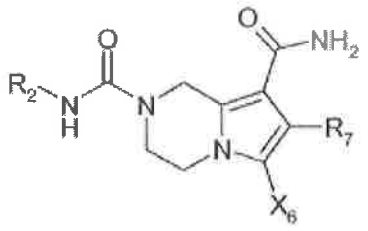
Claims

1. Compounds corresponding to the general formula (I)



(I)

in which

R_2 represents:

- a group C_{1-10}-alkyl, C_{3-7}-cycloalkyl-C_{1-6}-alkyl, C_{1-6}-alkylthio-C_{-1-10}-alkyl, C_{1-6}-alkoxy-C_{1-10}-alkyl, hydroxy-C_{1-10}-alkyl, hydroxy-C_{1-6}-alkyl-C_{3-7}-cycloalkyl-C_{1-6}-alkyl, C_{1-10}-fluoroalkyl, C_{1-10}-alkyl-oxyimino-C_{1-10}-alkyl,
- a group C_{3-10}-cycloalkyl, C_{3-10}-fluorocycloalkyl, hydroxy-C_{3-10}-cycloalkyl,
- a group C_{3-7}-cycloalkyl which may be substituted with one or two groups independently chosen from C_{1-6}-alkyl, C_{3-7}-cycloalkyl, hydroxyl, C_{1-10}-fluoroalkyl and C_{1-10}-alkyl-oxyimino,
- a heterocyclic group comprising from 3 to 8 carbon atoms and at least one heteroatom chosen from nitrogen, oxygen, sulfur and the oxide or dioxide form of sulfur, this heterocyclic group possibly being substituted with one or more groups from among hydroxyl, C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, C_{1-6}-fluoroalkyl, this heterocylic group being chosen from oxetanyl, tetrahydrofuryl, tetrahydro-2H-pyranyl, oxepanyl, thietanyl, tetrahydrothiophenyl, tetrahydro-2H-thiopyranyl, thiepanyl, 1,1-dioxydothietanyl, 1,1-dioxydotetrahydrothiophenyl, 1,1-dioxydotetrahydro-2H-thiopyranyl and 1,1-dioxydothiepanyl.
- a group C_{1-10}-alkyl substituted with a heterocyclic group comprising from 3 to 8 carbon atoms and at least one heteroatom chosen from nitrogen, oxygen, sulfur and the oxide or dioxide form of sulfur, this heterocyclic group possibly being substituted with one or more groups from

among hydroxyl, C_{1-6}-alkyl, hydroxy-C_{1-6}-alkyl, C_{1-6}-fluoroalkyl;

X_6 represents a hydrogen, fluorine, chlorine or bromine atom or a group C_{1-6}-alkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-6}-alkyl, C_{1-6}-fluoroalkyl or cyano;

R_7 represents a phenyl group or a naphthyl group, optionally substituted with one or more substituents X_7, which may be identical or different, chosen independently;

X_7 represents:

- a halogen atom chosen from fluorine, chlorine and bromine atoms,

or a group chosen from:

- hydroxyl,
- C_{1-6}-alkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-6}-alkyl,
- hydroxy-C_{1-6}-alkyl, hydroxy-C_{3-7}-cycloalkyl, hydroxy-C_{3-7}-cycloalkyl-C_{1-6}-alkyl,
- C_{1-6}-alkoxy, C_{3-7}-cycloalkoxy, C_{3-7}-cycloalkyl-C_{1-6}-alkoxy,
- C_{1-6}-alkylthio, C_{3-7}-cycloalkylthio, C_{3-7}-cycloalkyl-C_{1-6}-alkylthio,
- aryl, aryl-C_{1-6}-alkyl,
- aryloxy, aryl-C_{1-6}-alkoxy,
- C_{1-6}-fluoroalkyl, C_{3-7}-fluorocycloalkyl, C_{3-7}-fluorocycloalkyl-C_{1-6}-alkyl,
- C_{1-6}-fluoroalkoxy, C_{3-7}-fluorocycloalkoxy, C_{3-7}-fluorocycloalkyl-C_{1-6}-alkoxy,
- cyano, cyano-C_{1-6}-alkyl, cyano-C_{1-6}-alkoxy,
- NR_aR_b, NR_cCOR_d, $NR_cSO_2R_d$, $NR_cSO_2NR_aR_b$, $CONR_aR_b$, $CON(OR_c)R_d$,
- a heteroaryl group,

the aryl or heteroaryl groups being optionally substituted with one or more substituents chosen from fluorine, chlorine and bromine atoms or a group C_{1-6}-alkyl, C_{3-7}-cycloalkyl, C_{1-6}-alkoxy, C_{1-6}-fluoroalkyl, C_{1-6}-fluoroalkoxy or cyano, the aryl group being chosen from phenyl and naphthyl, and the heteroaryl group being chosen from pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, pyrrolyl, furyl, thienyl, imidazolyl, oxazolyl, thiazolyl,

pyrazolyl, isaoxazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl.

R_a and R_b represent, independently of each other, a hydrogen atom or a group C_{1-6}-alkyl, C_{3-7}-cycloalkyl or C_{3-7}-cycloalkyl-C_{1-6}-alkyl, or alternatively they form with the atom that bears them a ring chosen from azetidine, pyrrolidine, piperidine, morpholine, thiomorpholine, azepine and piperazine, this ring being optionally substituted with one or more groups C_{1-6}-alkyl,

R_c and R_d represent, independently of each other, a hydrogen atom or a group C_{1-6}-alkyl, C_{3-7}-cycloalkyl or C_{3-7}-cycloalkyl-C_{1-6}-alkyl;

in the form of the base or of an acid-addition salt,

wherein ~~the heterocyclic group is a saturated carbon-based cyclic group comprising at least one heteroatom,~~

~~the heteroaryl is an aromatic carbon-based cyclic group comprising at least one heteroatom,~~

~~the aryl is a monocylic or bicyclic aromatic group comprising between 6 and 10 carbon atoms; and~~

the aryloxy is a group -O-aryl.

~~2. Compounds of formula (I) according to Claim 1,~~

~~characterized in that~~

~~R_2 represents:~~

~~- a group C_{1-10}-alkyl, C_{3-7}-cycloalkyl-C_{1-6}-alkyl, C_{1-6}-alkoxy-C_{1-10}-alkyl, hydroxy-C_{1-10}-alkyl, hydroxy-C_{1-6}-alkyl-C_{3-7}-cycloalkyl-C_{1-6}-alkyl, C_{1-10}-fluoroalkyl,~~

~~- a group C_{3-10}-cycloalkyl, C_{3-10}-fluorocycloalkyl, hydroxy-C_{3-10}-cycloalkyl,~~

~~- a group C_{3-7}-cycloalkyl which may be substituted with one or two groups independently chosen from C_{1-6}-alkyl, C_{3-7}-cycloalkyl, hydroxyl, C_{1-10}-fluoroalkyl and C_{1-10}-alkyl-oxyimino,~~

~~- a heterocyclic group comprising from 3 to 8 carbon atoms and at least one heteroatom chosen from oxygen or a sulfur atom in dioxide form, this heterocyclic group possibly being substituted with one or more groups C_{1-6}-alkyl,~~

~~- a group C_{1-10}-alkyl substituted with a heterocyclic group comprising from 3 to 8 carbon atoms and at least one oxygen heteroatom, this heterocyclic group possibly being substituted with one or more groups C_{1-6}-alkyl,~~

~~R_7 represents a phenyl group optionally substituted with one or more substituents X_7, which may be identical or different, chosen independently from:~~

~~- a fluorine or chlorine atom~~

~~or a group chosen from~~

~~- C_{1-6}-alkyl, C_{3-7}-cycloalkyl,~~

~~- C_{1-6}-alkoxy, C_{3-7}-cycloalkyl-C_{1-6}-alkoxy,~~

~~- C_{1-6}-alkylthio,~~

~~- aryl,~~

~~- aryloxy, aryl-C_{1-6}-alkoxy,~~

~~- C_{1-6}-fluoroalkyl,~~

~~- C_{1-6}-fluoroalkoxy,~~

~~- cyano, cyano-C_{1-6}-alkoxy,~~

~~- NR_aR_b, $NR_cSO_2R_d$, $NR_cSO_2NR_aR_b$, $CONR_aR_b$, $CON(OR_c)R_d$,~~

~~- heteroaryl chosen from oxadiazolyl and pyrazolyl groups, optionally substituted with a group C_{1-6}-alkyl, the aryl group being optionally substituted with a fluorine atom,~~

~~R_a and R_b represent, independently of each other, a hydrogen atom or a group C_{1-6}-alkyl, C_{3-7}-cycloalkyl, or alternatively they form with the atom that bears them a ring chosen from pyrrolidine and morpholine,~~

~~R_c and R_d represent, independently of each other, a hydrogen atom or a group C_{1-6}-alkyl.~~

~~32~~. Compound ~~of formula (I)~~according to claim 1, ~~characterized in that it~~wherein said compound is chosen from:

N^2-tert-butyl-7-phenyl-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide,

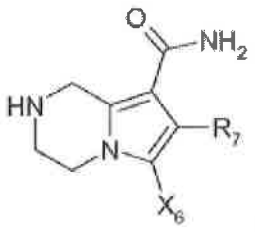
N^2- tert-butyl-7-(4-methoxyphenyl)-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide,

N^2- tert-butyl-6-methyl-7-phenyl-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide

N^2-tert-butyl-7-(4-methoxyphenyl)-6-methyl-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide,

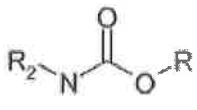
6-cyano-N^2-(4,4-difluoro-cyclohexyl)-7-(3-fluorophenyl)-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide.

~~43~~. Process for preparing compounds of formula (I) according to any one of Claims 1 to ~~32~~, comprising the step that consists in reacting a 1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-8-carboxamide derivative, which is a compound of formula (II) below:



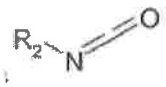
(II)

in which R_7 and X_6 are as defined in the general formula (I) defined in Claim 1,
with a compound of formula



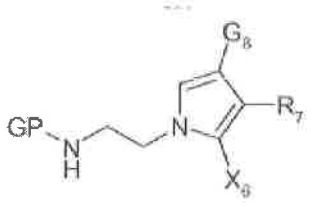
(IIb)

in which R_2 is as defined in the general formula (I) defined in Claim 1 and R represents a group such as phenyl, pentafluorophenyl or 4-nitrophenyl,
in an aprotic solvent such as acetonitrile and in the presence of a mineral base such as sodium carbonate,

or alternatively with a compound of formula  (IIa)

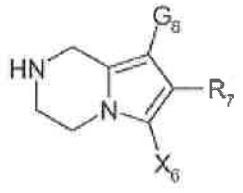
in which R_2 is as defined in the general formula (I) defined in Claim 1,
in an aprotic solvent such as dichloromethane and optionally in the presence of an organic amine such as triethylamine.

~~54~~. Process for preparing compounds of formula (XVII), comprising the step that consists in reacting a pyrrole derivative, which is a compound of formula (XVIII) below:



(XVIII)

with an acidic solution, for example an aqueous hydrochloric acid solution, and formaldehyde or paraformaldehyde, to give the 1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine derivatives of general formula (XVII)



(XVII)

in which X_6 represents a fluorine or chlorine atom, while R_7 is as defined according to either of Claims 1 and 2, and G_8 represents a nitrile group or an alkyl carboxylate group, such as a methyl or ethyl carboxylate.

~~65~~. Medicament comprising a compound of formula (I) according to any one of Claims 1 to ~~32~~, in the form of the base or of an addition salt with a pharmaceutically acceptable acid.

~~76~~. Pharmaceutical composition containing at least one compound of formula (I) according to any one of Claims 1 to ~~32~~, in the form of the base or of an addition salt with a pharmaceutically acceptable acid, and optionally one or more pharmaceutically acceptable excipients.

~~87~~. Use of a compound of formula (I) according to any one of Claims 1 to ~~32~~, in the form of the base or of an addition salt with a pharmaceutically acceptable acid, for the preparation of a medicament for preventing and/or treating sleep disorders and circadian rhythm disorders.

~~9~~8. Use of a compound of formula (I) according to any one of Claims 1 to ~~3~~2, in the form of the base or of an addition salt with a pharmaceutically acceptable acid, for the preparation of a medicament for preventing or treating inflammatory diseases, especially such as inflammatory diseases of the central nervous system, for instance multiple sclerosis, encephalitis, myelitis and encephalomyelitis and other inflammatory diseases, for instance vascular pathologies, atherosclerosis, joint inflammation, arthrosis and rheumatoid arthritis.

~~10~~9. Compound according to Claim 1, wherein the compound is N2-(tert-butyl)-6-chloro-7-phenyl-3,4-dihydropyrrolo[1,2-a]pyrazine-2,8(1H)-dicarboxamide.