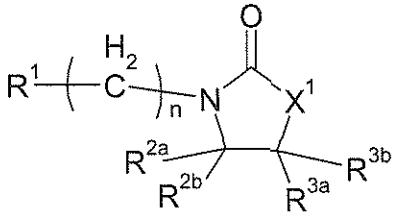
1995, *1*, 534) and slowed the growth of tumours in nude mice injected with human endometrial cancer cells (Z. Wang et al. *Oncogene* **2007**, *26*, 5107).

The invention is concerned with novel compounds of formula I,



I

wherein

X^1 is O or NH;

n is an integer between 1 to 4;

R^1 is hydrogen, cyano, $-C(O)R^{1a}$, $-C(O)NR^{1b}R^{1c}$, heteroaryl or CH_2OH;

R^{1a} is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl or heteroaryl;

R^{1b} and R^{1c} are each independently hydrogen, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said C_1-C_6 alkyl, said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of hydroxy, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, haloC_1-C_6 alkyl and haloC_1-C_6 alkoxy;

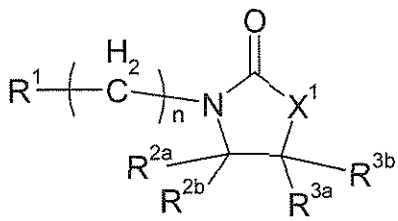
R^{2a} is hydrogen or C_1-C_6 alkyl;

R^{2b} is haloC_1-C_6alkyl, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly with one or two substituents independently selected from the group consisting of hydroxy, halogen, C_1-C alkyl and haloC_1-C_6alkyl;

R^{3a} and R^{3b} are each independently hydrogen, phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of halogen, C_1-C_6alkyl and haloC_1-C_6alkyl;

or pharmaceutically acceptable salts.

According to one aspect, there is provided a compound of formula (I):



(I)

wherein

X^1 is O or NH;

n is an integer between 1 to 4;

R^1 is hydrogen, cyano, $-C(O)R^{1a}$, $-C(O)NR^{1b}R^{1c}$, heteroaryl or CH_2OH;

R^{1a} is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl or heteroaryl;

R^{1b} and R^{1c} are each independently hydrogen, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said C_1-C_6 alkyl, said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of hydroxy, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, haloC_1-C_6 alkyl and haloC_1-C_6 alkoxy;

R^{2a} is hydrogen or C_1-C_6 alkyl;

R^{2b} is haloC_1-C_6alkyl, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly with one or two substituents independently selected from the group consisting of hydroxy, halogen, C_1-C alkyl and haloC_1-C_6alkyl;

R^{3a} and R^{3b} are each independently phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of halogen, C_1-C_6alkyl and haloC_1-C_6alkyl;

or pharmaceutically acceptable salts.

According to another aspect, there is provided a compound as defined above for use in the treatment or prophylaxis of polycystic kidney disease, asthma, brain edema, inflammatory bowel disease, transplant rejection, atherosclerosis, renal fibrosis, cancer, restenosis.

According to another aspect, there is provided a compound as defined above for use as a therapeutically active substance.

According to another aspect, there is provided a compound as defined above for use in the treatment or prophylaxis of polycystic kidney disease.

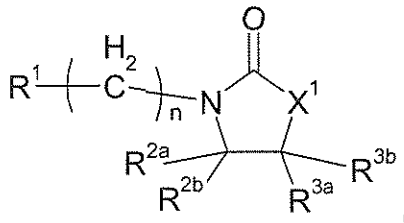
According to another aspect, there is provided the use of a compound as defined above for the preparation of a medicament for the treatment or prophylaxis of polycystic kidney disease, asthma, brain edema, inflammatory bowel disease, transplant rejection, atherosclerosis, renal fibrosis, cancer, restenosis.

The application provides a method for treating polycystic kidney disease comprising administering to a patient in need thereof a therapeutically effective amount of the compound of Formula I, I' or I".

Further, the disclosure is concerned with a process for the manufacture of the above compounds, pharmaceutical preparations which contain such compounds, the use of these compounds for the production of pharmaceutical preparations.

Claims

1. A compound of formula (I):



(I)

wherein

X^1 is O or NH;

n is an integer between 1 to 4;

R^1 is hydrogen, cyano, $-C(O)R^{1a}$, $-C(O)NR^{1b}R^{1c}$, heteroaryl or CH_2OH;

R^{1a} is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl or heteroaryl;

R^{1b} and R^{1c} are each independently hydrogen, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said C_1-C_6 alkyl, said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of hydroxy, halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, haloC_1-C_6 alkyl and haloC_1-C_6 alkoxy;

R^{2a} is hydrogen or C_1-C_6 alkyl;

R^{2b} is haloC_1-C_6alkyl, C_1-C_6 alkyl, phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly with one or two substituents independently selected from the group consisting of hydroxy, halogen, C_1-C alkyl and haloC_1-C_6alkyl;

R^{3a} and R^{3b} are each independently phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more, particularly one to three substituents independently selected from the group consisting of halogen, C_1-C_6alkyl and haloC_1-C_6alkyl;

or pharmaceutically acceptable salts.

2. The compound according to claim 1, wherein X^1 is O.

3. The compound according to any one of claim 1 or 2, wherein n is 1 or 2, more particularly wherein n is 1.

4. A compound according to any one of claims 1 to 3, wherein R^1 is cyano, $-C(O)R^{1a}$ or $-C(O)NR^{1b}R^{1c}$.

5. A compound according to any one of claims 1 to 4, wherein R^1 is $-C(O)R^{1a}$ or $-C(O)NR^{1b}R^{1c}$.

6. The compound according to any one of claims 1 to 5, wherein R^{1a} is hydrogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, more particularly wherein R^{1a} is C_1-C_3 alkoxy, most particularly wherein R^{1a} is methoxy or ethoxy.

7. The compound according to any one of claims 1 to 6, wherein R^{1b} and R^{1c} are each independently hydrogen, C_1-C_3 alkyl, phenyl or heteroaryl, more particularly wherein R^{1b} and R^{1c} are each independently hydrogen or C_1-C_3 alkyl, most particularly wherein R^{1b} and R^{1c} are each independently hydrogen, methyl or ethyl.

8. The compound according to any one of claims 1 to 7, wherein R^{2a} is hydrogen.

9. The compound according to any one of claims 1 to 8, wherein R^{2b} is perhaloC_1-C_3alkyl, C_1-C_3 alkyl, phenyl or pyridinyl, wherein said phenyl or said pyridinyl are optionally substituted with one or two substituents independently selected from the group consisting of halogen, C_1-C_3 alkyl and haloC_1-C_3alkyl.

10. A compound according to any one of claims 1 to 9, wherein R^{2b} is phenyl or pyridinyl, wherein said phenyl or said pyridinyl are optionally substituted with one or two substituents independently selected from the group consisting of halogen and C_1-C_3 alkyl.

11. A compound according to any one of claims 1 to 10, wherein R^{2b} is phenyl optionally substituted with one or two substituents independently selected from the group consisting of chloro, fluoro and methyl.

12. The compound according to any one of claims 1 to 11, wherein R^{3a} and R^{3b} are each independently phenyl or heteroaryl, wherein said phenyl or said heteroaryl are optionally substituted with one or more substituents independently selected from the group consisting of halogen, C_1-C_6alkyl and haloC_1-C_6alkyl.

13. A compound according to any one of claims 1 to 12, wherein R^{3a} and R^{3b} are each independently phenyl optionally substituted with one to two chloro or fluoro.

14. A compound according to any one of claims 1 to 13, wherein both R^{3a} and R^{3b} are phenyl substituted with one fluoro.

15. A compound according to any one of claims 1 to 14, selected from:

- 2-[(S)-4-(2,4-Difluoro-phenyl)-5,5-bis-(4-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- 2-[(S)-4,5,5-Tris-(4-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- 2-[(S)-5,5-Bis-(4-fluoro-phenyl)-4-(2-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- 2-[(S)-4,5,5-Tris-(2-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- 2-[(S)-5,5-Bis-(3-fluoro-phenyl)-4-(2-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- 2-[(S)-4-(2-Fluoro-phenyl)-2-oxo-5,5-diphenyl-oxazolidin-3-yl]-acetamide;

- 2-[(S)-4-(2-Chloro-phenyl)-5,5-bis-(4-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide;
- (S)-methyl 2-(4-(2-fluorophenyl)-5,5-bis(4-fluorophenyl)-2-oxooxazolidin-3-yl)acetate;
-(S)-2-(4-(2-fluorophenyl)-5,5-bis(4-fluorophenyl)-2-oxooxazolidin-3-yl)-N-methylacetamide;
-(S)-2-(5,5-bis(3,4-difluorophenyl)-2-oxo-4-phenyloxazolidin-3-yl)acetamide;

and pharmaceutically acceptable salts thereof.

16. A compound according to any one of claims 1 to 15, 2-[(S)-5,5-Bis-(4-fluoro-phenyl)-4-(2-fluoro-phenyl)-2-oxo-oxazolidin-3-yl]-acetamide.

17. A compound according to any one of claims 1 to 16 for use in the treatment or prophylaxis of polycystic kidney disease, asthma, brain edema, inflammatory bowel disease, transplant rejection, atherosclerosis, renal fibrosis, cancer, restenosis.

18. A compound according to any one of claims 1 to 16 for use as a therapeutically active substance.

19. A compound according to claim 15 or 16 for use in the treatment or prophylaxis of polycystic kidney disease.

20. The use of a compound according to any one of claims 1 to 16 for the preparation of a medicament for the treatment or prophylaxis of polycystic kidney disease, asthma, brain edema, inflammatory bowel disease, transplant rejection, atherosclerosis, renal fibrosis, cancer, restenosis.