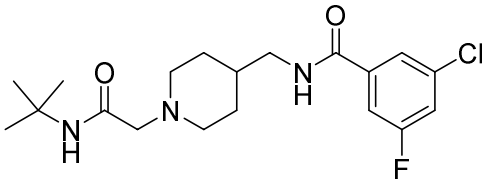
compliance and, thus, benefit patients with diseases or conditions involving T-type calcium channels, including, for example, essential tremor.

SUMMARY

[00010] Described herein are methods of preventing and/or treating a disease or condition relating to aberrant function or activity of T-type calcium channels, such as psychiatric disorders (e.g., mood disorder (e.g., major depressive disorder)), pain, tremor (e.g., essential tremor), seizures (e.g., absence seizures), epilepsy, or an epilepsy syndrome (e.g., juvenile myoclonic epilepsy). Also disclosed herein are methods for modulating the function of a T-type calcium channel and methods of administering a titrated dosage of a T-type calcium channel antagonist, such as the compound of formula (I) or a pharmaceutically acceptable salt thereof.

[0010a] In one aspect, the present disclosure provides the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, represented by the following structural formula:



(I),

in the manufacture of a medicament for treating essential tremor in a subject in need thereof; wherein the titrated dose comprises: (a) a first dose of the compound of formula (I), or a pharmaceutically acceptable salt thereof, of about 5 mg to about 40 mg formulated for administration to the subject daily for a first time period; (b) one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein the one or more increased doses are increased relative to the first dose to achieve a maximum titrated dose of about 20 mg to about 120 mg, formulated for administration to the subject daily.

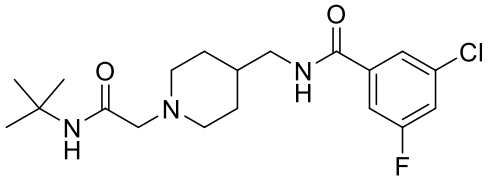
[00011] In one example, the methods of treating a disease or condition relating to aberrant function or activity of a T-type calcium channel in a subject in need thereof comprise (a) administering a first dose of a compound of formula (I) or a pharmaceutically acceptable salt thereof to the subject for a first period of time, wherein following administration of the first dose of the compound for the first period of time the subject has a maximum plasma drug concentration (C_{max}) ranging from about 30 ng/mL to about 130 ng/mL and/or an area under the plasma concentration-time curve from time of administration to 24 hours after administration (AUC_{24}) ranging from about 490 ng*h/mL to about 2030 ng*h/mL; (b) increasing the amount of the compound in the first dose and administering one or more increased doses of the compound to the

subject to arrive at a maximum titrated dose; and (c) administering the maximum titrated dose of the compound to the subject to maintain in the subject a C_{max} ranging from about 280 ng/mL to about 470 ng/mL and/or an AUC_{24} ranging from about 3480 ng*h/mL to about 5800 ng*h/mL. Typically, each dose is administered once daily; however, the frequency of administration may be altered as long as the desired C_{max} and/or AUC_{24} values are achieved, as discussed in other sections of this application.

[00012] In certain examples, step (b) comprises increasing the first dose to a second dose and administering the second dose of the compound to the subject for a second period of time, wherein following administration of the second dose of the compound for the second period of time, the subject has a C_{max} ranging from about 80 ng/mL to about 300 ng/mL and/or an AUC_{24} ranging from about 1220 ng*h/mL to about 4070 ng*h/mL. In certain examples, step (b) comprises increasing the first dose to a second dose and administering the second dose of the compound to the subject for a second period of time, wherein following administration of the second dose of the compound for the second period of time, the subject has a C_{max} ranging from about 80 ng/mL to about 220 ng/mL and/or an AUC_{24} ranging from about 1220 ng*h/mL to about 3330

CLAIMS

1. Use a compound of formula (I), or a pharmaceutically acceptable salt thereof, represented by the following structural formula:



(I),

in the manufacture of a medicament for treating essential tremor in a subject in need thereof; wherein the titrated dose comprises:

(a) a first dose of the compound of formula (I), or a pharmaceutically acceptable salt thereof, of about 5 mg to about 40 mg formulated for administration to the subject daily for a first time period; and

(b) one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein the one or more increased doses are increased relative to the first dose to achieve a maximum titrated dose of about 20 mg to about 120 mg, formulated for administration to the subject daily.

2. The use of claim 1, wherein in (b), the one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, are formulated for administration to the subject for a time period ranging from 3 days to 9 days.

3. The use of claim 1 or 2, wherein the first dose is about 20 mg to about 40 mg formulated for administration to the subject daily.

4. The use of any one of claims 1-3, wherein in (b) one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, comprises a second dose of about 40 mg to about 80 mg formulated for administration to the subject daily for a second time period.

5. The use of any one of claims 1-4, wherein in (b) the one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, comprises:

(i) a second dose of about 40 mg to about 60 mg formulated for administration to the subject daily for a second time period; and

(iii) a third dose of about 80 mg to about 100 mg formulated for administration to the subject daily for a third time period.

6. The use of claim 5, wherein in (b) the one or more increased doses of the compound of formula (I), or a pharmaceutically acceptable salt thereof, further comprises a fourth dose of about 120 mg formulated for administration to the subject daily for a fourth time period.

7. The use of any one of claims 1-6, wherein the first dose is about 20 mg formulated for administration to the subject daily and the second dose is about 40 mg formulated for administration to the subject daily.

8. The use of claim 1 or 2, wherein the titrated dose comprises:

(a) a first dose of about 5 mg to about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period;

(b) a second dose of about 10 mg to about 100 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period; and

(c) a third dose of about 20 mg to about 120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period.

9. The use of claim 1 or 2, wherein the titrated dose comprises:

(a) a first dose of about 5 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period;

(b) a second dose of about 10 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period; and

(c) a third dose of about 20 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period.

10. The use of claim 1 or 2, wherein the titrated dose comprises:

(a) a first dose of about 20-40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period;

(b) a second dose of about 40-80 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period; and

(c) a third dose of about 60-120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period.

11. The use of claim 10, wherein the titrated dose further comprises:

(d) a fourth dose of about 80-120 mg of the compound of formula (I) or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a fourth time period.

12. The use of claim 11, wherein the titrated dose further comprises:

(e) a fifth dose of about 100-120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a fifth time period.

13. The use of any one of claims 1-12, wherein the first time period is 3 days to 9 days.

14. The use of claim 13, wherein the first time period is 7 days.

15. The use of any one of claims 4-14, wherein the second time period is 3 days to 9 days.

16. The use of claim 15, wherein the second time period is 7 days.

17. The use of any one of claims 5-16, wherein the third time period is 3 days to 9 days.

18. The use of claim 17, wherein the third time period is 7 days.

19. The use of any one of claims 11-18, wherein the fourth time period is 3 days to 9 days.

20. The use of claim 19, wherein the fourth time period is 7 days.

21. The use of any one of claims 12-20, wherein the fifth time period is 3 days to 9 days.

22. The use of claim 21, wherein the fifth time period is 7 days.

23. The use of claim 1 or 2, wherein the titrated dose comprises:

(a) a first dose of about 5 mg to about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period ranging from 3 to 9 days;

(b) a second dose of about 10 mg to about 100 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period ranging from 3 to 9 days; and

(c) a third dose of about 20 mg to about 120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period ranging from 3 to 9 days.

24. The use of claim 23, wherein the titrated dose comprises:

(a) a first dose of about 20 mg or about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period ranging from 3 to 9 days;

(b) a second dose of about 40 mg, about 60 mg or about 80 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period ranging from 3 to 9 days; and

(c) a third dose of about 60 mg, about 80 mg, about 100 mg or about 120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period ranging from 3 to 9 days.

25. The use of claim 23 or 24, wherein the titrated dose comprises:

(a) a first dose of about 20 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period of 7 days;

(b) a second dose of about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period of 7 days;

(c) a third dose of about 60 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period of 7 days;

(d) a fourth dose of about 80 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a fourth time period of 7 days;

(e) a fifth dose of about 100 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a firth time period of 7 days; and

(f) a sixth dose of about 120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a sixth time period.

26. The use of claim 1, wherein the titrated dose comprises:

(a) a first dose of about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period of 7 days;

(b) a second dose of about 80 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period of 7 days; and

(c) a third dose of about 120 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period.

27. The use of claim 1, wherein the titrated dose comprises:

(a) a first dose of about 20 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a first time period of 7 days;

(b) a second dose of about 40 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a second time period of 7 days; and

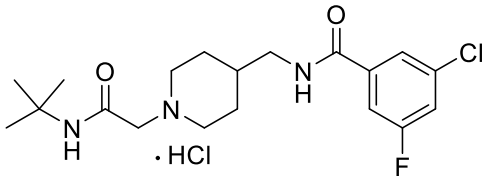
(c) a third dose of about 60 mg of the compound of formula (I), or a pharmaceutically acceptable salt thereof, formulated for administration to the subject daily for a third time period.

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

29. The use of claim 28, wherein the human is 0 to 100 years old.

30. The use of claim 29, wherein the human is 10 to 90 years old, 20 to 70 years old, 18 to 55 years old, or 55-75 years old.

31. The composition of any one of claims 1-30, wherein the compound of formula (I) is a compound of formula (II):



(II).