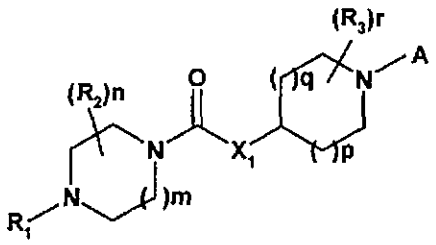
Claims:

1. A compound of the formula I



(I),

or a salt thereof, wherein

R_1 is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkinyl, C_{3-6}cycloalkyl, C_{5-6}cycloalkenyl or C_{3-6}cycloalkyl-C_{1-4}alkyl; wherein said C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkinyl or C_{3-6}cycloalkyl-C_{1-4}alkyl may be substituted once or more than once by halogen; and wherein said C_{3-6}cycloalkyl or C_{5-6}cycloalkenyl may be substituted once or more than once by halogen, C_{1-4}alkyl or C_{1-4}halogenalkyl;

m is 1 or 2;
n is 0, 1, 2, 3 or 4;

each R_2 independently is halogen, hydroxyl, amino, cyano, nitro, C_{1-6}alkyl, C_{1-6}halogenalkyl, C_{1-6}hydroxyalkyl, C_{1-4}alkoxy-C_{1-6}alkyl, amino-C_{1-6}alkyl, C_{1-4}alkyl-amino-C_{1-6}alkyl, di(C_{1-4}alkyl)-amino-C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}halogenalkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, C_{2-6}alkenyl, C_{2-6}halogenalkenyl, C_{2-6}alkinyl or C_{2-6}halogenalkinyl;
or C_{3-6}cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C_{3-6}cycloalkyl may be attached directly to the methylene or via a C_{1-2}alkylene, and wherein the C_{3-6}cycloalkyl may be substituted once or more than once by halogen;
or two R_2 at the same carbon atom form together with said carbon atom a C_{3-6}cycloalkyl;

X_1 is oxygen or $-N(R_4)$-;

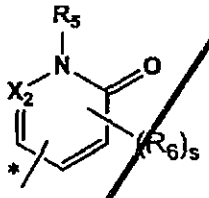
R_4 is hydrogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, or C_{3-6}cycloalkyl-C_{1-2}alkyl;

p is 1 and q is 1;
p is 0 and q is 1; or
p is 0 and q is 0;

r is 0, 1, 2, 3 or 4;

each R_3 independently is halogen, hydroxyl, amino, cyano, nitro, C_{1-6}alkyl, C_{1-6}halogenalkyl, C_{1-6}hydroxyalkyl, C_{1-4}alkoxy-C_{1-6}alkyl, amino-C_{1-6}alkyl, C_{1-4}alkyl-amino-C_{1-6}alkyl, di(C_{1-4}alkyl)-amino-C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}halogenalkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, C_{2-6}alkenyl, C_{2-6}halogenalkenyl, C_{2-6}alkinyl or C_{2-6}halogenalkinyl;
or C_{3-6}cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C_{3-6}cycloalkyl may be attached directly to the methylene or via a C_{1-2}alkylene, and wherein the C_{3-6}cycloalkyl may be substituted once or more than once by halogen;
or two R_3 at the same carbon atom form together with said carbon atom a C_{3-6}cycloalkyl;

A is



wherein the bond marked with the asterisk is attached to the nitrogen atom;

R_5 is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkinyl, C_{3-6}cycloalkyl, C_{5-6}cycloalkenyl or C_{3-6}cycloalkyl-C_{1-4}alkyl; wherein said C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkinyl or C_{3-6}cycloalkyl-C_{1-4}alkyl may be substituted once or more than once by halogen, hydroxyl or C_{1-6}alkoxy; and wherein said C_{3-6}cycloalkyl or C_{5-6}cycloalkenyl may be substituted once or more than once by halogen, C_{1-4}alkyl or C_{1-4}halogenalkyl;

X_2 is nitrogen or carbon;

s is 0, 1, 2 or 3;

each R_6 independently is halogen, hydroxyl, amino, cyano, nitro, C_{1-6}alkyl, C_{1-6}halogenalkyl, C_{1-6}hydroxyalkyl, C_{1-4}alkoxy-C_{1-6}alkyl, amino-C_{1-6}alkyl, C_{1-4}alkyl-amino-C_{1-6}alkyl, di(C_{1-4}alkyl)-amino-C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}halogenalkoxy, C_{1-6}alkylamino, di(C_{1-6}alkyl)amino, C_{2-6}alkenyl, C_{2-6}halogenalkenyl, C_{2-6}alkinyl or C_{2-6}halogenalkinyl;

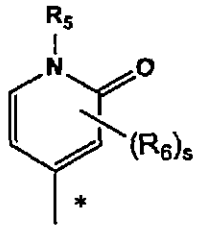
or C_{3-6}cycloalkyl, wherein one carbon atom may be replaced by an oxygen atom, wherein the C_{3-6}cycloalkyl may be attached directly to the methylene or via a C_{1-2}alkylene, and wherein the C_{3-6}cycloalkyl may be substituted once or more than once by halogen.

2. A compound of formula I according to claim 1, wherein X_1 is oxygen; or a salt thereof.

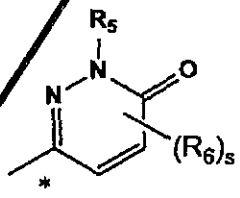
3. A compound of formula I according to any of claims 1 or 2, wherein p is 1 and q is 1; or a salt thereof.

4. A compound of formula I according to any of claims 1 to 3, wherein R_1 is isopropyl, cyclopropyl, cyclobutyl or cyclopentyl and m is 1; or a salt thereof.

5. A compound of formula I according any of claims 1 to 4, wherein A is selected from A3 and A4



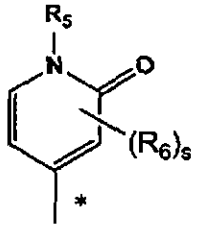
(A3);



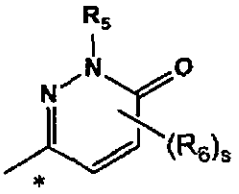
(A4);

wherein the bond marked with the asterisk is attached to the nitrogen atom;
or a salt thereof.

6. A compound of formula I according to claim 1, wherein
R_1 is isopropyl or cyclobutyl; m is 1; n is 0, 1 or 2; each R_2 independently is halogen, C_{1-4}alkyl, C_{1-4}halogenalkyl, C_{1-4}alkoxy, C_{1-4}halogenalkoxy or C_{3-4}cycloalkyl; or two R_2 at the same carbon atom form together with said carbon atom a C_{3-4}cycloalkyl;
X_1 is oxygen;
p is 1 and q is 1; r is 0, 1 or 2; wherein each R_3 independently is halogen, C_{1-4}alkyl, C_{1-4}halogenalkyl, C_{1-4}alkoxy, C_{1-4}halogenalkoxy or C_{3-4}cycloalkyl; or two R_3 at the same carbon atom form together with said carbon atom a C_{3-4}cycloalkyl; A is selected from A3 and A4



(A3);



(A4);

wherein the bond marked with the asterisk is attached to the nitrogen atom;

R_5 is hydrogen or methyl;

s is 0, 1 or 2; and

each R_6 independently is halogen, C_{1-4}alkyl, C_{1-4}halogenalkyl, C_{1-4}alkoxy, C_{1-4}halogenalkoxy or C_{3-4}cycloalkyl;

or a salt thereof.

7. A compound of formula I according to claim 1, wherein said compound is selected from the group consisting of

1-(6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate;

1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate;

1-(6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate;

1-(6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclopropylpiperazine-1-carboxylate;

1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate;

1-(1-ethyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate;

1-(1-methyl-2-oxo-1,2-dihydropyridin-4-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate;

1-(2-oxo-1,2-dihydropyridin-4-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate;

1-(2-oxo-1,2-dihydropyridin-4-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate; and

1-(6-oxo-1,6-dihydropyridin-3-yl)piperidin-4-yl 4-isopropylpiperazine-1-carboxylate;

or salts of these compounds.

8. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to any one of claims 1 to 7 and one or more pharmaceutically acceptable carriers.

9. A combination comprising a therapeutically effective amount of the compound according to any one of claims 1 to 7 and one or more therapeutically active agents.

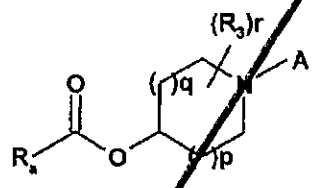
10. A method of treating a disorder or a disease in a subject mediated by H3 receptors, wherein the method comprises administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 7.

11. A compound according to any one of claims 1 to 7, for use as a medicament.

12. Use of a compound according to any one of claims 1 to 7, for the treatment of a disorder or disease in a subject mediated by H3 receptors.

13. Use of a compound according to any one of claims 1 to 7, for the treatment of a disorder or disease in a subject characterized by an abnormal activity of H3 receptors.

14. A compound of formula II-1



(II-1);

or a salt thereof; in which p, q, r, R_3 and A are as defined under formula I; and R_a is a leaving group.

15. A free form of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate in solid form; or a salt of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate in solid form, wherein said salt is the citrate, hydrochloride, fumarate, adipate, maleate or sebacate of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate.

16. A pharmaceutical composition, which comprises a free form or a salt as defined claim 15 as active ingredient and at least one pharmaceutically acceptable carrier.

17. A method of preparing a citrate salt of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate *in crystalline form* comprising the steps of

(a) preparing a solution of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate and citric acid in acetone, wherein the 1-(1-methyl-6-oxo-

1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate : citric acid ratio is about 1 : 2;

(b) adding to the solution of step (a) an ether antisolvent, e.g. diethyl ether, until an acetone : ether antisolvent volume ratio from 1 : 1 to 1 : 5 is reached; and

(e) isolate the solids by filtration to obtain the citrate salt of 1-(1-methyl-6-oxo-1,6-dihydropyridazin-3-yl)piperidin-4-yl 4-cyclobutylpiperazine-1-carboxylate in crystalline form.

CLAIMS

1. An invention not claimed in any divisional application.