediate release compressed tablet, the tablet comprising:

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

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

at least one lubricant in an amount of 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.

20. The use of any one of claims 16-19, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 150 mg.

21. The use of any one of claims 16-19, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 75 mg.

22. The use of any one of claims 16-19, wherein the amount of APC or a pharmaceutically acceptable salt thereof in the dosage form is about 37.5 mg.

23. The use any one of claims 1-22, wherein the subject is a human.

24. The use of any one of claims 1-23, wherein the subject is an adult.

25. The use of any one of claims 1-23, wherein the subject is a juvenile.