

Non Patent Literature 16: Azhary et al. American Family Physician, 2010, Vol. 81, p. 887-892

Non Patent Literature 17: McMahon et al. Current Opinion in Neurobiology, 1995, Vol. 5, p. 616-624

Non Patent Literature 18: Argyriou et al. Critical Reviews in Oncology/Hematology, 2012, Vol. 82, p. 51-77

Non Patent Literature 19: Apfel et al. JAMA, 2000, Vol. 284, p. 2215-2221

SUMMARY

TECHNICAL PROBLEM

[0020]

An object of the present disclosure is to provide a therapeutic or prophylactic agent for peripheral neuropathies.

SOLUTION TO PROBLEM

[0021]

As a result of intensive studies to achieve the above object, the present inventors have discovered that a specific cyclic amine derivative or a pharmacologically acceptable salt thereof has a significant effect of suppressing peripheral neuropathies.

[0022]

Specifically, the present disclosure provides a therapeutic agent or a prophylactic agent for peripheral neuropathies, comprising as an active ingredient, a cyclic amine derivative represented by the following general formula (I) or a pharmacologically acceptable salt thereof.

[Chemical Formula 1]

optionally substituted with a fluorine atom, and further preferably a methyl group, an ethyl group, a difluoromethyl group or a 2,2,2-trifluoroethyl group.

[0025]

In the above cyclic amine derivative, it is preferable that A is the group represented by general formula (IIa) and that the stereochemical configuration of the asymmetric carbon marked with * is preferably S, in which R¹ is more preferably a methyl group or an ethyl group optionally substituted with a fluorine atom, and further preferably a methyl group, an ethyl group, a difluoromethyl group or a 2,2,2-trifluoroethyl group.

[0026]

The present disclosure also provides a pharmaceutical composition for treating or preventing peripheral neuropathies, containing a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof, and a pharmacologically acceptable excipient, and the like.

[0027]

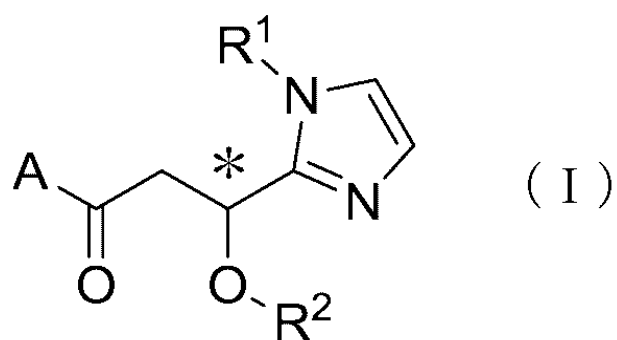
The present disclosure also provides a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof for use in treatment or prevention of peripheral neuropathies.

[0028]

The present disclosure also provides use of a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof in treatment or prevention of peripheral neuropathies.

[0029]

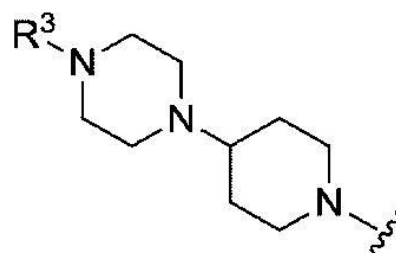
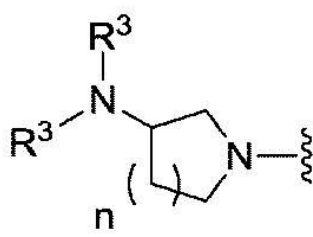
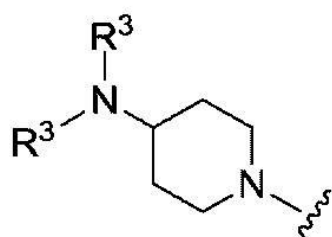
The present disclosure also provides use of a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof in producing a medicine for treatment or prevention of peripheral neuropathies. In one aspect, the present disclosure provides use of a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof in the manufacture of a medicament for treating or preventing peripheral neuropathies,



wherein,

carbon marked with * is asymmetric carbon; and

A represents a group represented by general formulae (IIa), (IIb) or (IIc):



wherein R¹ represents a methyl group or an ethyl group optionally substituted with one or more halogen atoms,

R² represents a hydrogen atom or an alkylcarbonyl group having 2 to 5 carbon atoms,

each R³ independently represents a methyl group or an ethyl group, and

n represents 1 or 2.

[0030]

The present disclosure also provides a method for treating or preventing peripheral neuropathies, which includes administering a therapeutically effective amount of a cyclic

amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof to a patient who needs treatment.

[0031]

In each example of the present disclosure, the above peripheral neuropathies are preferably drug-induced peripheral neuropathies, autoimmune peripheral neuropathies, metabolic peripheral neuropathies, hereditary peripheral neuropathies, vasculitic peripheral neuropathies, toxic peripheral neuropathies, infectious peripheral neuropathies, or peripheral neuropathies associated with malignant tumor, more preferably drug-induced peripheral neuropathies, autoimmune peripheral neuropathies, metabolic peripheral neuropathies, or hereditary peripheral neuropathies, and further preferably drug-induced peripheral neuropathies, autoimmune peripheral neuropathies, or metabolic peripheral neuropathies. The above drug-induced peripheral neuropathies are preferably anticancer agent-induced peripheral neuropathies. The above autoimmune peripheral neuropathies are preferably at least one type selected from Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), and paraproteinemic neuropathy (PPN). The above metabolic peripheral neuropathies are preferably diabetic peripheral neuropathy. The above hereditary peripheral neuropathy is preferably Charcot-Marie-Tooth disease.

ADVANTAGEOUS EFFECTS OF DISCLOSURE

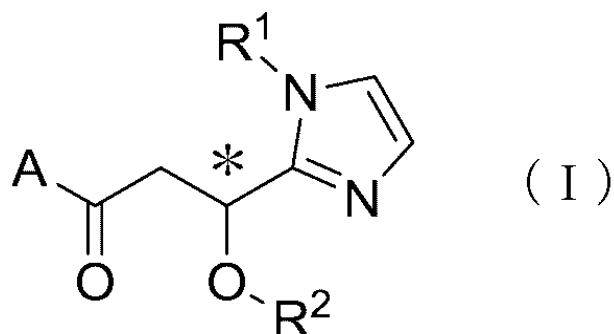
[0032]

With the cyclic amine derivative or the pharmacologically acceptable salt thereof of the present disclosure, peripheral neuropathies can be treated or prevented. The above peripheral neuropathies are for example, drug-induced peripheral neuropathies, autoimmune peripheral neuropathies, or metabolic peripheral neuropathies. The above drug-induced peripheral neuropathies are particularly anticancer agent-induced peripheral neuropathies. The above autoimmune peripheral neuropathies are particularly at least one type selected from Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN), and paraproteinemic neuropathy (PPN). The

CLAIMS

[Claim 1]

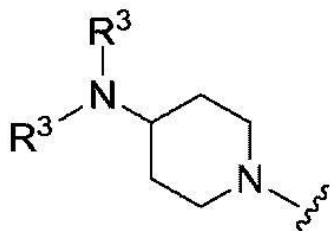
Use of a cyclic amine derivative represented by general formula (I) or a pharmacologically acceptable salt thereof in the manufacture of a medicament for treating or preventing peripheral neuropathies,



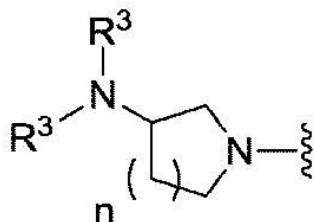
wherein,

carbon marked with * is asymmetric carbon; and

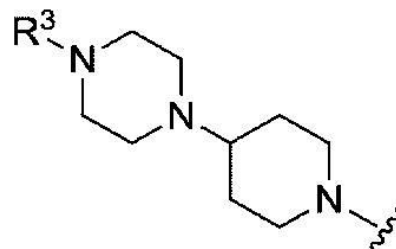
A represents a group represented by general formulae (IIa), (IIb) or (IIc):



(I I a)



(I I b)



(I I c)

wherein R¹ represents a methyl group or an ethyl group optionally substituted with one or more halogen atoms,

R² represents a hydrogen atom or an alkylcarbonyl group having 2 to 5 carbon atoms,

each R³ independently represents a methyl group or an ethyl group, and

n represents 1 or 2.

[Claim 2]

The use according to claim 1, wherein A is the group represented by general formula (IIa).

[Claim 3]

The use according to claim 1, wherein A is the group represented by general formulae (IIb) or (IIc).

[Claim 4]

The use according to claim 1, wherein A is the group represented by general formula (IIa) and the stereochemical configuration of the asymmetric carbon marked with * is S.

[Claim 5]

The use according to any one of claims 1 to 4, wherein R¹ represents a methyl group or an ethyl group optionally substituted with one or more fluorine atoms.

[Claim 6]

The use according to any one of claims 1 to 4, wherein R¹ is a methyl group, an ethyl group, a difluoromethyl group or a 2,2,2-trifluoroethyl group.

[Claim 7]

The use according to any one of claims 1 to 6, wherein the peripheral neuropathies are drug-induced peripheral neuropathies.

[Claim 8]

The use according to claim 7, wherein the drug-induced peripheral neuropathies are at least one type selected from anticancer agent-induced peripheral neuropathy, antiviral agent-induced peripheral neuropathy, antimicrobial agent-induced peripheral neuropathy, antitubercular agent-induced peripheral neuropathy, antiarrhythmic agent-induced peripheral neuropathy, lipid-lowering drug-induced peripheral neuropathy, immunosuppressive drug-induced peripheral neuropathy, gout therapeutic agent-induced peripheral neuropathy and peripheral neuropathies induced by other drugs.

[Claim 9]

The use according to any one of claims 1 to 6, wherein the peripheral neuropathies are autoimmune peripheral neuropathies.

[Claim 10]

The use according to claim 9, wherein the autoimmune peripheral neuropathies are at least one type selected from Guillain-Barré syndrome, chronic inflammatory demyelinating polyradiculoneuropathy, multifocal motor neuropathy and paraproteinemic neuropathy.

[Claim 11]

The use according to any one of claims 1 to 6, wherein the peripheral neuropathies are metabolic peripheral neuropathies.

[Claim 12]

The use according to claim 11, wherein the metabolic peripheral neuropathies are at least one type selected from diabetic peripheral neuropathy, uremic peripheral neuropathy, collagen-peripheral neuropathy and vitamin deficiency peripheral neuropathy.

[Claim 13]

The use according to any one of claims 1 to 6, wherein the peripheral neuropathies are hereditary peripheral neuropathies.

[Claim 14]

The use according to claim 13, wherein the hereditary peripheral neuropathies are at least one type selected from Charcot-Marie-Tooth disease, familial amyloid polyneuropathy, hereditary neuropathy to pressure palsies (HNPP) and hereditary neuralgic amyotrophy.