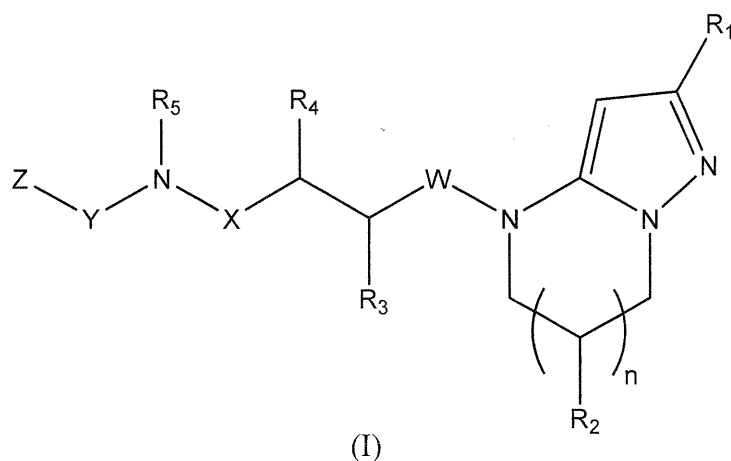


sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride and the like.

[0057] Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum and the like.

Summary of Invention

[0058] ~~According to the invention~~ In an aspect, there is provided a compound of formula (I),



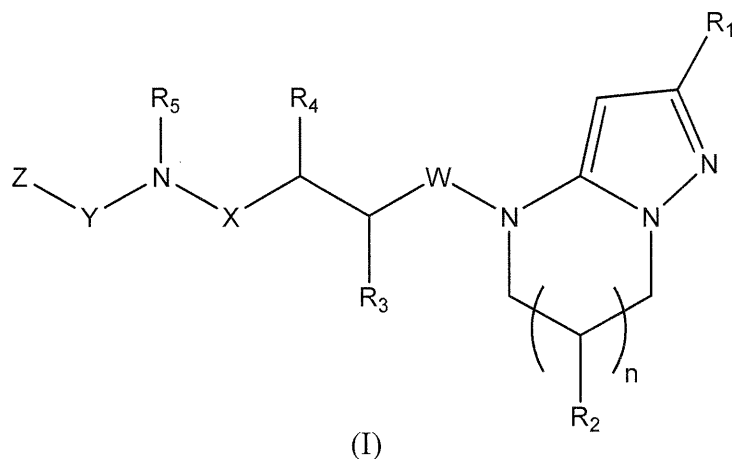
or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

[0059] R_1 represents H; optionally substituted alkyl (wherein optional substituents include one or more substituents each independently selected from C_{1-6} alkoxy, NH_2 , $-NHC_{1-3}$ alkyl and $-N(C_{1-3}alkyl)_2$); $-C(O)Oalkyl$; haloalkyl; haloalkoxy; or $-alkylaryl$;

[0060] each R_2 independently represents H; optionally substituted alkyl (wherein optional substituents include one or more substituents each independently selected from C_{1-6} alkoxy, NH_2 , $-NHC_{1-3}$ alkyl and $-N(C_{1-3}alkyl)_2$); $-alkylaryl$; optionally substituted carbocyclyl (wherein optional substituents include one or more substituents each independently selected from C_{1-6} alkyl, C_{1-6} alkoxy, $C_{1-6}haloalkyl$, $C_{1-6}haloalkoxy$ and halo); optionally substituted heterocyclyl (wherein optional substituents include one or more substituents each independently selected from C_{1-6} alkyl, C_{1-6} alkoxy, $-C(O)OC_{1-6}alkyl$, $-C(O)C_{1-6}alkyl$ and $-C(O)NHC_{1-6}alkyl$); $-NHalkyl$; $-N(alkyl)_2$; amino; hydroxyl; alkoxy or halo;

[0061] n represents 0, 1 or 2;

[0068] Further, according to the ~~invention~~ embodiments disclosed herein, there is provided a compound of formula (I),



or a pharmaceutically acceptable salt, solvate or polymorph thereof, including all tautomers and stereoisomers thereof wherein:

[0069] R_1 represents H; alkyl which is optionally substituted by one or more substituents each independently selected from C_{1-6} alkoxy, NH_2 , $-NHC_{1-3}$ alkyl and $-N(C_{1-3}alkyl)_2$; $-C(O)Oalkyl$; haloalkyl; haloalkoxy; or $-alkylaryl$;

[0070] each R_2 independently represents H; alkyl which is optionally substituted by one or more substituents each independently selected from C_{1-6} alkoxy, NH_2 , $-NHC_{1-3}$ alkyl and $-N(C_{1-3}alkyl)_2$; $-alkylaryl$; carbocyclyl which is optionally substituted by one or more substituents each independently selected from C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy and halo; heterocyclyl which is optionally substituted by one or more substituents each independently selected from C_{1-6} alkyl, C_{1-6} alkoxy, $-C(O)OC_{1-6}alkyl$, $-C(O)C_{1-6}alkyl$ and $-C(O)NHC_{1-6}alkyl$; $-NHalkyl$; $-N(alkyl)_2$; amino; hydroxyl; alkoxy or halo;

[0071] n represents 0, 1 or 2;

[0072] R_3 represents H or alkyl;

[0073] R_4 represents H or alkyl;

[0074] R_5 represents H or alkyl;

[0075] W and X each independently represent $C=O$; $C=S$; or CH_2 ;

[0076] Y represents aryl; heteroaryl; carbocyclyl which is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, C₁₋₆haloalkoxy and halo; or heterocyclyl which is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, -C(O)OC₁₋₆alkyl, -C(O)C₁₋₆alkyl and -C(O)NHC₁₋₆alkyl; and

[0077] Z represents alkyl which is optionally substituted by one or more substituents each independently selected from C₁₋₆alkoxy, NH₂, -NHC₁₋₃alkyl and -N(C₁₋₃alkyl)₂; aryl; heteroaryl; -alkylaryl; -alkylheteroaryl; carbocyclyl which is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkyl, C₁₋₆haloalkoxy and halo; heterocyclyl which is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, -C(O)OC₁₋₆alkyl, -C(O)C₁₋₆alkyl and -C(O)NHC₁₋₆alkyl; -alkylcarbocyclyl wherein carbocyclyl is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy and halo; -alkylheterocyclyl wherein heterocyclyl is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, -C(O)OC₁₋₆alkyl, -C(O)C₁₋₆alkyl and -C(O)NHC₁₋₆alkyl; -arylcarbocyclyl wherein carbocyclyl is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy and halo; or -arylheterocyclyl wherein heterocyclyl is optionally substituted by one or more substituents each independently selected from C₁₋₆alkyl, -C(O)OC₁₋₆alkyl, -C(O)C₁₋₆alkyl and -C(O)NHC₁₋₆alkyl.

[0077a] In another aspect, there is provided a compound as defined above for use as a medicament.

[0077b] In another aspect, there is provided a pharmaceutical composition comprising a compound as defined above in combination with one or more therapeutically acceptable adjuvants, diluters or carriers.

[0077c] In another aspect, there is provided the compound as defined above for use in modulation of the WNT pathway.

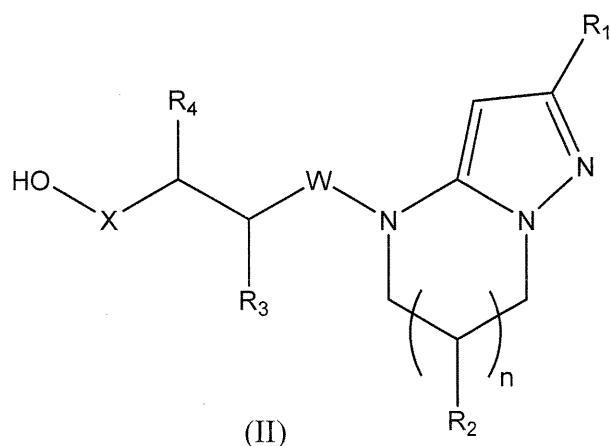
[0077d] In another aspect, there is provided a method of modulating WNT activity comprising exposing a WNT protein or a WNT receptor to a compound as defined above.

[0077e] In another aspect, there is provided the compound as defined above for use in the treatment of a disease or condition associated with WNT pathway activity.

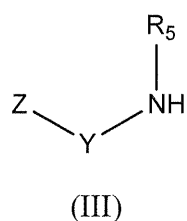
[0077f] In another aspect, there is provided the use of a compound as defined above in the manufacture of a medicament for the treatment of a disease or condition associated with WNT pathway activity.

[0077g] In another aspect, there is provided a compound as defined above for use in diagnosis.

[0077h] In another aspect, there is provided a process for preparation of a compound as defined above, wherein W and X each represent C=O, which process comprises reaction of a compound of formula (II)



wherein R_1 , R_2 , R_3 , n , R_4 and R_5 are as defined above, with a compound of formula (III)



or a protected derivative thereof, wherein R_5 , Y and Z are as defined above.

[0077i] A process for preparation of a compound as defined above, wherein W and X each represent CH_2 , which process comprises conversion of the W and X groups of compounds of formula (I) from C=O groups into CH_2 groups.

[0077j] A process for preparation of a compound as defined above, wherein W and X each represent C=S, which process comprises conversion of the W and X groups of compounds of formula (I) from C=O groups into C=S groups.

Brief Description of Drawings

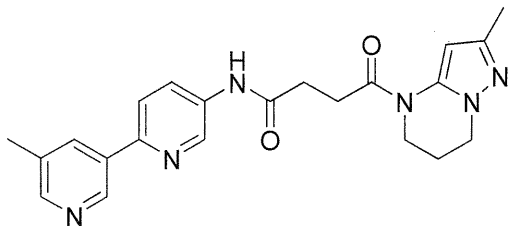
[0078] Figure 1: A bar chart illustrating inhibition of the activity of mammalian porcupine by Compound 51 and Compound 110.

[0079] Figure 2: A graph illustrating efficacy of Compound 51 on the MMTV-Wnt1 mouse model.

[0080] Figure 3: A graph illustrating efficacy data of Compound 110 in the MMTV-Wnt1 mouse model.

[0081] Figure 4: Images illustrating inhibition of Palmitoylation of Wnt3a by Compound 51.

20. The compound of claim 18 which is N-(5'-methyl-2,3'-bipyridin-5-yl)-4-(2-methyl-6,7-dihydropyrazolo[1,5-a]pyrimidin-4(5H)-yl)-4-oxobutanamide:



21. A compound according to any one of claims 1 to 20 for use as a medicament.
22. The compound of any one of claims 1 to 21 having an IC_{50} against HEK293-STF3A cells of less than about 10 micromolar.
23. A pharmaceutical composition comprising a compound according to any one of claims 1 to 22 in combination with one or more therapeutically acceptable adjuvants, diluents or carriers.
24. The compound of any one of claims 1 to 22 for use in modulation of the WNT pathway.
25. A method of modulating WNT activity comprising exposing a WNT protein or a WNT receptor to a compound according to any one of claims 1 to 22.
- ~~26. A method according to claim 25 wherein the method is an in vivo method.~~
- ~~27. Use of a compound according to any one of claims 1 to 22 for modulating WNT activity.~~
- ~~28-26. The compound of any one of claims 1 to 22 for use in the treatment of a disease or condition associated with WNT pathway activity.~~
- ~~29. A method of treating a disease or condition associated with WNT pathway activity comprising administering to a subject in need thereof a therapeutically effective amount of a compound according to any one of claims 1 to 22.~~
- ~~30. Use of a compound according to any one of claims 1 to 22 for treatment of a disease or condition associated with WNT pathway activity.~~

~~3127~~. Use of a compound according to any one of claims 1 to 22 in the manufacture of a medicament for the treatment of a disease or condition associated with WNT pathway activity.

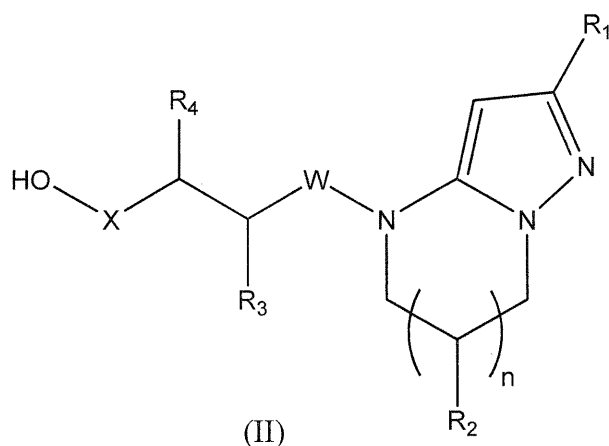
~~3228~~. The compound of claim ~~268~~, ~~method of claim 29~~, or use of claim ~~2730~~ or claim ~~31~~ wherein the disease or condition is selected from the group consisting of cancer, fibrosis, stem cell and diabetic retinopathy, rheumatoid arthritis, psoriasis and myocardial infarction.

~~3329~~. The compound, ~~method~~ or use of claim ~~3228~~ wherein the cancer is a cancer characterised by high WNT activity.

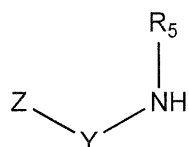
~~3430~~. The compound, ~~method~~ or use of claim ~~3228~~ wherein the disease or condition is a cancer, such as cervical, colon, breast, bladder, head and neck, gastric, lung, ovarian, prostate, thyroid, non-small-cell lung, chronic lymphocytic leukemia, mesothelioma, melanoma, pancreatic adenocarcinoma, basal cell carcinoma, osteosarcoma, hepatocellular carcinoma, Wilm's tumor or medulloblastoma, or a fibrotic disease, such as pulmonary fibrosis, liver fibrosis, skin fibrosis or renal fibrosis, or a degenerative disease, or a metabolic disease such as diabetic retinopathy.

~~3531~~. ~~Use of a~~ compound according to any one of claims 1 to 22 ~~for use~~ in diagnosis.

~~3632~~. A process for preparation of a compound according to any one of claims 1 to 22, wherein W and X each represent C=O, which process comprises reaction of a compound of formula (II)



wherein R₁, R₂, R₂, n, R₃ and R₄ are as defined in any one of claims 1 to 24, with a compound of formula (III)



(III)

or a protected derivative thereof, wherein R_5 , Y and Z are as defined any one of claims 1 to 24.

~~37~~33. A process for preparation of a compound according to any one of claims 1 to 9, wherein W and X each represent CH_2 , which process comprises conversion of the W and X groups of compounds of formula (I) from $\text{C}=\text{O}$ groups into CH_2 groups.

~~38~~34. A process for preparation of a compound according to any one of claims 1 to 9, wherein W and X each represent $\text{C}=\text{S}$, which process comprises conversion of the W and X groups of compounds of formula (I) from $\text{C}=\text{O}$ groups into $\text{C}=\text{S}$ groups.