

CLAIMS

[Claim 1]

A dihydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one.

[Claim 2]

The dihydrate according to claim 1 which has characteristic peaks at diffraction angles (2θ) of 8.1° , 8.9° , 15.1° , 15.6° , and 24.4° in an X-ray powder diffraction pattern measured by copper radiation of $\lambda = 1.5418\text{\AA}$ through a monochromator.

[Claim 3]

The dihydrate according to claim 1 or 2 which has characteristic peaks at 3509 cm^{-1} , 2934 cm^{-1} , 2812 cm^{-1} , 1651 cm^{-1} , 1626 cm^{-1} , 1447 cm^{-1} , 1223 cm^{-1} , and 839 cm^{-1} in an infrared absorption spectrum as measured by a potassium bromide tablet method.

[Claim 4]

The dihydrate according to any one of Claims 1 to 3 which has characteristic peaks at 1497 cm^{-1} , 1376 cm^{-1} , 1323 cm^{-1} , 1311 cm^{-1} , 1287 cm^{-1} , 1223 cm^{-1} , and 781 cm^{-1} in a Raman spectrum.

[Claim 5]

The dihydrate according to any one of claims 1 to 4 which contains water in an amount of 6.5 to 8.8 wt.%.

[Claim 6]

The dihydrate according to any one of Claims 1 to 5 which has peaks in a ^1H -NMR spectrum at:

- 1.64 ppm (tt, $J=7.4\text{Hz}$, $J=7.4\text{Hz}$, 2H),
- 1.80 ppm (tt, $J=7.0\text{Hz}$, $J=7.0\text{Hz}$, 2H),
- 2.44 ppm (t, $J=7.5\text{Hz}$, 2H),
- 2.62 ppm (br, 4H),
- 3.06 ppm (br, 4H),

3.32 ppm (s, 4H + H₂O) ,
4.06 ppm (t, J=6.5Hz, 2H) ,
6.29 ppm (d, J=9.5Hz, 1H) ,
6.80 ppm (d, J=2.5Hz, 1H) ,
6.80 ppm (dd, J=2.5Hz, J=9.0Hz, 1H) ,
6.88 ppm (d, J=7.5Hz, 1H) ,
7.27 ppm (dd, J=7.8Hz, J=7.8Hz, 1H) ,
7.40 ppm (dd, J=0.5Hz, J=5.5Hz, 1H) ,
7.55 ppm (d, J=9.0Hz, 1H) ,
7.61 ppm (d, J=8.0Hz, 1H) ,
7.69 ppm (d, J=5.5Hz, 1H) ,
7.80 ppm (d, J=9.5Hz, 1H) , and
11.57 ppm (s, 1H) .

[Claim 7]

A benzothiophene compound for use in treating and/or preventing a central nervous system disease, the compound comprising the dihydrate according to any one of claims 1 to 6 and an anhydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one, and the dihydrate being contained in an amount of 60 wt.% or more in the compound.

[Claim 8]

A dihydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one according to any one of claims 1 to 6 for use in preventing and/or treating a central nervous system disease.

[Claim 9]

The dihydrate for use according to claim 8 wherein the central nervous system disease is selected from the group consisting of schizophrenia, treatment-resistant, refractory and chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous

depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, adjustment disorder, substance-related disorder, anhedonia, delirium, cognitive impairment, cognitive impairment associated with Alzheimer's disease, Parkinson's disease, and other neurodegenerative diseases, BPSD caused by cognitive impairment, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autism, Tourette's syndrome, tic disorder, attention deficit hyperactivity disorder, conduct disorder, and Down's syndrome.

[Claim 10]

A dopamine D₂ receptor partial agonist and/or a 5-HT_{2A} receptor antagonist and/or a serotonin uptake inhibitor and/or a serotonin reuptake inhibitor and/or a α_1 receptor antagonist comprising the dihydrate according to any one of claims 1 to 6 as an active ingredient.

[Claim 11]

A pharmaceutical composition comprising the dihydrate according to any one of claims 1 to 6 and a pharmaceutically acceptable carrier.

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CLAIMS

[Claim 1]

A dihydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one or of a salt thereof.

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[Claim 2]

The dihydrate according to claim 1 which has characteristic peaks at diffraction angles (2θ) of 8.1° , 8.9° , 15.1° , 15.6° , and 24.4° in an X-ray powder diffraction pattern measured by copper radiation of $\lambda = 1.5418\text{\AA}$ through a monochromator.

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[Claim 3]

The dihydrate according to claim 1 or 2 which has characteristic peaks at 3509 cm^{-1} , 2934 cm^{-1} , 2812 cm^{-1} , 1651 cm^{-1} , 1626 cm^{-1} , 1447 cm^{-1} , 1223 cm^{-1} , and 839 cm^{-1} in an infrared absorption spectrum as measured by a potassium bromide tablet method.

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[Claim 4]

The dihydrate according to any one of Claims 1 to 3 which has characteristic peaks at 1497 cm^{-1} , 1376 cm^{-1} , 1323 cm^{-1} , 1311 cm^{-1} , 1287 cm^{-1} , 1223 cm^{-1} , and 781 cm^{-1} in a Raman spectrum.

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[Claim 5]

The dihydrate according to any one of claims 1 to 4 which contains water in an amount of 6.5 to 8.8 wt. %.

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[Claim 6]

The dihydrate according to any one of Claims 1 to 5 which has peaks in a $^1\text{H-NMR}$ spectrum at:

30 1.64 ppm (tt, $J=7.4\text{Hz}$, $J=7.4\text{Hz}$, 2H), 1.80 ppm (tt, $J=7.0\text{Hz}$, $J=7.0\text{Hz}$, 2H), 2.44 ppm (t, $J=7.5\text{Hz}$, 2H),

2.62 ppm (br, 4H),

3.06 ppm (br, 4H),

35 3.32 ppm (s, 4H + H_2O),

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4.06 ppm (t, J=6.5Hz, 2H),
6.29 ppm (d, J=9.5Hz, 1H),
6.80 ppm (d, J=2.5Hz, 1H),
6.80 ppm (dd, J=2.5Hz, J=9.0Hz, 1H),
5 6.88 ppm (d, J=7.5Hz, 1H),
7.27 ppm (dd, J=7.8Hz, J=7.8Hz, 1H),
7.40 ppm (dd, J=0.5Hz, J=5.5Hz, 1H),
7.55 ppm (d, J=9.0Hz, 1H),
7.61 ppm (d, J=8.0Hz, 1H),
10 7.69 ppm (d, J=5.5Hz, 1H),
7.80 ppm (d, J=9.5Hz, 1H), and
11.57 ppm (s, 1H).

[Claim 7]

15 A process for producing a dihydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one or of a salt thereof,
the process comprising:
(1) mixing at least one organic acid selected from the group
20 consisting of acetic acid and lactic acid, an ethanol-water mixed solution, and 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one to prepare an acid solution;
(2) cooling the solution obtained in step (1) to 5°C or less; and
(3) mixing the solution cooled in step (2) with an alkali to
25 adjust the pH of the solution to 7 or more.

[Claim 8]

A dihydrate of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one or of a salt thereof obtained by the
30 process according to claim 7.

[Claim 9]

A benzothiophene compound for use in treating and/or preventing a central nervous system disease, the compound comprising the
35 dihydrate according to any one of claims 1 to 6 and 8 and an

anhydride of 7-[4-(4-benzo[b]thiophen-4-yl-piperazin-1-yl)butoxy]-1H-quinolin-2-one or of a salt thereof, and the dihydrate being contained in an amount of 60 wt.% or more in the compound.

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[Claim 10]

A method for preventing and/or treating a central nervous system disease comprising the dihydrate according to any one of claims 1 to 6 and 8 as an active ingredient.

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[Claim 11]

The method according to claim 10 which is for preventing or treating a central nervous system disease selected from the group consisting of schizophrenia, treatment-resistant, refractory and chronic schizophrenia, emotional disturbance, psychotic disorder, mood disorder, bipolar disorder, mania, depression, endogenous depression, major depression, melancholic and treatment-resistant depression, dysthymic disorder, cyclothymic disorder, anxiety disorder, somatoform disorder, factitious disorder, dissociative disorder, sexual disorder, eating disorder, sleep disorder, adjustment disorder, substance-related disorder, anhedonia, delirium, cognitive impairment, cognitive impairment associated with Alzheimer's disease, Parkinson's disease, and other neurodegenerative diseases, BPSD caused by cognitive impairment, cognitive impairment in schizophrenia, cognitive impairment caused by treatment-resistant, refractory or chronic schizophrenia, vomiting, motion sickness, obesity, migraine, pain, mental retardation, autism, Tourette's syndrome, tic disorder, attention deficit hyperactivity disorder, conduct disorder, and Down's syndrome.

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[Claim 12]

A dopamine D₂ receptor partial agonist and/or a 5-HT_{2A} receptor antagonist and/or a serotonin uptake inhibitor and/or a serotonin reuptake inhibitor and/or a α_1 receptor antagonist comprising the

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dihydrate according to any one of claims 1 to 6 and 8 as an active ingredient.

[Claim 13]

- 5 A pharmaceutical composition comprising the dihydrate according to any one of claims 1 to 6 and 8 and a pharmaceutically acceptable carrier.