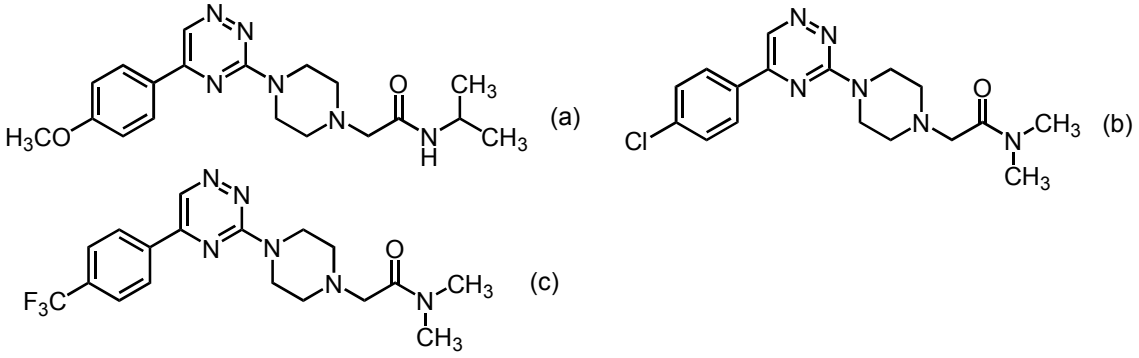
and (c):

[Chemical formula 1]



are listed in a commercial compound database (Registry) as Accession Nos: 1070398-58-1, 1069628-74-5, 1060824-77-2. However, it is not clarified what kind of physiological activity these compounds have.

PRIOR ART DOCUMENT(S)

PATENT DOCUMENT(S)

[0006]

[Patent document 1] WO2010/130796

[Patent document 2] WO2012/012478

NON-PATENT DOCUMENT(S)

[0007]

[Non-patent document 1] New England Journal of Medicine, 1999; 341: p.709-717

[Non-patent document 2] New England Journal of Medicine, 2003; 348: p.1309-1321

[Non-patent document 3] Current Topics in Medicinal Chemistry, 2013; 313: p.1385-1401

[Non-patent document 4] Current Hypertension Reports, 2013; 15: p.484-488

DISCLOSURE OF INVENTION

PROBLEM TO BE SOLVED BY THE INVENTION

[0008]

The present invention relates to a novel disubstituted 1,2,4-triazine compound or a pharmaceutically acceptable salt thereof which has an

The pcDNA3.1-human CYP11B2 plasmid was transfected into a Chinese hamster lung fibroblast V79 cell line to produce a cell line stably expressing human CYP11B2 gene.

The cells were cultured and grown in the Dulbecco's modified Eagle's/Ham's medium supplemented with 10% fetal bovine serum and 1% G418 disulfate solution under the environment of 37 °C, 95 % air, and 5 % CO_2, and the grown cells were harvested.

Then, the cells were fractionated to obtain mitochondria by reference to a method described in Chabre et al. JCE & M 85 (11) 4060-68, 2000. In particular, the cells suspended in a 5 mmol/L Tris-HCl buffer (pH 7.4) containing 250 mmol/L sucrose were homogenized in a Teflon (Registered Trademark) Potter Elvehjem homogenizer, and then the suspension was centrifuged (800×g, 15 min.). The supernatant was separated and again centrifuged (10000×g, 15min.) to obtain a pellet (mitochondrial fraction).

The mitochondrial fraction diluted with a buffer containing 10 mmol/L KH_2PO_4, 10 mmol/L Tris, 20 mmol/L KCl, 25 mmol/L sucrose, 5 mmol/L $MgCl_2$, and 0.05 % bovine serum albumin was dispensed to a 96-well plate. 0.5 μmol/L Deoxycorticosterone, 150 μmol/L NADPH and a compound of each concentration were added to each well, and incubated for 1.5-2 hours at room temperature to produce aldosterone. An amount of the produced aldosterone in the incubated solution was determined by using HTRF (Homogeneous Time Resolved Fluorescence) method.

IC 50 (nmol/L) was calculated by analyzing the aldosterone production inhibition rate (%) of each concentration of compounds by non-linear regression to a logistic curve.

[0297]

<Experimental Results>

[Table 44]

Example No.	hCYP11B2 IC_{50} (nmol/L)
12	6.9
16	16
18	7.9
19	17
22	17
26	8.5
27	13
28	8.4
29	18
38	14

dihydrobenzofuranyl group, a quinolyl group, an isoquinolyl group, an imidazopyridyl group, a tetrahydroimidazopyridyl group, a benzopyranyl group, or a dihydrobenzopyranyl group, or

when X^c is NR^{4c}, and $R^{B7}$and R^{4c} are bound to each other at their terminus to form an aliphatic heterocyclic group which may be substituted with an alkyl group which may be substituted with a hydroxyl group, together with a nitrogen atom to which they are bound, an aliphatic heterocyclic group is a group selected from azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, or homomorpholinyl,

or a pharmaceutically acceptable salt thereof.

4. The compound according to any of claims 1-3, wherein R^B is a group represented by the above formula (B-4),

or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 4,

wherein

R^A is

(1) a cycloalkyl group which may be substituted with an alkyl group,

(2) a cycloalkenyl group which may be substituted with an alkyl group,

(3) a phenyl group which may be substituted with 1-3 groups selected independently from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, an alkoxyalkyl group, an alkoxy group, and an alkylenedioxy group which may be substituted with 1-2 halogen atoms,

(4) a naphthyl group which may be partially hydrogenated and may be substituted with an alkyl group,

(5) a heteroaryl group which may be partially hydrogenated and may be substituted with 1-2 groups selected independently from the group consisting of a cyano group, and an alkyl group,

the heteroaryl moiety is pyridyl, indazolyl, thienyl, isoquinolyl, benzopyranyl, benzofuranyl, indolyl, or benzothiazolyl,

R^B is a group represented by the above formula (B-4),

R^{B7} is (i) an alkyl group which may be substituted, (ii) a cycloalkyl group which may be substituted, (iii) an aliphatic heterocyclic group which may be substituted, or (iv) a heteroaryl group which may be partially hydrogenated and may be substituted, or,

when X^c is NR^{4c}, R^{B7} and R^{4c} are bound to each other at their terminus to form an aliphatic heterocyclic group which may be substituted with an alkyl group (wherein the alkyl group may be substituted with a hydroxyl group), together with a nitrogen atom to which they are bound,

wherein

(i) a substituent of the alkyl group which may be substituted is 1-4 groups selected independently from the group consisting of a halogen atom; a hydroxyl group; a cycloalkyl group which may be substituted with 1-2 groups selected independently from the group consisting of a hydroxyl group and an alkylsulfonyl group; a phenyl group; a pyridyl group; an amino group which may be substituted with 1-2 groups selected independently from the group consisting of an alkyl group, an alkanoyl group, and an alkoxycarbonyl group; an alkylsulfonyl group; an alkoxy group; and an aliphatic heterocyclic group which may be substituted with 1-3 groups selected independently from the group consisting of a hydroxyl group, an oxo group, an alkyl group, an alkanoyl group, and an alkylsulfonyl group,

wherein the aliphatic heterocyclic group is selected from tetrahydrothiophenyl, piperidinyl, thiomorpholinyl, piperazinyl, or morpholinyl,

(ii) a substituent of the cycloalkyl group which may be substituted is 1-2 groups selected independently from the group consisting of a hydroxyl group; an aliphatic heterocyclic group which may be substituted with 1-3 groups selected independently from the group consisting of a hydroxyl group and an oxo group; an amino group which may be substituted with 1-2 groups selected independently from the group consisting of an alkyl group which may be substituted with an alkylsulfonyl group, and an alkanoyl group; an alkyl group which may be substituted with a hydroxyl group; a carbamoyl group which may be substituted with 1-2 alkyl groups; an alkoxy group which may be substituted with a carbamoyl group which may be substituted with 1-2 alkyl groups; a cycloalkyl group which may be substituted with a hydroxyl group; and an alkylsulfonyl group, or

two substituents on the same carbon atom in the above cycloalkyl group which may be substituted are bound to each other at the terminus thereof to form an alkylene group which may be substituted with 1-3 groups selected independently from the group consisting of an alkyl group and an oxo group (wherein the alkylene group may contain, in the alkylene chain, 1-2 heteroatoms selected independently from a nitrogen atom, an oxygen atom, and a sulfur atom),

wherein the aliphatic heterocyclic group is pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, or thiomorpholinyl, and

a cycloalkyl moiety of (ii) the cycloalkyl group which may be substituted is cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[2.2.2]octyl, or adamantyl,

(iii) a substituent of the aliphatic heterocyclic group which may be substituted is 1-3 groups selected independently from the group consisting of a halogen atom; a hydroxyl group; an oxo group; an alkyl group which may be substituted with 1-3 groups selected independently from the group consisting of an alkoxy group, an alkylsulfonyl group, an amino group which may be substituted with1-2 groups selected independently from the group consisting of an alkoxycarbonyl group and an alkylsulfonyl group, a carbamoyl group which may be substituted with 1-2 alkyl groups, a cycloalkyl group which may be substituted with a hydroxyl group, a morpholinylcarbonyl group, and a heteroaryl group which may be substituted with an alkyl group and may be partially hydrogenated (wherein the heteroaryl which may be partially hydrogenated is imidazolyl, imidazolinyl, oxazolyl, triazolyl, or pyridyl); an alkanoyl group which may be substituted with 1-3 groups selected independently from the group consisting of an a halogen atom and a hydroxyl group; a cycloalkylcarbonyl group which may be substituted with a hydroxyl group; an oxetanylcarbonyl group which may be substituted with an alkyl group; an alkoxy group; a carbamoyl group which may be substituted with 1-2 alkyl groups; an aliphatic heterocyclic group which may be substituted with an oxo group (wherein the aliphatic heterocyclic group is piperidinyl or tetrahydropyranyl); and a pyrimidinyl group,

wherein an aliphatic heterocyclic moiety of (iii) the aliphatic heterocyclic group which may be substituted is azetidinyl, pyrrolidinyl, piperidinyl, tetrahydrothiophenyl, tetrahydrothiopyranyl, tetrahydrofuranyl, tetrahydropyranyl,

1-azabicyclo[2.2.2]octyl, 8-azabicyclo[3.2.1]octyl, homomorpholinyl, 3-oxabicyclo[3.3.1]nonyl, or 3-oxo-9-azabicyclo[3.3.1]nonyl,

(iv) a substituent of the heteroaryl group which may be partially hydrogenated and may be substituted is 1-2 groups selected independently from the group consisting of a tetrahydropyranyl group; and an alkyl group which may be substituted with 1-2 groups selected independently from the group consisting of a carbamoyl group which may be substituted with 1-2 alkyl groups, an alkylsulfonyl group, and pyridazinyl group,

wherein heteroaryl of (iv) the heteroaryl group which may be partially hydrogenated and may be substituted is pyrazolyl, pyridyl, or imidazopyridinyl,

an aliphatic heterocyclic moiety of the aliphatic heterocyclic group which may be substituted with an alkyl group which may be substituted with a hydroxyl group is piperazinyl or pyrrolidinyl (wherein the aliphatic heterocyclic group is formed from $R^{B7}$and R^{4c} being bound to each other at their terminus, together with a nitrogen atom to which they are bound, when X^c is NR^{4c}),

or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 5,

wherein

R^A is

(1) a 3- to 7-membered monocyclic cycloalkyl group which may be substituted with an alkyl group,

(2) a 3- to 7-membered monocyclic cycloalkenyl group which may be substituted with an alkyl group,

(3) a phenyl group which may be substituted with 1-3 groups selected independently from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, an

alkoxyalkyl group, an alkoxy group, and a methylenedioxy group which may be substituted with1-2 halogen atoms,

(4) a naphthyl group which may be substituted with an alkyl group,

(5) a tetrahydronaphthyl group,

(6) a heteroaryl group which may be substituted with a cyano group or an alkyl group (wherein the heteroaryl group is pyridyl group, a thienyl group, a indazolyl group, a indolyl group, a benzothiazolyl group, or a isoquinolyl group), or

(7) a dihydrobenzopyranyl group,

R^{B7} is

(i) an alkyl group which may be substituted, wherein a substituent of the alkyl group is an aliphatic heterocyclic group which may be substituted with 1-2 groups selected independently from the group consisting of an oxo group, an alkylsulfonyl group, a hydroxyl group, an alkyl group, and an alkanoyl group (wherein the aliphatic heterocyclic ring is morpholinyl, thiomorpholinyl, or piperidinyl),

(ii) a cycloalkyl group which may be substituted (wherein the cycloalkyl group is a cyclopentyl group, a cyclohexyl group, a bicyclo[2.2.2]octyl group, or an adamantyl group), wherein a substituent of the cycloalkyl group is 1-2 groups selected independently from the group consisting of a hydroxyl group; an aliphatic heterocyclic group which may be substituted with 1-2 groups selected independently from the group consisting of a hydroxyl group and an oxo group (wherein the aliphatic heterocyclic group is selected from a thiomorpholinyl group, a piperidinyl group, a piperazinyl group, or a morpholinyl group); an amino group which may be substituted with 1-2 groups selected independently from the group consisting of an alkyl group and an alkanoyl group; an alkyl group which may

be substituted with a hydroxyl group; an alkoxy group which may be substituted with a carbamoyl group which may be substituted with 1-2 alkyl groups; and an alkylsulfonyl group,

(iii) an aliphatic heterocyclic group which may be substituted (wherein the aliphatic heterocyclic group is selected from an azetidinyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a tetrahydropyranyl group, a piperidinyl group, a tetrahydrothiopyranyl group, or 3-oxabicyclo[3.3.1]nonyl), wherein a substituent of the aliphatic heterocyclic group is 1-3 groups selected independently from the group consisting of a halogen atom; a hydroxyl group; an oxo group; an alkyl group which may be substituted with 1-3 groups selected independently from the group consisting of a hydroxyl group, a cycloalkyl group which may be substituted with a hydroxyl group, an alkoxy group, an alkylsulfonyl group, an alkylsulfonylamino group, a carbamoyl group which may be substituted with 1-2 alkyl groups, morpholinylcarbonyl group, and a heteroaryl group which may be substituted with an alkyl group and may be partially hydrogenated (wherein the heteroaryl which may be partially hydrogenated is pyridyl, imidazolyl, imidazolinyl, oxazolyl, or triazolyl); an alkanoyl group which may be substituted with a hydroxyl group; a pyrimidinyl group; and a cycloalkylcarbonyl group which may be substituted with a hydroxyl group, or

(iv) a pyrazolyl group which may be substituted with an alkyl group which may be substituted with a carbamoyl group which may be substituted with 1-2 alkyl groups,

or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 5,

wherein

R^A is

(1) a phenyl group which may be substituted with 1-3 groups selected independently from the group consisting of a halogen atom, an alkyl group, and a haloalkyl group,

(2) a pyridyl group which may be substituted with a cyano group, or

(3) a dihydrobenzopyranyl group,

R^B is a group of the above formula (B-4):

wherein X^a represents N,

X^b represents CH_2, and X^c represents NH, or

X^b represents NH, and X^c represents CH_2,

R^{B6} represents a hydrogen atom,

R^{B7} is

(i) an alkyl group which may be substituted, wherein a substituent of the alkyl group is an aliphatic heterocyclic group which may be substituted with 1-2 groups selected independently from the group consisting of an oxo group, a hydroxyl group, an alkyl group and an alkanoyl group (wherein the aliphatic heterocyclic ring is morpholinyl, thiomorpholinyl, or piperidinyl),

(ii) a cyclohexyl group which may be substituted, wherein a substituent of the cyclohexyl group is 1-2 groups selected independently from the group consisting of a piperidinyl group which may be substituted with a hydroxyl group; an amino group which may be substituted with 1-2 groups selected independently from the group consisting of an alkyl group and an alkanoyl group; and an alkoxy group which may be substituted with a carbamoyl group which may be substituted with1-2 alkyl groups,

(iii) an aliphatic heterocyclic group which may be substituted (wherein the aliphatic heterocyclic group is selected from an azetidinyl group, a tetrahydrofuranyl group, a pyrrolidinyl group, a tetrahydropyranyl group, a

piperidinyl group, a tetrahydrothiopyranyl group, or 3-oxabicyclo[3.3.1]nonyl), wherein a substituent of the aliphatic heterocyclic group is 1-3 groups selected independently from the group consisting of a hydroxyl group; an alkyl group which may be substituted with 1-3 groups selected independently from the group consisting of an amino group which may be substituted with an alkylsulfonyl group, a carbamoyl group which may be substituted with 1-2 alkyl groups, an imidazolinyl group which may be substituted with an alkyl group; an alkanoyl group which may be substituted with a hydroxyl group; and a cycloalkylcarbonyl group which may be substituted with a hydroxyl group, or

(iv) a pyrazolyl group which may be substituted with an alkyl group which may be substituted with a carbamoyl group which may be substituted with 1-2 alkyl groups,

or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 5,

wherein

R^A is a phenyl group which may be substituted with an alkyl group or a haloalkyl group,

R^B is a group of the above formula (B-4):

wherein

X^a is CR^{3a},

X^b is CHR^{3b},

R^{3a} is a hydrogen atom,

R^{3b} is a hydrogen atom or a hydroxyl group,

X^c is NR^{4c},

R^{4c} is a hydrogen atom or an alkyl group,

R^{B6} is a hydrogen atom, and

R^{B7} is a cycloalkyl group which may be substituted with an alkyl group or an amino group which may be substituted with 1-2 alkyl groups,
or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 5,
wherein
R^{A} is a phenyl group which may be substituted with a halogen atom,
R^{B} is a group of the above formula (B-4):
wherein
X^{a} is CR^{3a},
X^{b} is NR^{4b},
X^{c} is NR^{4c},
R^{3a} is a hydrogen atom,
R^{4b} is a hydrogen atom or an alkyl group,
R^{4c} is a hydrogen atom or an alkyl group,
R^{B6} is a hydrogen atom, and
R^{B7} is an alkyl group,
or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 5,
wherein
R^{B} is a group of the above formula (B-4):
wherein
X^{a} is N,
X^{b} is CHR^{3b}, and X^{c} is NR^{4c}, or
X^{b} is NR^{4b}, and X^{c} is CHR^{3c},
R^{3b} and R^{3c} is a hydrogen atom,
R^{4b} and R^{4c} is a hydrogen atom, and
R^{B6} is a hydrogen atom,
or a pharmaceutically acceptable salt thereof.

11. The compound according to any of claim 4 or 5, wherein

X^a is N, X^b is CHR^{3b} or C(=O), X^c is NR^{4c},

R^{3b} is a hydrogen atom or an alkyl group, and

R^{4c} is a hydrogen atom, an alkyl group, or a cycloalkyl group,

or a pharmaceutically acceptable salt thereof.

12. The compound according to any of claim 4 or 5, wherein

X^a is N, X^b is CH_2, X^c is NH, and

R^{B6} is a hydrogen atom,

or a pharmaceutically acceptable salt thereof.

13. The compound according to any of claim 4, 5, 11 or 12, wherein

R^A is a phenyl group which may be substituted with 1-3 groups selected independently from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, an alkoxyalkyl group, an alkoxy group, and an alkylenedioxy group which may be substituted with 1-2 halogen atoms,

or a pharmaceutically acceptable salt thereof.

14. The compound according to any of claim 4, 5, 11, 12 or 13,

wherein

R^{B7} is a cycloalkyl group which may be substituted,

wherein a substituent of the cycloalkyl group which may be substituted is 1-2 groups selected independently from the group consisting of a hydroxyl group; an aliphatic heterocyclic group which may be substituted with 1-3 groups selected independently from the group consisting of a hydroxyl group and an oxo group; an amino group which may

be substituted with 1-2 groups selected independently from the group consisting of an alkyl group which may be substituted with an alkylsulfonyl group, and an alkanoyl group; an alkyl group which may be substituted with a hydroxyl group; a carbamoyl group which may be substituted with 1-2 alkyl groups; an alkoxy group which may be substituted with a carbamoyl group which may be substituted with 1-2 alkyl groups; a cycloalkyl group which may be substituted with a hydroxyl group; and an alkylsulfonyl group, or

two substituents on the same carbon atom in the above cycloalkyl group which may be substituted are bound to each other at the terminus thereof to form an alkylene group which may be substituted with 1-3 groups selected independently from the group consisting of an alkyl group and an oxo group (wherein the alkylene group may contain, in the alkylene chain, 1-2 heteroatoms selected independently from a nitrogen atom, an oxygen atom, and a sulfur atom),

wherein the aliphatic heterocyclic group is pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, or thiomorpholinyl, and

a cycloalkyl moiety of the above cycloalkyl group which may be substituted is cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[2.2.2]octyl, or adamantyl,

or a pharmaceutically acceptable salt thereof.

15. The compound selected from the group consisting of:

3-[4-[(cis-3-hydroxytetrahydrofuran-4-yl)carbamoylmethyl]piperazin-1-yl]-5-(4-trifluoromethylphenyl)-1,2,4-triazine,

5-(4-fluorophenyl)-3-[4-[[trans-4-(N-methylcarbamoylmethyloxy) cyclohexyl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[(1-acetyl-4-hydroxypiperidin-4-yl)methyl]carbamoylmethyl]piperazin-1-yl]-5-(4-chlorophenyl)-1,2,4-triazine,
3-[4-[[(7-exo-9-endo)-9-hydroxy-3-oxabicyclo[3.3.1]nonan-7-yl]carbamoylmethyl]piperazin-1-yl]-5-(4-trifluoromethylphenyl)-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[[1-[2-(methylsulfonylamino)ethyl]piperidin-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(2-cyano-5-pyridyl)-3-[4-[[1-[(1-hydroxycyclopropyl)carbonyl]piperidin-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[trans-4-(4-hydroxypiperidino) cyclohexyl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[[1-((R)-2-hydroxybutanoyl)piperidin-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[(3S)-1-[(1-hydroxycyclopropyl)carbonyl]pyrrolidin-3-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[cis-3-(dimethylamino) cyclohexyl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
3-[4-[[1-[(4,5-dihydro-1H-imidazol-2-yl)methyl]piperidin-4-yl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
3-[4-[[trans-4-(acetoamino) cyclohexyl]carbamoylmethyl]piperazin-1-yl]-5-(p-tolyl)-1,2,4-triazine,

3-[4-[[1-(N,N-dimethylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[1-[(1-hydroxycyclopropyl)carbonyl]azetidin-3-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[trans-4-(N-methylcarbamoylmethyloxy)cyclohexyl]carbamoylmethyl]piperazin-1-yl]-5-(4-trifluoromethylphenyl)-1,2,4-triazine,
3-[4-[[cis-3-(acetoamino)cyclohexyl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
5-(4-chlorophenyl)-3-[(3S,4S)-4-[(cis-3-hydroxytetrahydropyran-4-yl)carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[1-(N,N-dimethylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-5-(p-tolyl)-1,2,4-triazine,
5-(4-chlorophenyl)-3-[4-[[1-(N,N-dimethylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-chlorophenyl)-3-[4-[(trans-3-hydroxytetrahydropyran-4-yl)carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[1-(N-methylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-5-(p-tolyl)-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[[1-(N-methylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-chlorophenyl)-3-[4-[[1-(N-methylcarbamoylmethyl)-1H-pyrazol-4-yl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(4-chlorophenyl)-3-[4-[(3-methylbutanoyl)amino]piperazin-1-yl]-1,2,4-triazine,

5-(4-fluorophenyl)-3-[4-[[((2R)-4-methylmorpholyn-2-yl)methyl]carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
3-[4-[[1-(N-methylcarbamoylmethyl) piperidin-4-yl]carbamoylmethyl]piperazin-1-yl]-5-(p-tolyl)-1,2,4-triazine,
3-[4-[[2-(1,1-dioxothiomorholino) ethyl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
3-[4-[[trans-4-(dimethylamino) cyclohexyl]carbamoylmethyl]piperazin-1-yl]-5-(4-fluorophenyl)-1,2,4-triazine,
5-(4-fluorophenyl)-3-[4-[(piperazin-1-yl)carbamoylmethyl]piperazin-1-yl]-1,2,4-triazine,
5-(dihydrobenzopyran-5-yl)-3-[4-(isopropylcarbamoylmethyl) piperazin-1-yl]-1,2,4-triazine,
3-[4-(4-fluorophenyl) piperazin-1-yl]-5-(o-tolyl)-1,2,4-triazine, and
5-(2-cyano-5-pyridyl)-3-[4-(isopropylcarbamoylmethyl) piperazin-1-yl]-1,2,4-triazine,
or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising the compound according to any of claims 1-15 or a pharmaceutically acceptable salt thereof as an active ingredient.

17. The pharmaceutical composition according to claim 16, which is used for preventing or treating various diseases and/or disease states evoked by an increased level of aldosterone and/or overproduction of aldosterone, or for improving prognosis of these diseases.

18. The pharmaceutical composition according to claim 16, which is a therapeutic or prophylactic agent for primary

aldosteronism, secondary aldosteronism, hypertension, heart failure, cardiomyopathy, cardiac hypertrophy, myocardial infarction, myocardial necrosis lesion, failure after myocardial ischemia, coronary artery disease, fibrosis or remodeling of myocardium or blood vessels, vascular restenosis, blood vessel wall thickening, arterial sclerosis, acute renal disorder, chronic kidney disease, renal fibrosis, nephropathy, hypokalemia, metabolic syndrome, obesity, sleep apnea syndrome, retinopathy, hepatic disease, idiopathic and/or cyclic edema, or sympathetic hyperactivity.

19. The pharmaceutical composition according to claim 16, which is a therapeutic or prophylactic agent for primary aldosteronism, secondary aldosteronism, hypertension, heart failure, arterial sclerosis, nephropathy, or retinopathy.

20. The pharmaceutical composition according to any of claim 18 or 19, wherein primary aldosteronism is unilateral or bilateral adrenal adenomas, unilateral or bilateral adrenal hyperplasia, aldosterone-producing adrenal carcinoma, unilateral adrenal multiple nodules aldosteronism, glucocorticoid reactive aldosteronism, familial aldosteronism, or ectopic aldosterone-producing tumors.

21. The pharmaceutical composition according to any of claim 18 or 19, wherein secondary aldosteronism is hypertension caused by an estrogen preparation, renal vascular hypertension, pregnancy hypertension, malignant hypertension, pheochromocytoma, congestive heart failure, pseudohypoaldosteronism, chronic liver disease associated with ascites, inappropriate use of a medicament such as a

laxative and a diuretic, or hyperaldosteronemia associated with nephrotic syndrome, Bartter's syndrome or Gitelman syndrome.

22. The pharmaceutical composition according to any of claim 18 or 19, wherein heart failure is congestive heart failure, left ventricular failure, right ventricular failure, systolic dysfunction, or diastolic dysfunction.

23. The pharmaceutical composition according to any of claim 18 or 19, wherein nephropathy is diabetic nephropathy.

24. The pharmaceutical composition according to claim 21, wherein chronic liver disease associated with ascites is hepatic cirrhosis.

25. The pharmaceutical composition according to any of claim 18 or 19, wherein retinopathy is diabetic retinopathy.

26. The pharmaceutical composition according to any of claim 18 or 19, wherein hypertension is essential hypertension, secondary hypertension, treatment-resistant hypertension, or mineralocorticoid-related hypertension.

27. The pharmaceutical composition according to claim 26, wherein secondary hypertension is renal vascular hypertension, renal parenchymal hypertension, primary aldosteronism, pheochromocytoma, sleep apnea syndrome, Cushing's syndrome, drug induced hypertension, aortostenosis, or hyperparathyroidism.

28. Use of the compound according to any of claims 1-15 or a pharmaceutically acceptable salt thereof in the

manufacture of a medicament for treating various diseases and/or disease states evoked by an increased level of aldosterone and/or overproduction of aldosterone.

29. The use according to claim 28, wherein the diseases and/or disease states is primary aldosteronism, secondary aldosteronism, hypertension, heart failure, cardiomyopathy, cardiac hypertrophy, myocardial infarction, myocardial necrosis lesion, failure after myocardial ischemia, coronary artery disease, fibrosis or remodeling of myocardium or blood vessels, vascular restenosis, blood vessel wall thickening, arterial sclerosis, acute renal disorder, chronic kidney disease, renal fibrosis, nephropathy, hypokalemia, metabolic syndrome, obesity, sleep apnea syndrome, retinopathy, hepatic disease, idiopathic and/or cyclic edema, or sympathetic hyperactivity.