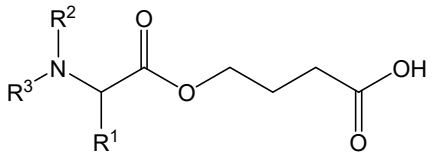
CLAIMS

1. A pharmaceutical composition comprising a plurality of coated granules, wherein,

the coated granules comprise a core and a controlled release coating surrounding the core;

the core comprises from 90.0 wt% to 99.5 wt% of a compound of Formula (2):



(2)

or a pharmaceutically acceptable salt thereof, wherein,

R^1 is selected from hydrogen and C_{1-6} alkyl; and

each of R^2 and R^3 is independently selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxycarbonyl, and C_{3-6} cycloalkoxycarbonyl;

wherein wt% is based on the total weight of the core, wherein

the coated granules are characterized by a particle size distribution (PSD) (D50) from 150 μm to 500 μm, wherein the particle size distribution is determined by laser diffraction;

the coated granules comprise from 50 wt% to 95 wt% of the compound of Formula (2), wherein wt% is based on the total weight of the coated granules;

the controlled release coating comprising:

from 60 wt% to 85 wt% of a matrix polymer, wherein the matrix polymer comprises:

from 92 wt% to 98 wt% of a water-insoluble polymer; and

from 2 wt% to 8 wt% of a water-soluble polymer,

wherein wt% is based on the total weight of the matrix polymer;

from 10 wt% to 20 wt% of talc; and

from 3 wt% to 13 wt% of dibutyl sebacate,

wherein wt% is based on the total weight of the controlled release coating; and

the controlled release coating has a thickness from 5 μm to 40 μm.

2. The pharmaceutical composition of claim 1, wherein the core is characterized by:

an average sphericity greater than 0.90, wherein sphericity is determined using wet dispersion

particle shape methods or by dynamic image analysis; and/or

a friability value less than 2 wt%, wherein friability is determined using a sonic sifter.

3. The pharmaceutical composition of any one of claims 1 to 2, wherein,

the core has a bulk density from 0.5 g/mL to 1.0 g/mL; and/or

the coated granulation has a bulk density from 0. 55 g/mL to 0.80 g/mL,

wherein the bulk density is determined using a bulk density cylinder.

4. The pharmaceutical composition of any one of claims 1 to 3, wherein,

the water-insoluble polymer comprises ethylcellulose; and

the water soluble polymer comprises hydroxypropyl cellulose.

5. The pharmaceutical composition of any one of claims 1 to 4, wherein the coated granules comprise:

from 55 wt% to 90 wt% of the core; and

from 10 wt% to 45 wt% of the controlled release coating,

wherein wt% is based on the total weight of the coated granules.

6. The pharmaceutical composition of any one of claims 1 to 5, wherein the compound of Formula (2) comprises:

4-(((*tert*-butoxycarbonyl)glycyl)oxy)butanoic acid;

4-(glycyloxy)butanoic acid;

4-((*D*-valyl)oxy)butanoic acid;

4-((*L*-alanyl)oxy)butanoic acid;

4-(((ethoxycarbonyl)glycyl)oxy)butanoic acid;

4-(((isopropoxycarbonyl)glycyl)oxy)butanoic acid;

4-((((cyclohexyloxy)carbonyl)glycyl)oxy)butanoic acid;

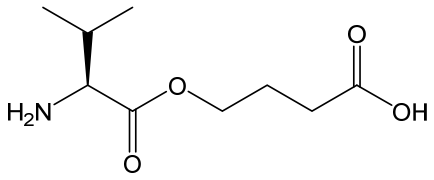
4-(((ethoxycarbonyl)-*D*-valyl)oxy)butanoic acid;

4-((*L*-valyl)oxy)butanoic acid;

a pharmaceutically acceptable salt of any of the foregoing; or

a combination of any of the foregoing.

7. The pharmaceutical composition of any one of claims 1 to 5, wherein the compound of Formula (2) comprises 4-((*L*-valyl)oxy)butanoic acid (2a) or a pharmaceutically acceptable salt thereof:



(2a).

8. The pharmaceutical composition of any one of claims 1 to 7, wherein the pharmaceutical composition comprises from 500 mg equivalents to 12 g equivalents of γ-hydroxybutyric acid.

9. The pharmaceutical composition of any one of claims 1 to 8, wherein the pharmaceutical composition comprises:

a controlled release portion, wherein the controlled release portion comprises the pharmaceutical granulation; and

an immediate release portion, an extended release portion, or a combination thereof.

10. The pharmaceutical composition of any one of claims 1 to 9, wherein the

pharmaceutical composition comprises an oral formulation comprising a suspension of the pharmaceutical granulation.

11. Use of the pharmaceutical granulation of any one of claims 1 to 10, in the manufacture of a medicament for the treatment of a disease selected from the group consisting of excessive daytime sleepiness associated with narcolepsy, excessive daytime sleepiness associated with Parkinson's disease, excessive daytime sleepiness associated with multiple sclerosis, cataplexy associated with narcolepsy, fatigue in a patient with Parkinson's disease, fatigue in a patient with multiple sclerosis, fibromyalgia, insomnia associated with schizophrenia, idiopathic hypersomnia, and chronic fatigue syndrome.