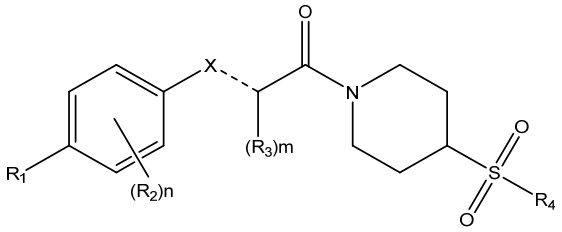
CLAIMS

1. A compound of formula I,



(I)

wherein;

the dotted line [- - - -] represents a single or a double bond;

X is O, CH_2 or CH, provided that when X is O or CH_2 the dotted line is a single bond, and when X is CH the dotted line is a double bond;

R_1 is halogen, halo(C_{1-3})alkyl or halo(C_{1-3})alkoxy;

R_2 is halogen;

or R_1 and R_2 attached to adjacent carbon ring atoms form, together with the carbon ring atoms a fused 2,2-difluoro-1,3-dioxolane ring;

R_3 is hydrogen;

R_4 is (C_{2-6})alkyl, halo(C_{1-3})alkyl, (C_{1-3})alkoxy(C_{1-6})alkyl, (C_{3-6})cycloalkyl, 6-membered heterocyclyl, heterocyclyl(C_{1-3})alkyl, NHR_5 or NR_6R_7, wherein said (C_{3-6})cycloalkyl or heterocyclyl is unsubstituted or substituted with one or more substituents independently selected from hydroxy, (C_{1-3})alkyl and (C_{1-3})alkoxy;

R_5 is hydrogen, (C_{2-6})alkyl, (C_{1-3})alkoxy(C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl(C_{1-3})alkyl, or heterocyclyl(C_{1-3})alkyl, wherein said (C_{3-6})cycloalkyl or heterocyclyl is unsubstituted or substituted with one or more substituents independently selected from hydroxy, (C_{1-3})alkyl and phenyl(C_{1-3})alkyl;

R_6 and R_7 form, together with the nitrogen atom to which they are attached, a pyrrolidine ring wherein said pyrrolidine ring is substituted with 1 or 2 substituents independently selected from (C_{1-3})alkyl, hydroxy(C_{1-6})alkyl and heterocyclyl;

n is an integer selected from 0, 1 or 2;

m is an integer selected from 1 or 2;

or a pharmaceutically acceptable salt thereof;

with the proviso that the compound is not

2-(4-chlorophenoxy)-1-(4-(ethylsulfonyl)piperidin-1-yl)ethan-1-one,

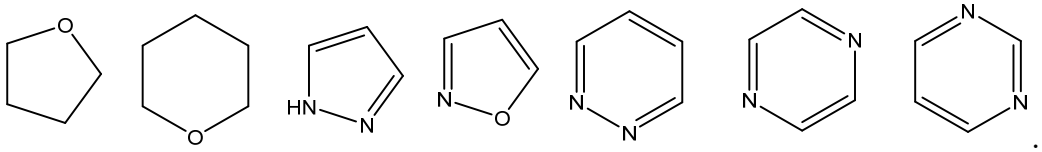
2-(4-fluorophenoxy)-1-(4-(isobutylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-(isobutylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(2,4-dichlorophenoxy)-1-(4-(ethylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(2,4-dichlorophenoxy)-1-(4-(isobutylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-fluorophenoxy)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)ethan-1-one,
2-(2,4-dichlorophenoxy)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)ethan-1-one,
3-(4-chlorophenyl)-1-(4-(ethylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
1-(4-(ethylsulfonyl)piperidin-1-yl)-3-(4-fluorophenyl)prop-2-en-1-one,
3-(4-chlorophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
3-(2,4-dichlorophenyl)-1-(4-(ethylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
3-(4-bromophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)propan-1-one,
3-(3,4-dichlorophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)propan-1-one,
3-(3-chloro-4-fluorophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)propan-1-one,
3-(4-chloro-3-fluorophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)propan-1-one,
3-(2,4-dichlorophenyl)-1-(4-(isobutylsulfonyl)piperidin-1-yl)propan-1-one,
3-(4-chlorophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
1-(4-(isobutylsulfonyl)piperidin-1-yl)-3-(4-(trifluoromethyl)phenyl)propan-1-one,
3-(4-bromophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)propan-1-one,
3-(3-chloro-4-fluorophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)propan-1-one,
3-(3,4-dichlorophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)propan-1-one,
3-(2,4-dichlorophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)propan-1-one,
3-(4-chloro-3-fluorophenyl)-1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)propan-1-one,
1-(4-((furan-2-ylmethyl)sulfonyl)piperidin-1-yl)-3-(4-(trifluoromethyl)phenyl)-propan-1-one,
1-(4-(ethylsulfonyl)piperidin-1-yl)-3-(4-fluorophenyl)propan-1-one,

1-(3-(4-chlorophenyl)propanoyl)piperidine-4-sulfonamide, or
1-(3-(4-fluorophenyl)propanoyl)piperidine-4-sulfonamide.

2. The compound according to claim 1, wherein
X is O;
R_1 is halogen;
R_3 is hydrogen;
R_4 is (C_{3-6})alkyl, (C_{1-3})alkoxy(C_{2-6})alkyl, heterocyclyl(C_{1-3})alkyl, or NHR_5, wherein said heterocyclyl is unsubstituted;
R_5 is (C_{1-3})alkoxy(C_{2-6})alkyl, hydroxy(C_{3-6})alkyl, (C_{3-6})cycloalkyl(C_{1-3})alkyl, or heterocyclyl(C_{1-3})alkyl, wherein said (C_{3-6})cycloalkyl or heterocyclyl is unsubstituted or substituted with one substituent independently selected from hydroxy and (C_{1-2})alkyl;
n is 0;
m is 2;
or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1, wherein
X is CH;
R_1 is halogen;
R_3 is hydrogen;
R_4 is (C_{3-6})alkyl, (C_{1-3})alkoxy(C_{2-6})alkyl, heterocyclyl(C_{1-3})alkyl, or NHR_5, wherein said heterocyclyl is unsubstituted;
R_5 is (C_{1-3})alkoxy(C_{2-6})alkyl, hydroxy(C_{3-6})alkyl, (C_{3-6})cycloalkyl(C_{1-3})alkyl, or heterocyclyl(C_{1-3})alkyl, wherein said (C_{3-6})cycloalkyl or heterocyclyl is unsubstituted or substituted with one substituent independently selected from hydroxy and (C_{1-2})alkyl;
n is 0;
m is 1;
or a pharmaceutically acceptable salt thereof.

4. The compound according to any one of claims 1 to 3, wherein the heterocyclyl is any one of the following groups:



5. The compound according to claim 1, wherein the compound is;

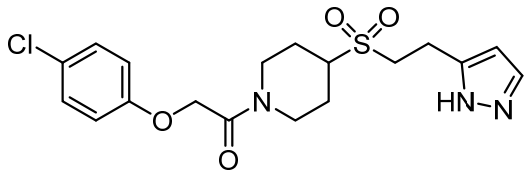
2-(3,4-dichlorophenoxy)-1-(4-(isopropylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-(((tetrahydro-2H-pyran-3-yl)methyl)sulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-(difluoromethyl)phenoxy)-1-(4-(isopropylsulfonyl)piperidin-1-yl)ethan-1-one,
1-(4-((2-(1H-pyrazol-5-yl)ethyl)sulfonyl)piperidin-1-yl)-2-(4-chlorophenoxy)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-(2-ethoxyethyl)piperidine-4-sulfonamide,
2-(4-chlorophenoxy)-1-(4-(pentan-3-ylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(3,4-difluorophenoxy)-1-(4-(isopropylsulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-((difluoromethyl)sulfonyl)piperidin-1-yl)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-(isopropylsulfonyl)piperidin-1-yl)ethan-1-one,
1-(4-(isopropylsulfonyl)piperidin-1-yl)-2-(4-(trifluoromethoxy)phenoxy)ethan-1-one,
2-(4-chloro-3-fluorophenoxy)-1-(4-(isopropylsulfonyl)piperidin-1-yl)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-(2-methoxyethyl)piperidine-4-sulfonamide,
N-butyl-1-(2-(4-chlorophenoxy)acetyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(4-hydroxy-4-methylpentyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(3-hydroxy-3-methylbutyl)piperidine-4-sulfonamide,
2-(4-chlorophenoxy)-1-(4-((2,2-dimethylpyrrolidin-1-yl)sulfonyl)piperidin-1-yl)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-cyclopropylpiperidine-4-sulfonamide,
2-(4-chlorophenoxy)-1-(4-((3-methoxypropyl)sulfonyl)piperidin-1-yl)ethan-1-one,
1-(4-(sec-butylsulfonyl)piperidin-1-yl)-2-(4-chlorophenoxy)ethan-1-one,
2-(4-chlorophenoxy)-1-(4-((2-(tetrahydrofuran-2-yl)ethyl)sulfonyl)piperidin-1-

yl)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-(2-hydroxy-2-methylbutyl)piperidine-4-sulfonamide,
N-((1H-pyrazol-5-yl)methyl)-1-(2-(4-chlorophenoxy)acetyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(isoxazol-3-ylmethyl)piperidine-4-sulfonamide,
(R)-1-(4-((3-(1H-pyrazol-5-yl)pyrrolidin-1-yl)sulfonyl)piperidin-1-yl)-2-(4-chlorophenoxy)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-((1-hydroxycyclobutyl)methyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-((1-methyl-1H-pyrazol-3-yl)methyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-((1-ethyl-1H-pyrazol-3-yl)methyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(pyridazin-3-ylmethyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-((1-hydroxycyclopentyl)methyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(3-methoxypropyl)piperidine-4-sulfonamide,
1-(2-(4-chlorophenoxy)acetyl)-N-(pyrazin-2-ylmethyl)piperidine-4-sulfonamide,
2-(4-chlorophenoxy)-1-(4-(propylsulfonyl)piperidin-1-yl)ethan-1-one,
1-(4-(isopropylsulfonyl)piperidin-1-yl)-2-(4-(trifluoromethyl)phenoxy)ethan-1-one,
1-(2-(4-chlorophenoxy)acetyl)-N-(2-hydroxy-2-methylpropyl)piperidine-4-sulfonamide,
1-(3-(4-chlorophenyl)propanoyl)-N-(3-methoxypropyl)piperidine-4-sulfonamide,
(E)-3-(4-chlorophenyl)-1-(4-(isopropylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-1-(3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)acryloyl)-N-((1-ethyl-1H-pyrazol-3-yl)methyl)piperidine-4-sulfonamide,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-((1-ethyl-1H-pyrazol-3-yl)methyl)piperidine-4-sulfonamide,
(E)-3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-(4-(isopropylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-(2-hydroxy-2-methylpropyl)piperidine-4-

sulfonamide,
(E)-3-(4-bromophenyl)-1-(4-((3-methoxypropyl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-1-(3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)acryloyl)-N-(3-hydroxy-3-methylbutyl)piperidine-4-sulfonamide,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-(3-hydroxy-3-methylbutyl)piperidine-4-sulfonamide,
(R,E)-1-(3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)acryloyl)-N-((tetrahydrofuran-2-yl)methyl)piperidine-4-sulfonamide,
(R,E)-3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-(4-((3-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-(2-ethoxyethyl)piperidine-4-sulfonamide,
(E)-1-(4-((2-(1H-pyrazol-1-yl)ethyl)sulfonyl)piperidin-1-yl)-3-(4-chlorophenyl)prop-2-en-1-one,
(E)-N-(2-(1H-pyrazol-1-yl)ethyl)-1-(3-(4-chlorophenyl)acryloyl)piperidine-4-sulfonamide,
(R,E)-3-(4-chlorophenyl)-1-(4-((3-(2-hydroxypropan-2-yl)pyrrolidin-1-yl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
(R,E)-1-(3-(4-chlorophenyl)acryloyl)-N-((tetrahydrofuran-2-yl)methyl)piperidine-4-sulfonamide,
(E)-N-((1-benzyl-1H-pyrazol-3-yl)methyl)-1-(3-(4-chlorophenyl)acryloyl)piperidine-4-sulfonamide,
(E)-N-(3-methoxypropyl)-1-(3-(4-(trifluoromethyl)phenyl)acryloyl)piperidine-4-sulfonamide,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-(3-methoxypropyl)piperidine-4-sulfonamide,
(E)-3-(4-chlorophenyl)-1-(4-(propylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-3-(4-chlorophenyl)-1-(4-((difluoromethyl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-3-(4-chlorophenyl)-1-(4-(cyclobutylsulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-3-(4-chlorophenyl)-1-(4-((2-methoxypyrimidin-5-yl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
1-(4-((2-(1H-pyrazol-1-yl)ethyl)sulfonyl)piperidin-1-yl)-2-(4-chlorophenoxy)ethan-

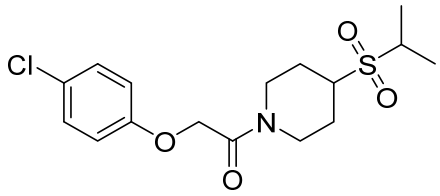
1-one,
N-((1-benzyl-1H-pyrazol-3-yl)methyl)-1-(2-(4-chlorophenoxy)acetyl)piperidine-4-sulfonamide,
(E)-1-(3-(4-chlorophenyl)acryloyl)-N-(2-methoxyethyl)piperidine-4-sulfonamide,
(E)-3-(2,2-difluorobenzo[d][1,3]dioxol-5-yl)-1-(4-((3-methoxypropyl)sulfonyl)-piperidin-1-yl)prop-2-en-1-one,
(E)-3-(4-chlorophenyl)-1-(4-((3-methoxypropyl)sulfonyl)piperidin-1-yl)prop-2-en-1-one,
(E)-N-((1H-pyrazol-5-yl)methyl)-1-(3-(4-chlorophenyl)acryloyl)piperidine-4-sulfonamide, or
(E)-1-(3-(4-chlorophenyl)acryloyl)piperidine-4-sulfonamide,
or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 1, wherein the compound is



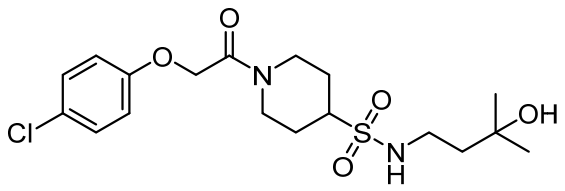
or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1, wherein the compound is



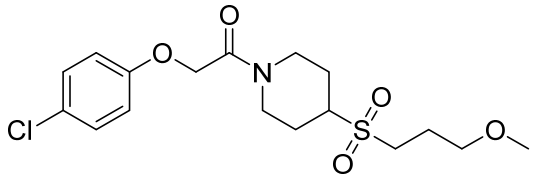
or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 1, wherein the compound is



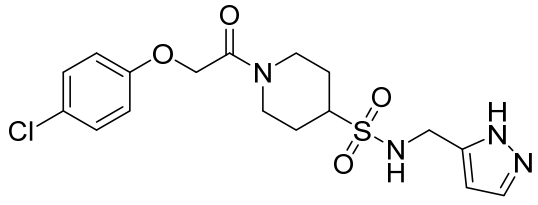
or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 1, wherein the compound is



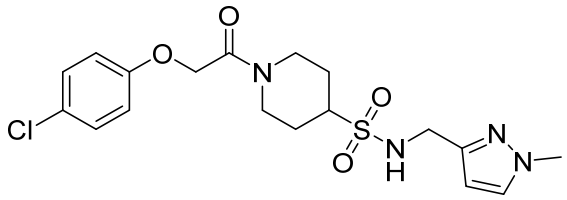
or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 1, wherein the compound is



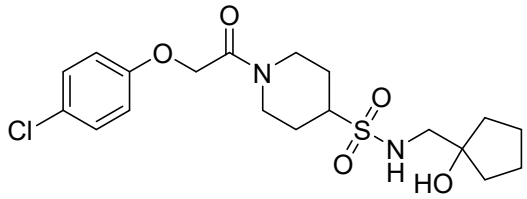
or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 1, wherein the compound is



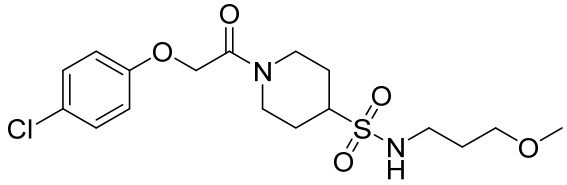
or a pharmaceutically acceptable salt thereof.

12. The compound according to claim 1, wherein the compound is



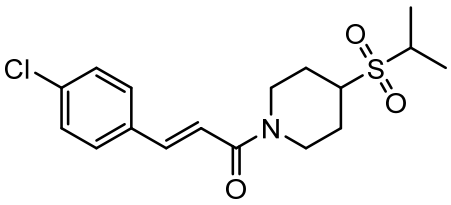
or a pharmaceutically acceptable salt thereof.

13. The compound according to claim 1, wherein the compound is



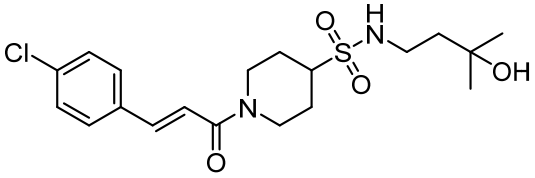
or a pharmaceutically acceptable salt thereof.

14. The compound according to claim 1, wherein the compound is



or a pharmaceutically acceptable salt thereof.

15. The compound according to claim 1, wherein the compound is



or a pharmaceutically acceptable salt thereof.

16. The compound according to any one of claims 1 to 15 for use as a medicament.

17. Use of the compound according to any one of claims 1 to 15 in the manufacture of a medicament for treatment of a disorder, condition, or disease where a GPR183 antagonist is indicated to be useful.

18. The use according to claim 17, wherein the disorder, condition, or disease is chronic pain e.g osteoarthritis, chronic low back pain, neuropathic pain and immune system diseases e.g inflammatory bowel diseases e.g. Colitis and Chron's diseases, multiple sclerosis, rheumatoid arthritis, inflammatory pulmonary diseases e.g. asthma and psoriasis ameliorated by inhibition of GPR183 receptors.

19. A pharmaceutical composition comprising at least one compound according to any one of claims 1 to 15 and a pharmaceutically acceptable carrier, diluent and/or excipient.

20. The pharmaceutical composition according to claim 19 wherein the composition comprises further at least one other active ingredient.