[0010]

[Patent Document 1] International Publication WO00/75113

[Patent Document 2] JP Patent Publication (Kokai) No. 2008-013499 A

[Patent Document 3] International Publication WO07/120980

[Patent Document 4] International Publication WO07/124221

[Patent Document 5] International Publication WO09/026107

[Patent Document 6] International Publication WO09/131687

[Patent Document 7] International Publication WO09/136995

[Patent Document 8] International Publication WO09/145856

[Non Patent Documents]

[0011]

[Non Patent Document 1] The Journal of Biological Chemistry, Vol. 266, pp. 15790-15796, 1991

[Non Patent Document 2] International Journal of Hematology, Vol. 75, No. 4, pp. 357-362, 2002

[Non Patent Document 3] The Journal of Biological Chemistry, Vol. 270, pp. 16189-16197, 1995

[Non Patent Document 4] The Journal of Immunology, Vol. 167, No. 11, pp. 6292-6302, 2001

[Non Patent Document 5] Expert Opinion on Investigational Drugs, Vol. 13, No. 7, pp. 743-762, 2004

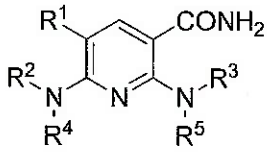
[Non Patent Document 6] Expert Opinion on Therapeutic Targets, Vol. 9, No. 5, pp. 901-921, 2005

[Non Patent Document 7] IDrugs, Vol. 12, No. 3, pp. 174-185, 2009

[Summary]

[0011a]

In one aspect of the present disclosure, there is provided a nicotinamide derivative represented by the following formula (I) or a salt thereof:

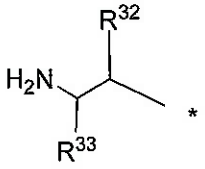


(I)

wherein

R^1 represents a halogen atom;

R^2 represents a substituent represented by the following formula (II-1):



(II-1)

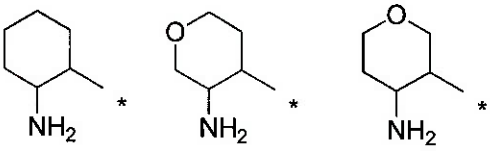
wherein R^{32} represents a hydrogen atom, or

C_{1-6} alkyl, C_{3-8} cycloalkyl, phenyl, pyridyl or thiophenyl group, each optionally having a substituent selected from the group consisting of a halogen atom, C_{1-6} alkyl, C_{3-8} cycloalkyl and phenyl group, or

an alkoxyalkyl group containing 2 to 4 carbon atoms in total,

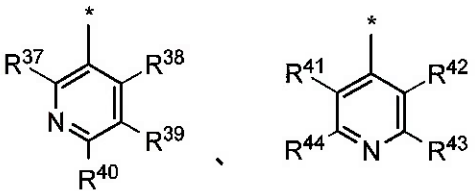
R^{33} represents a hydrogen atom, C_{1-6} alkyl or C_{3-8} cycloalkyl group;

or a substituent represented by the following;



(III-4)

R^3 represents a pyridyl group represented by the following formula (VIII-1) or (VIII-2):



(VIII-1)

(VIII-2)

wherein R^{37} and R^{38} each independently represent a hydrogen atom or a halogen atom;

R^{39} represents a hydrogen atom, a halogen atom or C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, pyrrolyl, pyrrolidinyl, pyrazolyl, oxazolyl, oxadiazolyl, imidazolyl, triazolyl or furanyl group, each

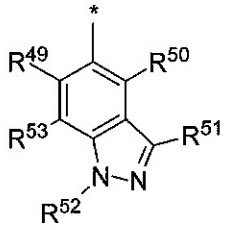
optionally having a substituent selected from the group consisting of a halogen atom, C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5 represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group);

R^{40} represents a hydrogen atom, a halogen atom or C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, pyrrolyl, pyrrolidinyl, pyrazolyl, oxazolyl, oxadiazolyl, imidazolyl, triazolyl, furanyl or morpholinyl group, each optionally having a substituent selected from the group consisting of a halogen atom, C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5 represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group);

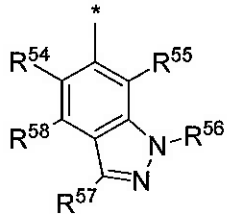
R^{41} and R^{42} each independently represent a hydrogen atom or a halogen atom;

R^{43} and R^{44} each independently a hydrogen atom, a halogen atom or C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, pyrrolyl, pyrrolidinyl, pyrazolyl, oxazolyl, oxadiazolyl, imidazolyl, triazolyl or furanyl group, each optionally having a substituent selected from the group consisting of a halogen atom, C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5 represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group);

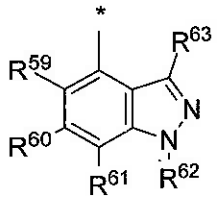
an indazolyl group represented by any one of the following formulae (IX-1) to (IX-6):



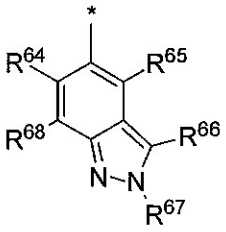
(IX-1)



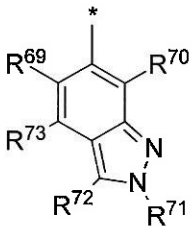
(IX-2)



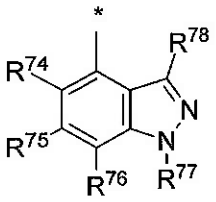
(IX-3)



(IX-4)



(IX-5)



(IX-6)

wherein R^{49}, R^{50}, R^{54}, R^{55}, R^{59}, R^{60}, R^{64}, R^{65}, R^{69}, R^{70}, R^{74} and R^{75} each independently represent a hydrogen atom or a halogen atom;

R^{53}, R^{58}, R^{61}, R^{68}, R^{73} and R^{76}, each independently represent a hydrogen atom, a halogen atom, C_{1-6} alkyl, or C_{1-6} alkoxy group;

R^{51}, R^{57}, R^{63}, R^{66}, R^{72} and R^{78} each independently represent a hydrogen atom, a halogen atom or C_{1-6} alkyl, C_{3-8} cycloalkyl or C_{1-6} alkoxy group, each optionally having a substituent selected from the group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5

represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group), each optionally having a halogen atom;

R^{52}, R^{56}, R^{62}, R^{67}, R^{71} and R^{77} each independently represent a hydrogen atom, a halogen atom or C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-6} alkoxy or phenyl group, each optionally having a substituent selected from the group consisting of C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5 represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group), each optionally having a halogen atom;

or phenyl group optionally having one or two substituents selected from the group consisting of a halogen atom or C_{1-6} alkyl, phenyl, C_{1-6} alkoxy, pyrrolyl, pyrrolidinyl, pyrazolyl, oxazolyl, oxadiazolyl, imidazolyl, triazolyl, furanyl or morpholinyl group, each optionally having a substituent selected from the group consisting of a halogen atom, C_{1-6} alkyl, C_{3-8} cycloalkyl and $-Q^5-R^{36}$ (wherein Q^5 represents C_{1-3} alkyleneoxy group, and R^{36} represents a hydrogen atom, C_{1-3} alkyl, or cyclopropyl group):

R^4 and R^5 represent a hydrogen atom.

[0011b]

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the nicotinamide derivative or a salt thereof as defined herein.

[0011c]

In yet another aspect of the present disclosure, there is provided the pharmaceutical composition as defined herein, which is for use in the treatment of a disease selected from the group consisting of rheumatism and idiopathic thrombocytopenic purpura.

[0011d]

In a further aspect of the present disclosure, there is provided a compound which is selected from the group consisting of:

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-phenylpyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(3-methylphenylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(4-(morpholin-4-yl)phenylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(3,4,5-trimethoxyphenylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methoxypyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(2,6-dimethoxypyridin-4-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-(morpholin-4-yl)pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(6-(morpholin-4-yl)pyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(pyrimidin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1,5-naphthyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1,6-naphthyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1,6-naphthyridin-8-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(8-nitroquinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-c]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrrolo[2,3-c]pyridin-4-ylamino)nicotinamide;

2-(8-acetylaminoquinolin-3-ylamino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-(anilinocarbonyl)pyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

methyl5-(3-aminocarbonyl-6-(cis-2-aminocyclohexylamino)-5-fluoropyridin-2-

ylamino)nicotinate;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(6-methylpyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methylpyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrrolo[2,3-b]pyridin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-(morpholin-4-yl)ethyl)-1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-([1,3]thiazolo[4,5-b]pyridin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1-(2-(diethylamino)ethyl)-1H-pyrrolo[2,3-b]pyridin-4-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-methoxyethyl)-1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-isobutyl-1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1-cyclopropyl-1H-pyrrolo[2,3-b]pyridin-4-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1-(cyclopropylmethyl)-1H-pyrrolo[2,3-b]pyridin-4-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-(2H-1,2,3-triazol-2-yl)pyridin-3-ylamino)-nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-(1H-pyrrol-2-yl)pyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-(2-thienyl)pyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(5-cyclopropylpyridin-3-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-(2-furyl)pyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(8-aminoquinolin-3-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1H-pyrrolo[2,3-b]pyridin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1H-pyrrolo[2,3-b]pyridin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1H-pyrrolo[2,3-c]pyridin-4-ylamino)nicotinamide;

2-(8-(aminocarbonyl)aminoquinolin-3-ylamino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(2-aminoethylamino)-5-fluoro-2-(pyridin-4-ylamino)nicotinamide;

6-(2-aminoethylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(2,1,3-benzothiadiazol-5-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1,3-benzothiazol-6-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-indazol-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methyl-1,3-benzoxazol-6-ylamino)nicotinamide;

6-(2-aminoethylamino)-2-(1,3-benzothiazol-6-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methyl-1,3-benzoxazol-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-methylpyridin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1,3-dimethyl-1H-pyrazolo[3,4-b]pyridin-5-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(2,3-dihydro-1,4-benzodioxin-6-ylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(3-(2H-1,2,3-triazol-2-yl)phenylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(6-methoxyquinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinolin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinoxalin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(1,3-benzothiazol-5-ylamino)-5-fluoronicotinamide;

6-(2-aminoethylamino)-5-fluoro-2-(isoquinolin-4-ylamino)nicotinamide;

6-(2-aminoethylamino)-5-fluoro-2-(quinolin-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-indazol-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-benzoimidazol-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinazolin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinazolin-7-ylamino)nicotinamide;

cis-6-(2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-benzoimidazol-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methylquinolin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinolin-7-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-methyl-1H-indazol-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-methylquinoxalin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1-(2-(pyrrolidin-1-yl)ethyl)-1H-indazol-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(2-(2-(pyrrolidin-1-yl)ethyl)-2H-indazol-5-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1H-indazol-5-ylamino)nicotinamide;

6-(2-aminoethylamino)-2-(3,5-dimethoxyphenylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(3-chlorophenylamino)-5-fluoronicotinamide;

6-(2-aminoethylamino)-5-fluoro-2-(quinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(isoquinolin-4-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(1,8-naphthyridin-3-ylamino)nicotinamide;

5-fluoro-6-(2-(1H-imidazol-5-yl)ethylamino)-2-(quinolin-3-ylamino)nicotinamide;

6-((1R)-2-amino-2-oxo-1-phenylethylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2R)-1-amino-4-methyl-1-oxopentan-2-ylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2R)-1-amino-1-oxobutan-2-ylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2S)-2-aminobutylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2S)-2-amino-3-methylbutylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2S)-2-amino-2-phenylethylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2R)-2-amino-3-methoxypropylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2S)-2-aminopropylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-((2S)-2-amino-4-methylpentylamino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-(3-aminopropylamino)-2-(3,5-dimethoxyphenylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(3,5-dimethoxyphenylamino)-5-fluoronicotinamide;

6-((1R,2S)-2-aminocyclohexylamino)-2-(3,5-dimethoxyphenylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-chloro-2-(quinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-bromo-2-(quinolin-3-ylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-chloro-2-(3-methoxyphenylamino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-chloro-2-(5-methylpyridin-3-ylamino)nicotinamide; and

6-(cis-2-aminocyclohexylamino)-5-bromo-2-(5-methylpyridin-3-ylamino)nicotinamide.

[0011e]

In another aspect of the present disclosure, there is provided a compound which is selected from the group consisting of:
6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(6-methylpyridin-3-ylamino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-2-((5-cyano-6-morpholinopyridin-3-yl)amino)-5-fluoronic otinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-(5-methylpyridin-3-ylamino)nicotinamide;

(R)-6-((1-amino-4-methylpentan-2-yl)amino)-5-fluoro-2-((quinolin-6-yl)amino)nicotinamide;

(R)-6-((1-amino-4-methylpentan-2-yl)amino)-5-fluoro-2-((2-(2-methoxyethoxy)pyridin-4-yl) amino)nicotinamide;

6-((1R,2S)-2-aminocyclohexylamino)-5-fluoro-2-((6-morpholinopyridin-3-yl)amino)nicotinamide;

2-((5-(1H-pyrazol-1-yl)pyridin-3-yl)amino)-6-((1R,2S)-2-aminocyclohexylamino)-5-fluoronicotinamide;

(R)-6-((1-amino-4-methylpentan-2-yl)amino)-2-((5,6-dimethylpyridin-3-yl)amino)-5-fluoronicotinamide;

6-(((2S,3R)-2-aminopentane3-yl)amino)-2-((1-ethyl-1H-indazol-5-yl)amino)-5-fluoronicotinamide;

6-(((2S,3R)-2-aminohexane3-yl)amino)-5-fluoro-2-((2-methoxypyridin-4-yl)amino)nicotinamide;

6-(((2S,3R)-2-aminopentane3-yl)amino)-5-fluoro-2-((5-(2-fluorophenyl)pyridin-3-yl)amino)nicotinamide;

6-(((2S,3R)-2-aminopentane3-yl)amino)-5-fluoro-2-((1-methoxyisoquinolin-6-yl)amino)nicotinamide;

6-(((2S,3R)-2-aminopentane3-yl)amino)-5-fluoro-2-((1-methyl-1H-indazol-4-yl)amino)nicotinamide;

6-(((2S,3R)-2-aminohexane3-yl)amino)-2-((5,6-dimethylpyridin-3-yl)amino)-5-fluoronicotinamide;

6-(((2S,3R)-2-aminohexane3-yl)amino)-5-fluoro-2-((5-fluoropyridin-3-yl)amino)nicotinamide;

6-(((2S,3R)-2-aminohexane3-yl)amino)-5-fluoro-2-((2-propoxypyridin-4-yl)amino)nicotinamide;

(R)-6-((1-amino-4-methylpentan-2-yl)amino)-2-((1-ethyl-1H-indazol-5-yl)amino)-5-fluoronicotinamide;

6-(((2R,3S)-3-amino-1-cyclopropylbutan-2-yl)amino)-2-((1-ethyl-1H-indazol-5-yl)amino)-5-fluoronicotinamide;

6-(((1R,2S)-2-amino-1-cyclopropylpropyl)amino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-(((1R,2S)-2-aminocyclohexyl)amino)-5-fluoro-2-((6-methyl-5-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)amino)nicotinamide;

6-(((1R,2S)-2-aminocyclohexyl)amino)-5-fluoro-2-((6-methoxy-5-(2H-1,2,3-triazol-2-yl)pyridin-3-yl)amino)nicotinamide;

6-(((2S,3R)-2-amino-5-methylhexane3-yl)amino)-5-fluoro-2-((1-methyl-1H-indazol-5-yl)amino)nicotinamide;

6-(((2S,3R)-2-amino-5-methylhexane3-yl)amino)-2-((1-ethyl-1H-indazol-5-yl)amino)-5-fluoronicotinamide;

6-(((1R,2S)-2-aminocyclohexyl)amino)-5-fluoro-2-((5-fluoro-6-morpholinopyridin-3-yl)amino)nicotinamide;

6-(((1R,2S)-2-aminocyclohexyl)amino)-2-((2-ethoxy-3-fluoropyridin-4-yl)amino)-5-fluoronicotinamide;

6-(((2R,3S)-3-amino-1-cyclopropylbutan-2-yl)amino)-2-((5,6-dimethylpyridin-3-yl)amino)-5-fluoronicotinamide;

6-(((2S,3S)-3-amino-1-methoxybutan-2-yl)amino)-5-fluoro-2-(quinolin-6-ylamino)nicotinamide;

6-(2-aminoethylamino)-2-(3,5-dimethoxyphenylamino)-5-fluoronicotinamide;

6-(((1R,2S)-2-aminocyclohexylamino)-5-fluoro-2-((5-methylpyridin-3-yl) amino) nicotinamide; and

6-(((1R,2S)-2-aminocyclohexylamino)-5-fluoro-2-((6-methylpyridin-3-yl) amino) nicotinamide.

[0011f]

In yet another aspect of the present disclosure, there is provided a compound which is selected from the group consisting of:

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((6-methyl-5-phenylpyridin-3-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((5,6-dimethylpyridin-3-yl) amino)-5-fluoronicotinamide;

2-(1H-indazol-4-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((1-(2-(pyrrolidin-1-yl)ethyl)-1H-indazol-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((1-(2-morpholinoethyl)-1H-indazol-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((1-(cyclopropylmethyl)-1H-indazol-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((1-(2-methoxyethyl)-1H-indazol-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((1-(2-(2-ethoxyethoxy)ethyl)-1H-indazol-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(cyclopropylmethyl)-2H-indazol-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-benzyl-2H-indazol-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-methoxyethyl)-2H-indazol-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-benzyl-2H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((5-ethylpyridin-3-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-methyl-2H-indazol-5-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((1-(cyclopropylmethyl)-1H-indazol-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((1-(2-methoxyethyl)-1H-indazol-6-yl) amino)nicotinamide;

2-(2-(1H-pyrrol-2-yl)pyridin-4-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-phenylpyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(furan-2-yl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-isopropoxypyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(furan-3-yl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(methylamino)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(2-ethoxypyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-(2,6-diethoxypyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((5-(5-methylfuran-2-yl)pyridin-3-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-((5-methylfuran-2-yl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-methoxy-6-phenylpyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-methoxyethoxy)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-morpholino-6-phenylpyridin-4-yl) amino)nicotinamide;

2-((5-(1H-pyrazol-4-yl)pyridin-3-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

2-(2-(1H-pyrazol-4-yl)pyridin-4-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-propoxypyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-butoxypyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-isobutoxypyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-methoxyquinolin-7-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-methoxyethoxy)quinolin-7-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-((1-methoxypropan-2-yl)oxy)quinolin-7-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(3-methoxybutoxy)quinolin-7-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2-(2-ethoxyethoxy)ethoxy)quinolin-7-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((5-(1-cyclohexen-1-yl)pyridin-3-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-methoxyethoxy)quinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-((1-methoxypropan-2-yl)oxy)quinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(3-methoxybutoxy)quinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2-(2-ethoxyethoxy)ethoxy)quinolin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-methoxyquinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-ethoxyquinolin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-propoxyquinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2-ethoxyethoxy)quinolin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-(2-methoxyethoxy)ethoxy)quinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-((tetrahydrofuran-2-yl)methoxy)quinolin-6-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-(2-oxopyrrolidin-1-yl)ethoxy)quinolin-6-yl) amino)nicotinamide;

2-((2-(1H-1,2,4-triazol-1-yl)pyridin-4-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((5-(furan-3-yl)-6-methylpyridin-3-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2,3-dimethoxyquinoxalin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2,3-diethoxyquinoxalin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((4-methyl-3,4-dihydro-2H-[1,4]oxazino[2,3-b]quinoxalin-7-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2,3-dimethylquinoxalin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2,3-diethylquinoxalin-6-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((1-ethyl-1H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((1-propyl-1H-indazol-5-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-fluorophenyl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2,4-difluorophenyl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((6-methyl-5-(2H-1,2,3-triazol-2-yl)pyridin-3-yl) amino)nicotinamide;

2-((5-(1H-1,2,4-triazol-1-yl)pyridin-3-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-fluoro-3-methoxyphenyl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-fluoro-4-methoxyphenyl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(2-fluoro-5-methoxyphenyl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((6-cyclopropylpyridin-3-yl) amino)-5-fluoronicotinamide;

2-((3-(1H-pyrazol-1-yl)quinolin-7-yl) amino)-6-(cis-2-aminocyclohexylamino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2,3-difluorophenyl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(2,5-difluorophenyl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(3-chloro-2-fluorophenyl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-((5-chloro-2-fluorophenyl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((5-(benzo[d][1,3]dioxol-5-yl)pyridin-3-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-2-((2-(benzo[d][1,3]dioxol-5-yl)pyridin-4-yl) amino)-5-fluoronicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((5-(3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)pyridin-3-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(3-methoxyphenyl)pyridin-4-yl) amino)nicotinamide;

6-(cis-2-aminocyclohexylamino)-5-fluoro-2-((2-(4-methoxyphenyl)pyridin-4-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino) -2-((1-ethyl-1H-indazol-6-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino) -2-((1-ethyl-1H-indazol-4-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino) -2-((1-(2,2-difluoroethyl)-1H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino) -2-((1-(2,2-difluoroethyl)-1H-indazol-6-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino) -5-fluoro-2-((5-(quinolin-7-yl)pyridin-3-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino) -5-fluoro-2-((5-(isoquinolin-6-yl)pyridin-3-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((5-(isoquinolin-7-yl)pyridin-3-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((2-(quinolin-7-yl)pyridin-4-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((2-(isoquinolin-6-yl)pyridin-4-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((2-(isoquinolin-7-yl)pyridin-4-yl) amino)nicotinamide;

6-(((cis)-2-aminocyclohexyl)amino)-2-((benzofuro[2,3-b]pyridin-3-yl)amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((3-fluoro-1-methyl-1H-indazol-5-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-2-((1-ethyl-3-fluoro-1H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((3-fluoro-1-methyl-1H-indazol-6-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-2-((1-ethyl-3-fluoro-1H-indazol-6-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((1-(2-fluoroethyl)-1H-indazol-5-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((1-(2-fluoroethyl)-1H-indazol-6-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((3-fluoro-1-(2-fluoroethyl)-1H-indazol-5-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((3-fluoro-1-(2-fluoroethyl)-1H-indazol-6-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-2-((1,3-dimethyl-1H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino)-2-((1-ethyl-3-methyl-1H-indazol-5-yl) amino)-5-fluoronicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((1-(2-methoxyethyl)-3-methyl-1H-indazol-5-yl) amino)nicotinamide;

6-((cis-2-aminocyclohexyl)amino)-5-fluoro-2-((1-(2-fluoroethyl)-3-methyl-1H-indazol-5-yl)amino)nicotinamide; and

6-((cis-2-aminocyclohexyl)amino)-2-((1-(2,2-difluoroethyl)-3-methyl-1H-indazol-5-yl)amino)-5-fluoronicotinamide.

[Object to be Solved by the Invention]

[0012]

To date, various Syk inhibitors have been reported, but they have not been placed on the market yet. It has been desired to develop a compound and a pharmaceutical composition, which have excellent Syk-inhibitory activity.

[Means for Solving the Object]

[0013]

As a result of intensive studies directed towards achieving the aforementioned object, the present inventors have found that a nicotinamide