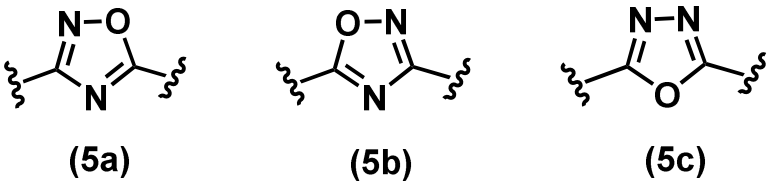
(5b), or (5c).

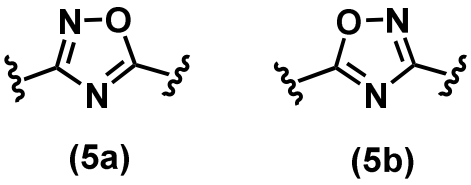


[0017]

(Item 8)

The compound of Item 7 or a pharmaceutically acceptable salt thereof, wherein

the ring containing X, Y, and Z is the following (5a) or (5b).

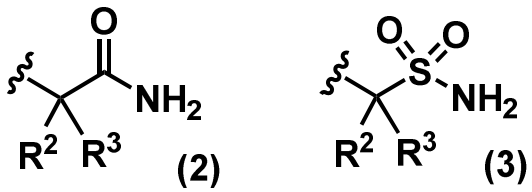


[0018]

(Item 9)

The compound of any one of ~~claims~~ Items 1 to 3 and 6 to 8 or a pharmaceutically acceptable salt thereof, wherein

R^1 is the following (2) or (3).



[0019]

(Item 10)

The compound of any one of Items 1 and 4 to 8 or a pharmaceutically acceptable salt thereof, wherein

(Item 18)

The medicament of Item 14 or 17, wherein the neurological disease or psychiatric disease is epileptic seizure (generalized seizure including tonic seizure, clonic seizure, absence seizure, myoclonic seizure, and~~generalized seizure including~~ atonic seizure, focal seizure, an unknown seizure), status epilepticus, West syndrome, Dravet syndrome, Lennox-Gastaut syndrome, autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE), mesial temporal lobe epilepsy associated with hippocampal sclerosis which is a definitely identified symptom, Rasmussen syndrome, depressive symptom accompanying or unaccompanying epilepsy, anxiety disorder, obsessive-compulsive disorder, REM sleep behavior disorder associated with Parkinson's disease/dementia with Lewy bodies, neuropathic pain, developmental disorder, autism, bipolar disorder, schizophrenia, Alzheimer's disease and the other dementia, amyotrophic lateral sclerosis, or Parkinson's disease.

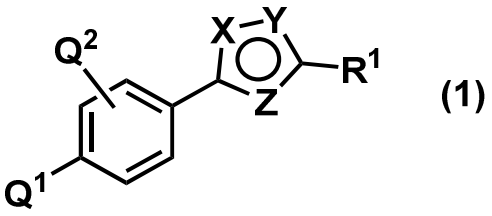
[0028]

(Item 19)

The medicament of Item 14 or 17, wherein the neurological disease or psychiatric disease is epilepsy, neuropathic pain, neurodevelopmental disorders, bipolar disorder and its related disorders, schizophrenia spectrum disorder, Alzheimer's disease and the other neurocognitive

CLAIMS

1. A compound of formula (1):



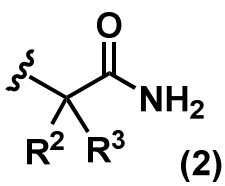
or a pharmaceutically acceptable salt thereof, wherein

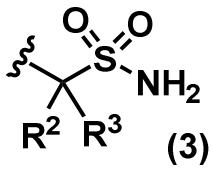
Q^1 is halogen,

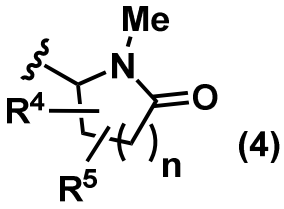
Q^2 is hydrogen, halogen, cyano, C_{1-3} alkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{1-3} alkoxy (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy),

X, Y, and Z are the same or different and are nitrogen atom or oxygen atom, provided that the ring containing X, Y, and Z is a heteroaryl wherein any two of X, Y, and Z are nitrogen atom and the other is oxygen atom,

R^1 is any one of the following formulae (2) to (4):







R^2 and R^3 are the same or different and are C_{1-6} alkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy) or C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy); or R^2 and R^3 may be taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{4-6} saturated hetero ring containing one or two heteroatoms selected independently from nitrogen atom and oxygen atom (said saturated hetero ring may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy),

R^4 and R^5 are the same or different and are hydrogen, halogen, hydroxy, C_{1-6} alkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{3-6} cycloalkyl, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy); or when R^4 and R^5 are attached to the same carbon atom or

to two adjacent carbon atoms respectively, R^4 and R^5 may be taken together with the carbon atom(s) to which they are attached to form C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{4-6} saturated hetero ring containing one or two heteroatoms selected independently from nitrogen atom and oxygen atom (said saturated hetero ring may be substituted with 1 to 3 substituents selected independently from the group consisting of halogen, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), and

n is an integer of 0 to 2.

2. The compound of claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^2 and R^3 are the same or different and are C_{1-3} alkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy); or R^2 and R^3 may be taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{4-6} saturated hetero ring containing one or two heteroatoms selected independently from nitrogen atom and

oxygen atom (said saturated hetero ring may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy).

3. The compound of claim 2 or a pharmaceutically acceptable salt thereof, wherein

R^2 and R^3 are the same or different and are C_{1-3} alkyl which may be substituted with fluorine; or R^2 and R^3 may be taken together with the carbon atom to which they are attached to form C_{3-6} cycloalkyl (which may be substituted with fluorine), or C_{4-6} saturated hetero ring containing one or two heteroatoms selected independently from nitrogen atom and oxygen atom (said saturated hetero ring may be substituted with fluorine).

4. The compound of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof, wherein

R^4 and R^5 are the same or different and are hydrogen, fluorine, hydroxy, C_{1-3} alkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, and C_{1-3} alkoxy), or C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3}

alkoxy); or when R^4 and R^5 are attached to the same carbon atom or to two adjacent carbon atoms respectively, R^4 and R^5 may be taken together with the carbon atom(s) to which they are attached to form C_{3-6} cycloalkyl (which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy), or C_{4-6} saturated hetero ring containing one or two heteroatoms selected independently from nitrogen atom and oxygen atom (said saturated hetero ring may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine, hydroxy, C_{1-3} alkyl, and C_{1-3} alkoxy).

5. The compound of claim 4 or a pharmaceutically acceptable salt thereof, wherein

R^4 and R^5 are the same or different and are hydrogen, fluorine, hydroxy, C_{1-3} alkyl (which may be substituted with fluorine), or C_{3-6} cycloalkyl (which may be substituted with fluorine); or when R^4 and R^5 are attached to the same carbon atom or to two adjacent carbon atoms respectively, R^4 and R^5 may be taken together with the carbon atom(s) to which they are attached to form C_{3-6} cycloalkyl which may be substituted with 1 to 3 substituents selected independently from the group consisting of fluorine and C_{1-3} alkyl.

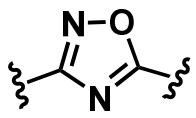
6. The compound of any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein

Q^1 is fluorine, chlorine, or bromine, and

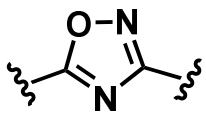
Q^2 is hydrogen, fluorine, chlorine, bromine, cyano, C_{1-3} alkyl (which may be substituted with fluorine), or C_{1-3} alkoxy (which may be substituted with fluorine).

7. The compound of any one of claims 1 to 6 or a pharmaceutically acceptable salt thereof, wherein

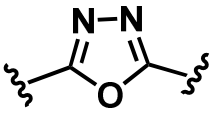
the ring containing X, Y, and Z is the following (5a), (5b), or (5c).



(5a)



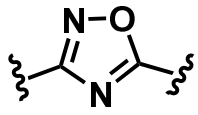
(5b)



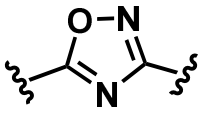
(5c)

8. The compound of claim 7 or a pharmaceutically acceptable salt thereof, wherein

the ring containing X, Y, and Z is the following (5a) or (5b).



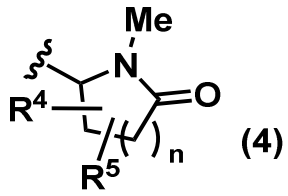
(5a)



(5b)

9. The compound of any one of claims 1 and 4 to 8 or a pharmaceutically acceptable salt thereof, wherein

R^1 is the following (4).



(4)

10. The compound of claim 1 or a pharmaceutically acceptable salt thereof, which is selected from the following compounds:

2-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-2-methylpropanamide,

2-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-2-methylpropanamide,

2-[3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl]-2-methylpropanamide,

1-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]cyclopropane-1-carboxamide,

1-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]cyclopropane-1-carboxamide,

1-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-3-fluorocyclobutane-1-carboxamide,

1-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-3,3-difluorocyclobutane-1-carboxamide,

1-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]cyclobutane-1-carboxamide,

1-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-

yl]cyclopentane-1-carboxamide,

4-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]tetrahydro-2H-pyran-4-carboxamide,

2-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-2-ethylbutanamide,

2-[5-(4-fluorophenyl)-1,2,4-oxadiazol-3-yl]-2-methylpropanamide,

2-[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]-2-methylpropanamide,

2-[5-(4-bromophenyl)-1,2,4-oxadiazol-3-yl]-2-methylpropanamide,

2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-2-methylpropanamide,

2-[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]-2-methylpropanamide,

2-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]propane-2-sulfonamide,

2-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]propane-2-sulfonamide,

2-[3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl]propane-2-sulfonamide,

2-[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]propane-2-sulfonamide,

2-[5-(4-bromophenyl)-1,2,4-oxadiazol-3-yl]propane-2-sulfonamide,

2-[5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl]propane-2-sulfonamide,

2-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]propane-2-sulfonamide,

2-[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]propane-2-sulfonamide,

5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

5-[3-(2,4-difluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

5-[3-(3,4-difluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1,5-dimethylpyrrolidin-2-one,

5-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

5-[3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

(S)-5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one, and

(R)-5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one.

11. The compound of claim 1 or a pharmaceutically acceptable salt thereof, which is selected from the

following compounds:

2-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-2-methylpropanamide,

2-[3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl]-2-methylpropanamide,

2-[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]-2-methylpropanamide,

2-[5-(4-chlorophenyl)-1,2,4-oxadiazol-3-yl]propane-2-sulfonamide,

5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

5-[3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one,

(S)-5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one, and

(R)-5-[3-(4-fluorophenyl)-1,2,4-oxadiazol-5-yl]-1-methylpyrrolidin-2-one.

12. A pharmaceutical composition comprising the compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof.

13. A medicament for treating and/or preventing diseases associated with hypofunction of GABAergic system, comprising the compound of any one of claims 1 to 11 or a

pharmaceutically acceptable salt thereof as an active ingredient.

14. The medicament of claim 13, wherein the diseases associated with hypofunction of GABAergic system are neurological disease or psychiatric disease.

15. The medicament of claim 14, wherein the neurological disease or psychiatric disease is epilepsy, neuropathic pain, neurodevelopmental disorders, bipolar disorder and its related disorders, schizophrenia spectrum disorder, Alzheimer's disease and the other neurocognitive disorders, amyotrophic lateral sclerosis, Parkinson's disease, depressive syndrome, anxiety disorders, obsessive-compulsive disorder, trauma- and stressor-related disorders, sleep-wake disorders, and/or REM sleep behavior disorder associated with Parkinson's disease/dementia with Lewy bodies.

~~16. A method for treating and/or preventing diseases associated with hypofunction of GABAergic system, comprising administering a therapeutically effective amount of the compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof to a patient in need thereof.~~

~~17~~16. Use of the compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating and/or preventing diseases associated with hypofunction of GABAergic system.

~~18~~17. The compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof for use in treating and/or preventing diseases associated with hypofunction of GABAergic system.

~~19~~18. A pharmaceutical combination comprising the compound of any one of claims 1 to 11 or a pharmaceutically acceptable salt thereof, and at least one drug selected from drugs classified into antiepileptic drug, antidepressant drug, or antipsychotic drug.

~~20~~19. A medicament for treating diseases associated with hypofunction of GABAergic system, comprising the compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, which is used in combination with at least one drug selected from drugs classified into antiepileptic drug, antidepressant drug, or antipsychotic drug.