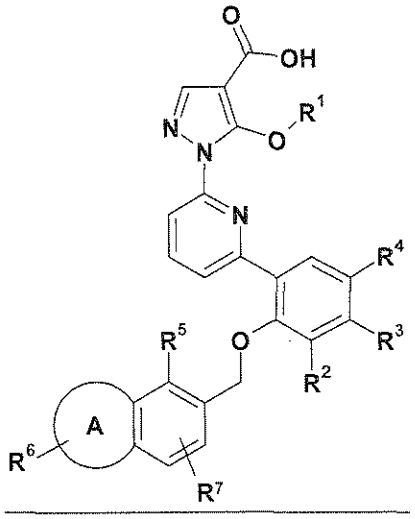
BRIEF SUMMARY ~~OF THE INVENTION~~

The present ~~invention~~ disclosure provides novel compounds which activate or potentiate sGC and are thus useful for treating a variety of diseases and disorders that can be alleviated by sGC activation or potentiation including cardiovascular, inflammatory and renal diseases. This disclosure ~~invention~~ also relates to pharmaceutical compositions comprising these compounds, methods of using these compounds in the treatment of various diseases and disorders, processes for preparing these compounds and intermediates useful in these processes.

In a first aspect, the present disclosure provides for a compound of the formula I



I

wherein:

A is a 5-7 membered saturated heterocyclyl group containing one nitrogen and optionally one oxygen, wherein one carbon of said heterocyclyl group is optionally substituted with one or two groups selected from C_{1-3}alkyl and oxo ;

R^1 is C_{1-4} alkyl optionally substituted with a methoxy group;

R^2 is selected from H, F, Cl, C_{1-3}alkyl, -CN, -OMe and $-CF_3$;

R^3 is selected from H and $-CH_3$;

R^4 is selected from H, F, $-CH_3$ and -OMe;

R^5 is selected from H, Cl, $-CH_3$, $-CH_2CH_3$, $-CF_3$, F, and -OMe;

R^6 is bonded to the nitrogen on A and is selected from H, C_{1-6}alkyl, -$(CH_2)_n$$C_{3-6}$cycloalkyl, -C(O)$C_{1-6}$alkyl, -$(CH_2)_n$ heterocyclyl, -$(CH_2)_n$ aryl -$(CH_2)_n$ heteroaryl, -SO_2aryl, SO_2C_{1-6}alkyl wherein said C_{1-6}alkyl, -$(CH_2)_n$ heterocyclyl, -$(CH_2)_n$ cycloalkyl, -$(CH_2)_n$ aryl and -$(CH_2)_n$ heteroaryl are optionally substituted with one to four groups independently selected from C_{1-3}alkyl, halogen, C_{1-3}alkoxy, $-CF_3$, -OH, oxo, -$(CH_2)_{1-3}O(CH_2)_{2-3}OH$, and $-SO_2CH_3$;
R^7 is selected from H, $-CH_3$, $-CH_2CH_3$, $-CF_3$, F, and –CN;
n is 0, 1 or 2
or a salt thereof.

~~In a further aspect, t~~The present ~~invention~~ disclosure also provides for activators of soluble guanylate cyclase having solubility properties consistent with acceptable pharmacokinetic properties. As is known in the art, poorly soluble compounds may suffer from poor human exposure. The compounds of the present ~~invention~~ disclosure would be expected to have exposure properties consistent with being a suitable drug.

~~In a further aspect, t~~The present ~~invention~~ disclosure provides compounds with metabolic stability properties consistent with acceptable pharmacokinetic properties. As is known in the art, compounds having poor metabolic stability may not readily achieve desirable therapeutic levels. The compounds of the present ~~invention~~ disclosure would be expected to have metabolic stability properties consistent with being a suitable drug.

In another aspect, the present disclosure provides a pharmaceutical composition comprising a compound as defined herein and a pharmaceutically acceptable excipient or carrier.

In another aspect, the present disclosure provides a compound as defined herein for use in treating a disease or disorder that can be alleviated by sGC activation or potentiation.

In another aspect, the present disclosure provides use of a compound as defined herein in the manufacture of a medicament for the treatment of a disease or disorder selected from the group consisting of a cardiovascular disease, inflammatory disease, hepatic fibrotic disorder, renal fibrotic disorder, pulmonary fibrotic disorder and cardiac fibrotic disorder.

In another aspect, the present disclosure provides use of a compound as defined herein in the manufacture of a medicament for the treatment of a disease selected from the group consisting of a renal disease, overactive bladder, benign prostatic hyperplasia, erectile dysfunction, Alzheimer's disease, Parkinson's disease and neuropathic pain.

In another aspect, the present disclosure provides use of a compound as defined herein in the manufacture of a medicament for the treatment of diabetic nephropathy.

DETAILED DESCRIPTION OF THE INVENTION

In an embodiment, there are provided compounds of the formula I

116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 136, 137, 139, 140, 141, 142, 145, 146, 152, 153, 154, 155, 157, 158, 159,161, 162, 163, 164, 165, 166, 167, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 184, 185, 186, 187, 188, 189, 191, 193, 194, 195, 196, 197, 198, 199, 201, 202, 203, 204, 205, 206, 207, 208, 210, 211, 212, 213, 214, 215, 216, 220, 222, 223, 224, 225, 227, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257 and the pharmaceutically acceptable salts thereof.

13. A pharmaceutical composition comprising a compound according to any of claims 1 to 12 and a pharmaceutically acceptable excipient or carrier.

14. A compound according to any of claims 1 to 12 for use in ~~method of~~ treating a disease or disorder that can be alleviated by sGC activation or potentiation ~~comprising administering a therapeutically effective amount of a compound according to any of claims 1 to 12 to patient in need thereof~~.

15. The compound ~~method~~ according to claim 14 wherein the disease or disorder is selected from a cardiovascular disease, inflammatory disease, hepatic fibrotic disorder, renal fibrotic disorder, pulmonary fibrotic disorder and cardiac fibrotic disorder.

16. The compound ~~method~~ according to claim 14 wherein the disease is selected from renal disease, overactive bladder, benign prostatic hyperplasia, erectile dysfunction, Alzheimer's disease, Parkinson's disease and neuropathic pain.

17. The compound ~~method~~ according to claim 14 wherein the disease is diabetic nephropathy.

18. Use of a compound according to any of claims 1 to 12 in the manufacture of a medicament for the treatment of a disease or disorder selected from the group consisting of a cardiovascular disease, inflammatory disease, hepatic fibrotic disorder, renal fibrotic disorder, pulmonary fibrotic disorder and cardiac fibrotic disorder.

19. Use of a compound according to any of claims 1 to 12 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of a renal disease, overactive bladder, benign prostatic hyperplasia, erectile dysfunction, Alzheimer's disease, Parkinson's disease and neuropathic pain.

20. Use of a compound according to any of claims 1 to 12 in the manufacture of a medicament for the treatment of diabetic nephropathy.