FORMULATIONS OF RADIPRODIL

CROSS-REFERENCE

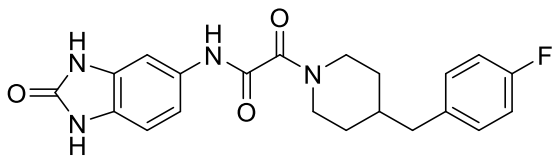
[0001] This application claims priority to U.S. Provisional Application Number 63/230,331 filed August 6, 2021, which is incorporated herein by reference in its entirety.

BACKGROUND

[0002] N-methyl-D-aspartate (NMDA) receptors are ligand-gated cation-channels embedded in the cell membranes of neurons. Overactivation of NMDA receptors by glutamate, their natural ligand, can lead to calcium overload of cells. This triggers a cascade of intracellular events that alters the cell function and ultimately may lead to death of neurons. Modulators of the NMDA receptors may be used for treating many disorders that are accompanied with excess release of glutamate, the main excitatory neurotransmitter in the central nervous system. For example, NR2B subtype selective antagonists of NMDA receptors are expected to possess little or no untoward side effects that are typically caused by the non-selective antagonists of NMDA receptors, namely psychotomimetic effects such as dizziness, headache, hallucinations, dysphoria and disturbances of cognitive and motor function. There is a need for NMDA receptor modulators that are useful for the treatment of disorders.

SUMMARY

[0002a] In a first aspect of the present disclosure, there is provided a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 0.5% by weight to about 15% by weight of the compound of Formula I based on the total weight of the composition;

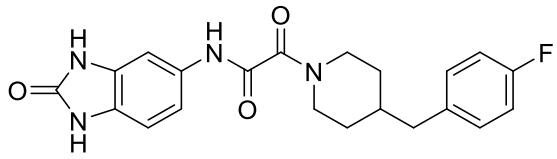
at least one filler;

a disintegrant;

a binder; and

a surfactant.

[0002b] In another aspect of the present disclosure, there is provided a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

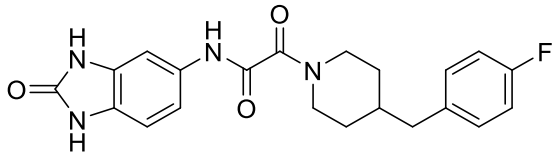
about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition.

[0002c] In yet another aspect of the present disclosure, there is provided a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

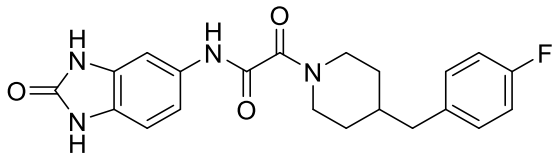
about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition.

[0002d] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

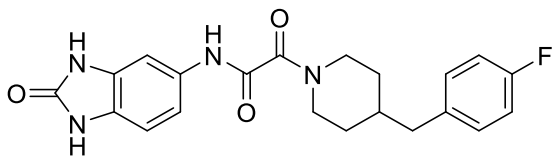
about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

not more than about 0.1% to 0.5% of an impurity with respect to the quantity of the compound as measured by HPLC; and

one or more pharmaceutically acceptable excipients.

[0002e] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable aqueous suspension comprising the pharmaceutically acceptable composition as disclosed herein and an aqueous medium.

[0002f] In yet another aspect of the present disclosure, there is provided a pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising:

(i) a solid pharmaceutically acceptable composition comprising:

about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

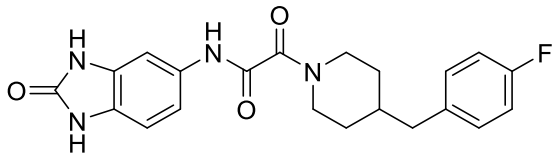
about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition; and

(ii) an aqueous medium.

[0002g] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

(i) a solid pharmaceutically acceptable composition comprising:

about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-

ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

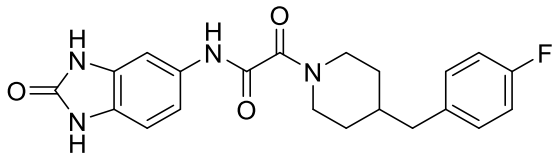
about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition; and

(ii) an aqueous medium.

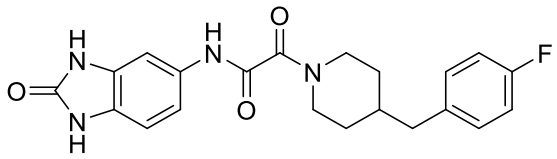
[0002h] In another aspect of the present disclosure, there is provided a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

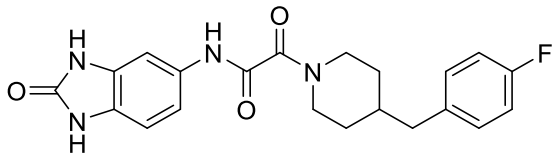
[0002i] In yet another aspect of the present disclosure, there is provided a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

[0002j] In a further aspect of the present disclosure, there is provided a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:

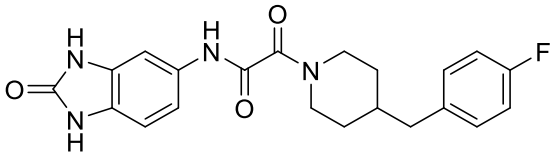


Formula I

comprising: about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; not more than about 0.1% to

0.5% of an impurity (e.g., 6-amino-2-benzoxazolone) with respect to the quantity of the compound as measured by HPLC; and one or more pharmaceutically acceptable excipients.

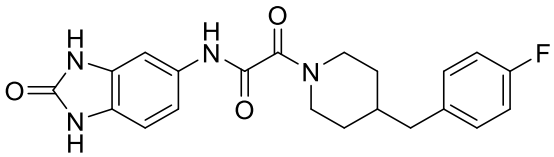
[0002k] In another aspect of the present disclosure, there is provided a pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising: (i) a solid pharmaceutically acceptable composition comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

[0002l] In yet another aspect of the present disclosure, there is provided a pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

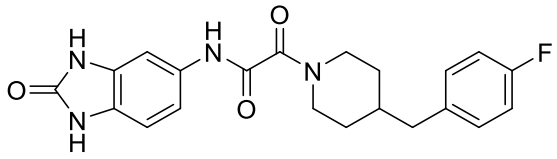
(i) a solid pharmaceutically acceptable composition comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

[0002m] In a further aspect of the present disclosure, there is provided a use of the pharmaceutical composition as disclosed herein, or the suspension as disclosed herein, in the manufacture of a medicament for treating a convulsive disorder in a subject in need thereof.

[0002n] In another aspect of the present disclosure, there is provided a pharmaceutical composition as disclosed herein, or a suspension as disclosed herein, for use in therapy.

[0003] The present disclosure provides, in an example, compositions comprising radiprodil, and methods of use thereof.

[0004] In one example, described herein is a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



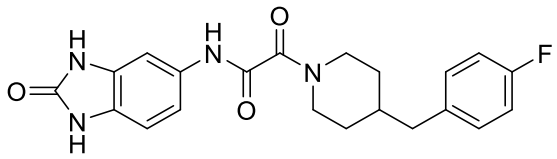
Formula I

comprising: about 0.5% by weight to about 15% by weight of the compound of Formula I based on the total weight of the composition; at least one filler; a disintegrant; a binder; and a surfactant.

[0005] In some examples, compositions described herein comprise Form A of the compound of Formula I. Form A may be characterized by an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ.

[0006] In some examples, compositions described herein comprise Form C of the compound of Formula I. Form C may be characterized by an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ.

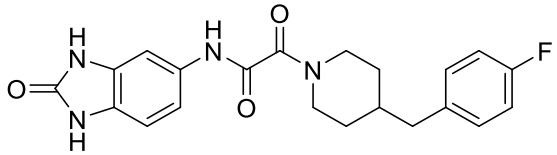
[0007] In one example, provided herein is a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

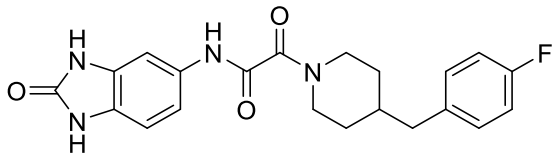
[0008] In one example, described herein is a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

[0009] In one example, described herein is a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:

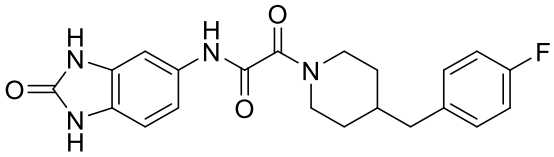


Formula I

comprising: about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ; not more than about 0.1% to 0.5% of an impurity (e.g., 6-amino-2-benzoxazolone) with respect to the quantity of the compound as measured by HPLC; and one or more pharmaceutically acceptable excipients.

[00010] In one example, provided herein is a pharmaceutically acceptable aqueous suspension comprising a pharmaceutically acceptable composition described herein and an aqueous medium.

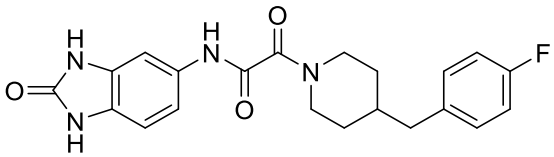
[00011] In one example, described herein is a pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising: (i) a solid pharmaceutically acceptable composition comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

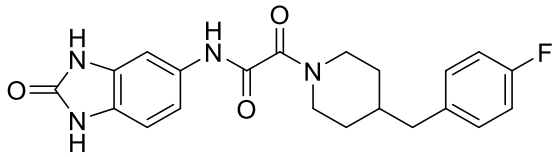
[00012] In one example, provided herein is a pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

(i) a solid pharmaceutically acceptable composition comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium. In some examples, the aqueous medium comprises a starch-based suspension (e.g., SYRSPEND® SF).

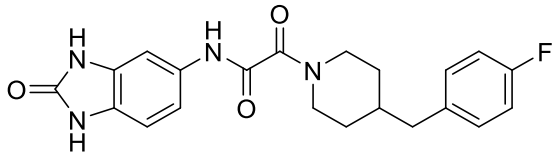
[00013] In one example, provided herein is a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

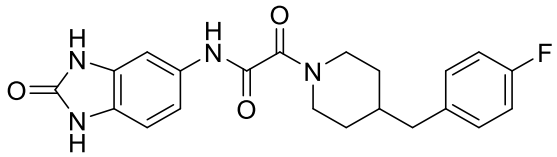
[00014] In one example, described herein is a solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

[00015] In one example, described herein is a pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:

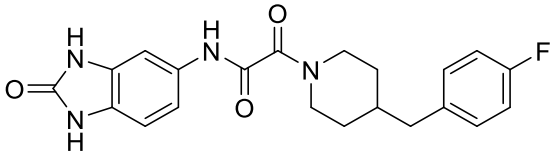


Formula I

comprising: about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; not more than about 0.1% to 0.5% of an impurity (e.g., 6-amino-2-benzoxazolone) with respect to the quantity of the compound as measured by HPLC; and one or more pharmaceutically acceptable excipients.

[00016] In one example, provided herein is a pharmaceutically acceptable aqueous suspension comprising a pharmaceutically acceptable composition described herein and an aqueous medium.

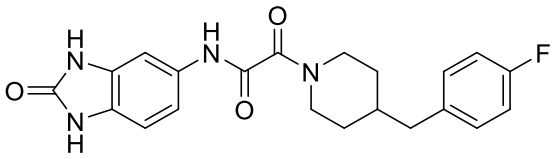
[00017] In one example, described herein is a pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising: (i) a solid pharmaceutically acceptable composition comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

[00018] In one example, provided herein is a pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

(i) a solid pharmaceutically acceptable composition comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the

composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium. In some examples, the aqueous medium comprises a starch-based suspension (e.g., SYRSPEND® SF).

BRIEF DESCRIPTION OF THE DRAWINGS

[00019] **Figure 1** depicts an exemplary manufacturing process of 1 weight% and 10 weight% radiprodil granules.

[00020] **Figure 2** depicts dissolution profiles for exemplary radiprodil samples that were not reconstituted prior to dissolution testing.

[00021] **Figure 3** depicts dissolution profiles for exemplary radiprodil samples that were reconstituted prior to dissolution testing.

[00022] **Figure 4** depicts dissolution profiles for exemplary radiprodil samples that underwent extemporaneous reconsistution prior to dissolution testing.

DETAILED DESCRIPTION

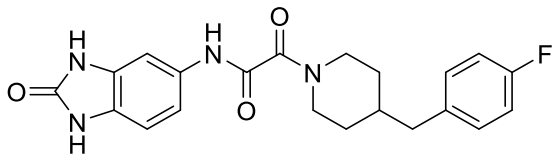
[00023] The features and other details of the disclosure will now be more particularly described. Certain terms employed in the specification, examples and appended claims are collected here. These definitions should be read in light of the remainder of the disclosure and as understood by a person of skill in the art. Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by a person of ordinary skill in the art.

Compounds

[00024] In one embodiment, provided herein is a compound of the formula:

CLAIMS

1. A pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 0.5% by weight to about 15% by weight of the compound of Formula I based on the total weight of the composition;

at least one filler;

a disintegrant;

a binder; and

a surfactant.

2. The pharmaceutically acceptable composition of claim 1, comprising about 1% by weight of the compound based on the total weight of the pharmaceutically acceptable composition.

3. The pharmaceutically acceptable composition of claim 1, comprising about 10% by weight of the compound based on the total weight of the pharmaceutically acceptable composition.

4. The pharmaceutically acceptable composition of any one of claims 1-3, comprising an anhydrous crystalline form of the compound of Formula I.

5. The pharmaceutically acceptable composition of claim 4, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ.

6. The pharmaceutical composition of any one of claims 1-5, wherein the pharmaceutical composition comprises about 10% by weight to about 80% by weight of at least one filler based on the total weight of the pharmaceutical composition.

7. The pharmaceutical composition of any one of claims 1-6, wherein the at least one filler is selected from the group consisting of confectioner's sugar, compressible sugar, dextrates, dextrin, dextrose, lactose, mannitol, microcrystalline cellulose, powdered cellulose, sorbitol, sucrose, talc, and combinations thereof.

8. The pharmaceutical composition of any one of claims 1-7, wherein the composition comprises two fillers.

9. The pharmaceutical composition of any one of claims 1-8, wherein the pharmaceutical composition comprises about 1% by weight to about 10% by weight of the disintegrant based on the total weight of the pharmaceutical composition.

10. The pharmaceutical composition of any one of claims 1-9, wherein the disintegrant is selected from the group consisting of crospovidone, croscarmellose sodium, sodium starch glycolate, microcrystalline cellulose, pregelatinized starch, and combinations thereof.

11. The pharmaceutical composition of any one of claims 1-10, wherein the pharmaceutical composition comprises about 1% by weight to about 10% by weight of the binder based on the total weight of the pharmaceutical composition.

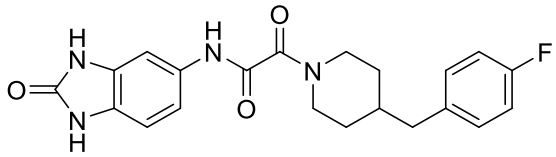
12. The pharmaceutical composition of any one of claims 1-11, wherein the binder is selected from the group consisting of povidone, starch, gelatin, sugars, natural and synthetic gums, alginates, polyethylene oxide, polyethylene glycol, inorganic calcium salts, silicic acid, polymethacrylates, waxes, water, alcohol, and combinations thereof.

13. The pharmaceutical composition of any one of claims 1-12, wherein the pharmaceutical composition comprises about 0.01% by weight to about 5% by weight of the surfactant based on the total weight of the pharmaceutical composition.

14. The pharmaceutical composition of any one of claims 1-13, wherein the surfactant is selected from the group consisting of polyoxyethylene stearates, polyoxyethylene alkyl ethers, sorbitan fatty acid esters, poloxamers, polyoxyethylene castor oil derivatives, phospholipids, sodium lauryl sulphate, polysorbate (polyoxyethylene sorbitan fatty acid esters), and combinations thereof.

15. The pharmaceutical composition of any one of claims 1-14, wherein the composition is a granule for an oral solution.

16. A solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

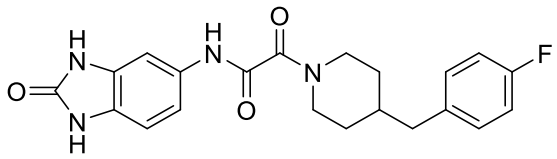
about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition.

17. A solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

about 5% by weight of crospovidone based on the total weight of the composition;

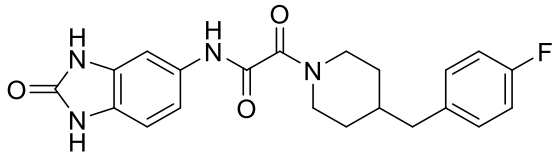
about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition.

18. The pharmaceutically acceptable composition of any one of claims 1-17, comprising not more than about 0.1% to 0.5% of an impurity with respect to the quantity of the compound as measured by HPLC.

19. The pharmaceutically acceptable composition of any one of claims 1-18, comprising not more than about 0.1% to 0.5% of 6-amino-2-benzoxazolone with respect to the quantity of the compound as measured by HPLC.

20. A pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising:

about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

not more than about 0.1% to 0.5% of an impurity with respect to the quantity of the compound as measured by HPLC; and

one or more pharmaceutically acceptable excipients.

21. The pharmaceutically acceptable composition of claim 20, comprising not more than about 0.5% of an impurity with respect to the quantity of the compound as measured by HPLC.

22. The pharmaceutically acceptable composition of claim 20 or 21, comprising not more than about 0.05% of an impurity with respect to the quantity of the compound as measured by HPLC.

23. The pharmaceutically acceptable composition of any one of claims 1-22, comprising not more than about 0.5% of an impurity with respect to when exposed to 60% relative humidity at 25 °C for about 6 months.

24. The pharmaceutically acceptable composition of any one of claims 1-23, comprising not more than about 0.05% of an impurity with respect to when exposed to 60% relative humidity at 25 °C for about 6 months.

25. The pharmaceutically acceptable composition of any one of claims 1-24, comprising not more than about 0.5% of an impurity with respect to when exposed to 60% relative humidity at 25 °C for about 36 months.

26. The pharmaceutically acceptable composition of any one of claims 1-25, comprising not more than about 0.05% of an impurity with respect to when exposed to 60% relative humidity at 25 °C for about 36 months.

27. The pharmaceutically acceptable composition of any one of claims 18-26, comprising about 10% of the anhydrous crystalline form based on the total weight of the composition.

28. The pharmaceutically acceptable composition of any one of claims 18-26, comprising about 1% of the anhydrous crystalline form based on the total weight of the composition.

29. The composition of any one of claims 1-28, wherein the composition releases at least 80% of the compound after 30 minutes when the composition is tested in 900 mL sodium lauryl sulfate solution in water using a USPII Paddle Apparatus at 37 °C, with a paddle speed of 75 rpm.

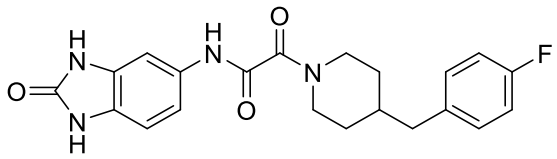
30. The composition of any one of claims 1-29, wherein the composition releases at least 80% of the compound when the composition is stirred in an aqueous medium from at least 1 minute to about 24 hours after reconstitution.

31. The composition of claim 30, wherein the aqueous medium comprises a starch-based suspension.

32. A pharmaceutically acceptable aqueous suspension comprising the pharmaceutically acceptable composition of any one of claims 1-31 and an aqueous medium.

33. The pharmaceutically acceptable suspension of claim 32, wherein the aqueous medium comprising a starch-based suspension.

34. A pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising:

(i) a solid pharmaceutically acceptable composition comprising:

about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

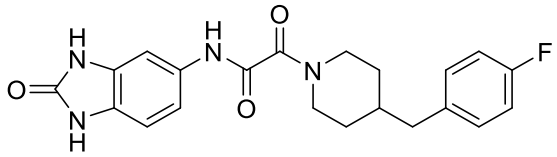
about 5% by weight of crospovidone based on the total weight of the composition;

about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition; and

(ii) an aqueous medium.

35. A pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

(i) a solid pharmaceutically acceptable composition comprising:

about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 7.8, 22.0, 23.7, 27.0 and 27.6 ± 0.2° 2θ;

about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition;

about 5% by weight of crospovidone based on the total weight of the composition;

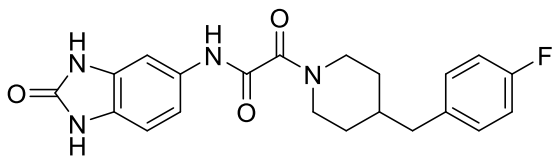
about 4% of povidone based on the total weight of the composition; and

about 1% of a polysorbate based on the total weight of the composition; and

(ii) an aqueous medium.

36. The pharmaceutically acceptable suspension of claim 34 or 35, wherein the aqueous medium comprises a starch-based suspension.

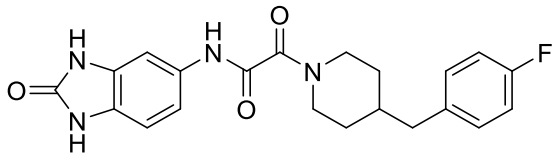
37. A solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

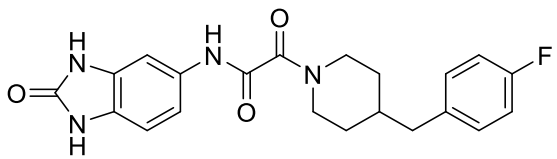
38. A solid pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition.

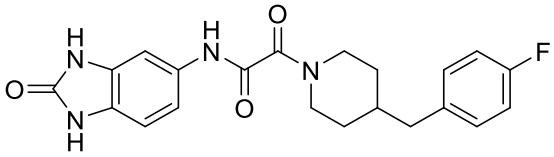
39. A pharmaceutically acceptable composition formulated for oral administration of a compound of Formula I:



Formula I

comprising: about 0.5% to 15% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; not more than about 0.1% to 0.5% of an impurity (e.g., 6-amino-2-benzoxazolone) with respect to the quantity of the compound as measured by HPLC; and one or more pharmaceutically acceptable excipients.

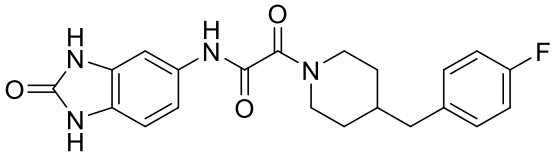
40. A pharmaceutically acceptable aqueous suspension for orally delivering about 0.1 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

comprising: (i) a solid pharmaceutically acceptable composition comprising: about 10% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 50% to 80% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

41. A pharmaceutically acceptable aqueous suspension for orally delivering about 0.2 mg/kg to 2 mg/kg of a compound of Formula I:



Formula I

(i) a solid pharmaceutically acceptable composition comprising: about 1% by weight of an anhydrous crystalline form of the compound of Formula I based on the total weight of the composition, wherein the anhydrous crystalline form has an X-ray powder diffraction pattern with characteristic peaks between and including the following values of 2θ in degrees: 6.4, 13.7, and 25.8 ± 0.2° 2θ; about 70% to 89% by weight of a filler selected from the group consisting of mannitol, microcrystalline cellulose, and a combination thereof, based on the total weight of the composition; about 5% by weight of crospovidone based on the total weight of the composition; about 4% of povidone based on the total weight of the composition; and about 1% of a polysorbate based on the total weight of the composition; and (ii) an aqueous medium.

42. Use of the pharmaceutical composition of any one of claims 1-31 and 37-39, or the suspension of any one of claims 32-36 and 40-41, in the manufacture of a medicament for treating a convulsive disorder in a subject in need thereof.

43. The use of claim 42, wherein the convulsive disorder is epilepsy.

44. The use of claim 42 or 43, wherein the subject is a pediatric subject.

45. The use of any one of claims 42-44, wherein the convulsive disorder is infantile spasm syndrome.

46. A pharmaceutical composition of any one of claims 1-31 and 37-39, or a suspension of any one of claims 32-36 and 40-41, for use in therapy.