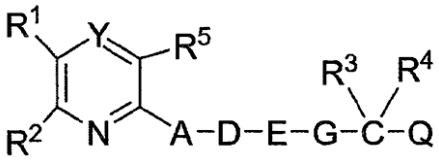
Claims

[Claim 1]

A therapeutic agent for gait disturbance in a patient with ischemic disease, comprising a heterocyclic derivative represented by formula (1) below or a pharmaceutically acceptable salt thereof as an active component:

[Chem. 1]



(1)

wherein R^1 and R^2 are the same or different and each represents aryl optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro;

R^3 and R^4 are the same or different and each represents a hydrogen atom or alkyl;

R^5 represents a hydrogen atom, alkyl, or a halogen atom;

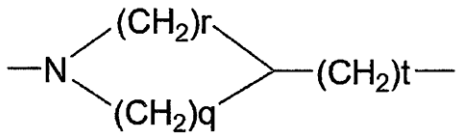
Y represents N or N -> O;

A represents NR^6 and R^6 represents a hydrogen atom, alkyl, alkenyl, or cycloalkyl; and

D represents alkylene or alkenylene optionally substituted with hydroxy, or A and D are combined with each

other to form a divalent group represented by formula (2) below:

[Chem. 2]

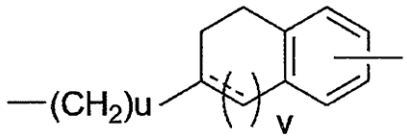


(2)

wherein r represents an integer of 0 to 2, q represents 2 or 3, and t represents an integer of 0 to 4; and

E represents phenylene or a single bond, or D and E are combined with each other to form a divalent group represented by formula (3) below:

[Chem. 3]



(3)

wherein

 represents a single bond or a double bond,

wherein u represents an integer of 0 to 2; v represents 0 or 1;

G represents O, S, SO, or SO_2; and

Q represents carboxy, alkoxycarbonyl, tetrazolyl, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl, or a group represented by formula (4) below:

[Chem. 4]

$$—CONH—SO_2—R^7$$

(4)

wherein R^7 represents amino, monoalkylamino, dialkylamino, or hydroxy; or any of groups 1) to 4) below:

1) alkyl,

2) aryl,

3) aryloxy, and

4) a heterocyclic group,

optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro.

[Claim 2]

The therapeutic agent for gait disturbance according to claim 1, wherein

in the heterocyclic derivative represented by formula(1), R^1 and R^2 are the same or different and each represents phenyl optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, and alkoxy;

R^3 and R^4 are the same or different and each represents a hydrogen atom or alkyl;

R^5 is a hydrogen atom;

Y is N;

A is NR^6, R^6 is alkyl;

D is alkylene;

E is a single bond;

G is O; and

Q is carboxy or a group represented by formula (4), and R^7 is amino, monoalkylamino, dialkylamino, or hydroxy; or any of groups 1) to 4) below:

1) alkyl,

2) aryl,

3) aryloxy, and

4) a heterocyclic group,

optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro.

[Claim 3]

The therapeutic agent for gait disturbance according to claim 1, wherein the patient with ischemic disease is a patient with arteriosclerosis obliterans.

[Claim 4]

The therapeutic agent for gait disturbance according to claim 3, wherein the patient with arteriosclerosis obliterans is a patient classified into at least one selected from Fontaine Classifications I to IV.

[Claim 5]

A therapeutic agent for gait disturbance in a patient with ischemic disease, comprising 2-{4-[N-(5,6-diphenylpyrazine-2-yl)-N-isopropylamino]butyloxy}acetic acid or 2-{4-[N-(5,6-diphenylpyrazine-2-yl)-N-isopropylamino]butyloxy}-N-(methylsulfonyl)acetamide, or a pharmaceutically acceptable salt thereof as an active component.

[Claim 6]

The therapeutic agent for gait disturbance according to claim 5, wherein the patient with ischemic disease is a patient with arteriosclerosis obliterans.

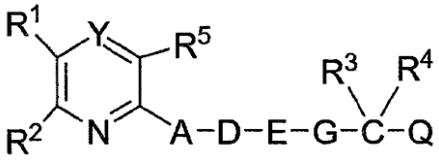
[Claim 7]

The therapeutic agent for gait disturbance according to claim 6, wherein the patient with arteriosclerosis obliterans is a patient classified into at least one selected from Fontaine Classifications I to IV.

[Claim 8]

Use of a heterocyclic derivative represented by formula (1) below or a pharmaceutically acceptable salt thereof

[Chem. 1]



(1)

wherein R^1 and R^2 are the same or different and each represents aryl optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro;

R^3 and R^4 are the same or different and each represents a hydrogen atom or alkyl;

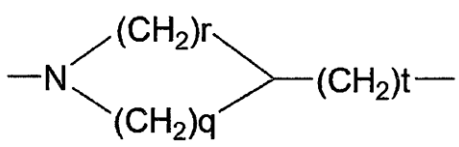
R^5 represents a hydrogen atom, alkyl, or a halogen atom;

Y represents N or N -> O;

A represents NR^6 and R^6 represents a hydrogen atom, alkyl, alkenyl, or cycloalkyl; and

D represents alkylene or alkenylene optionally substituted with hydroxy, or A and D are combined with each other to form a divalent group represented by formula (2) below:

[Chem. 2]

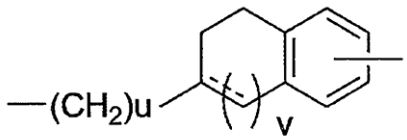


(2)

wherein r represents an integer of 0 to 2, q represents 2 or 3, and t represents an integer of 0 to 4; and

E represents phenylene or a single bond, or D and E are combined with each other to form a divalent group represented by formula (3) below:

[Chem. 3]



(3)

wherein

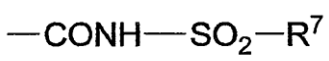
 represents a single bond or a double bond,

wherein u represents an integer of 0 to 2; v represents 0 or 1;

G represents O, S, SO, or SO_2; and

Q represents carboxy, alkoxycarbonyl, tetrazolyl, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl, or a group represented by formula (4) below:

[Chem. 4]



(4)

wherein R^7 represents amino, monoalkylamino, dialkylamino, or hydroxy; or any of groups 1) to 4) below:

1) alkyl,

2) aryl,

3) aryloxy, and

4) a heterocyclic group,

optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro; in the manufacture of a medicament for treating gait disturbance in a patient with ischemic disease.

[Claim 9]

The use according to claim 8, wherein

in the heterocyclic derivative represented by formula (1), R^1 and R^2 are the same or different and each represents phenyl optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, and alkoxy;

R^3 and R^4 are the same or different and each represents a hydrogen atom or alkyl;

R^5 is a hydrogen atom;

Y is N;

A is NR^6, R^6 is alkyl;

D is alkylene;

E is a single bond;

G is O; and

Q is carboxy or a group represented by formula (4), and R^7 is amino, monoalkylamino, dialkylamino, or hydroxy; or any of groups 1) to 4) below:

1) alkyl,

2) aryl,

3) aryloxy, and

4) a heterocyclic group,

optionally substituted with 1 to 3 substituents selected from the group consisting of a halogen atom, alkyl, haloalkyl, arylalkyl, alkoxy, alkylthio, alkoxyalkyl, alkylsulfonyl, hydroxy, amino, monoalkylamino, dialkylamino, carboxy, cyano, and nitro.

[Claim 10]

The use according to claim 8, wherein the patient with ischemic disease is a patient with arteriosclerosis obliterans.

[Claim 11]

The use according to claim 10, wherein the patient with arteriosclerosis obliterans is a patient classified into at least one selected from Fontaine Classifications I to IV.

[Claim 12]

Use of 2-{4-[N-(5,6-diphenylpyrazine-2-yl)-N-isopropylamino]butyloxy}acetic acid or 2-{4-[N-(5,6-diphenylpyrazine-2-yl)-N-isopropylamino]butyloxy}-N-(methylsulfonyl)acetamide, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating gait disturbance in a patient with ischemic disease.

[Claim 13]

The use according to claim 12, wherein the patient with ischemic disease is a patient with arteriosclerosis obliterans.

[Claim 14]

The use according to claim 13, wherein the patient with arteriosclerosis obliterans is a patient classified into at least one selected from Fontaine Classifications I to IV.