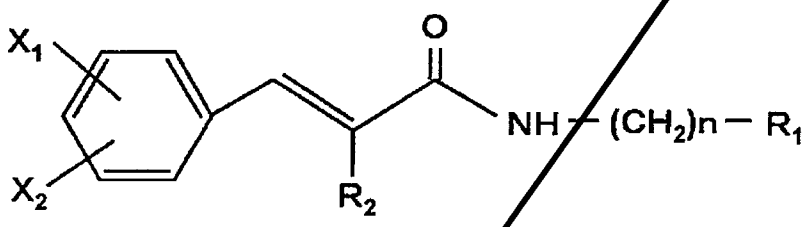
Claims

[Claim 1] A compound or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from guanidino, indazolyl, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms, with proviso that in a case of n=0, R_1 stands for a substituent other than a phenyl substituted with morpholino.

[Claim 2] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, wherein R_2 is a hydrogen, and wherein either one of X_1 and X_2 is a hydrogen, and the other is a fluorine.

[Claim 3] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is an imidazolyl substituted with alkyl having 1 to 6 carbon atoms or phenyl.

[Claim 4] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms.

[Claim 5] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a phenyl substituted with amino, isoxazolyl, or morpholino.

[Claim 6] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a phenyl substituted with thiomorpholino which may be substituted with oxo.

[Claim 7] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl.

[Claim 8] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a thiomorpholino which may be

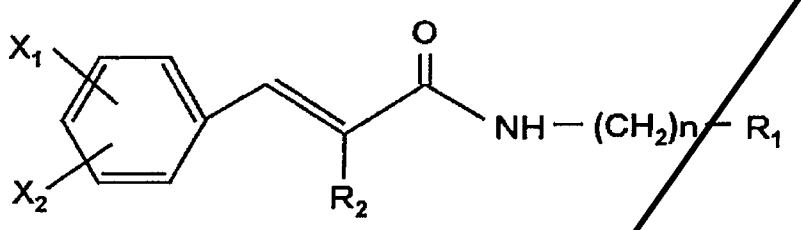
substituted with one or two oxos.

[Claim 9] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is any one of substituents selected from guanidino, indazolyl, and cyclohexylamino.

[Claim 10] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, which is selected from the group consisting of (*E*)-*N*-[2-(4-cyclohexylpiperazin-1-yl)ethyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(4-cyclohexylpiperazin-1-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(4-methylpiperazin-1-yl)propyl]-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(isoxazol-5-yl)phenyl]-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

[Claim 11] The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, which is selected from the group consisting of (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

[Claim 12] A pharmaceutical agent, comprising, as an active ingredient, at least one member of a compound, and salt and hydrate thereof that are pharmaceutically acceptable, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 13] The pharmaceutical agent according to claim 12, which is an analgesic.

[Claim 14] The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for chronic pains.

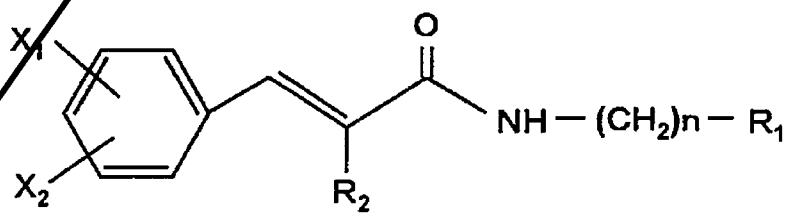
[Claim 15] The pharmaceutical agent according to claim 14, wherein the therapeutic agent for chronic pains is a therapeutic agent for lumbago, arthralgia, or neuropathic pains.

[Claim 16] The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for neuropathic pains.

[Claim 17] The pharmaceutical agent according to any one of claims 12 to 16, which is an oral preparation.

[Claim 18] The pharmaceutical agent according to any one of claims 12 to 16, which is an injectable preparation.

[Claim 19] Use of a compound or a pharmaceutically acceptable salt or hydrate thereof as a pharmaceutical agent, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 0 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

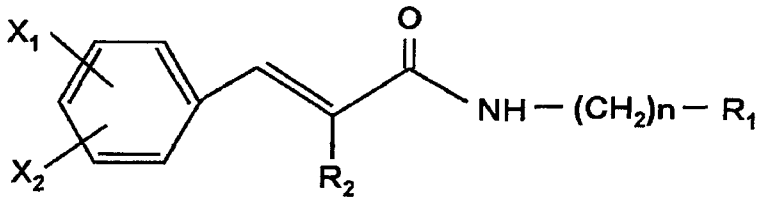
- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from amino, carboxy, guanidino, indolyl, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

[Claim 20] The use according to claim 19, wherein the pharmaceutical agent is an analgesic.

Claims

1. A compound or a pharmaceutically acceptable salt or hydrate thereof, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 1 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl substituted with alkyl having 2 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;
- a thiomorpholino which may be substituted with one or two oxos; or
- any one of substituents selected from guanidino, indazolyl, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms, with proviso that in a case of n=0, R_1 stands for a substituent other than a phenyl substituted with morpholino.

2. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, wherein R_2 is a hydrogen, and wherein either one of X_1 and X_2 is a hydrogen, and the other is a fluorine.

3. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is an imidazolyl substituted with alkyl having 2 to 6 carbon atoms or phenyl.

4. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms.

5. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a phenyl substituted with amino, isoxazolyl, or morpholino.

6. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2,whrerin R_1 is a phenyl substituted with thiomorpholino which may be substituted with oxo.

7. The compound or a pharmaceutically acceptable salt or hydrate thereof

according to claim 2, wherein R_1 is a piperazino substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl.

8. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is a thiomorpholino which may be substituted with one or two oxos.

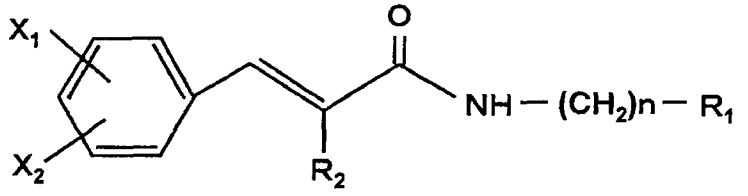
9. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 2, wherein R_1 is any one of substituents selected from guanidino, indazolyl, and cyclohexylamino.

10. The compound or a pharmaceutically acceptable salt or hydrate thereof according to claim 1, which is selected from the group consisting of (*E*)-*N*-[2-(4-cyclohexylpiperazin-1-yl)ethyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(4-cyclohexylpiperazin-1-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-[3-(4-methylpiperazin-1-yl)-propyl]-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholino-propyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholino-propyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(2-fluorophenyl)-2-propenamide, (*E*)-*N*-[3-(1,1-dioxo-1,4-thiazinan-4-yl)propyl]-3-(4-fluorophenyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluoro-phenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

11. The compound or a pharmaceutically acceptable salt or hydrate thereof

according to claim 1, which is selected from the group consisting of (*E*)-3-(4-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(2-fluorophenyl)-*N*-(3-thiomorpholinopropyl)-2-propenamide, (*E*)-3-(4-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide and (*E*)-3-(2-fluorophenyl)-*N*-[3-(1-oxo-1,4-thiazinan-4-yl)propyl]-2-propenamide.

12. A pharmaceutical agent, comprising, as an active ingredient, at least one member of a compound, and salt and hydrate thereof that are pharmaceutically acceptable, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 1 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 2 to 4 carbon atoms,

pyrazolyl, isoxazolyl or morpholino;

- a phenyl substituted with thiomorpholino which may be substituted with oxo;

- a piperazino which may be substituted with alkyl having 1 to 4 carbon atoms or cyclohexyl;

- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from amino, carboxy, guanidino, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.

13. The pharmaceutical agent according to claim 12, which is an analgesic.

14. The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for chronic pains.

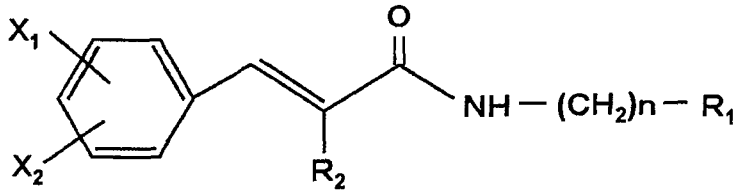
15. The pharmaceutical agent according to claim 14, wherein the therapeutic agent for chronic pains is a therapeutic agent for lumbago, arthralgia, or neuropathic pains.

16. The pharmaceutical agent according to claim 13, wherein the analgesic is a therapeutic agent for neuropathic pains.

17. The pharmaceutical agent according to any one of claims 12 to 16, which is an oral preparation.

18. The pharmaceutical agent according to any one of claims 12 to 16, which is an injectable preparation.

19. Use of a compound or a pharmaceutically acceptable salt or hydrate thereof in the manufacture of a pharmaceutical agent for the treatment of a pain disease, wherein the compound is represented by the following general formula (I):



(I)

wherein n stands for an integer of from 1 to 4;

X_1 and X_2, which are identical or different, stand for a hydrogen, a fluorine, a trifluoromethyl, or a carboxy, and either one of X_1 and X_2 stands for a substituent other than a hydrogen;

R_1 stands for:

- an imidazolyl which may be substituted with alkyl having 1 to 6 carbon atoms or phenyl;
- a pyrrolyl which may be substituted with alkyl having 1 to 4 carbon atoms;
- a phenyl substituted with amino, alkoxy having 1 to 4 carbon atoms, pyrazolyl, isoxazolyl or morpholino;
- a phenyl substituted with thiomorpholino which may be substituted with oxo;
- a piperazino which may be substituted with alkyl having 1 to 4 carbon

atoms or cyclohexyl;

- a thiomorpholino which may be substituted with one or two oxos; or

- any one of substituents selected from amino, carboxy, guanidino, benzoimidazolyl, indazolyl, pyrazolyl, triazolyl, pyridyl, pyrrolidinyl, piperidino, hexamethyleneimino, morpholino, and cyclohexylamino; and

R_2 stands for a hydrogen, a cyano or an alkyl having 1 to 4 carbon atoms.