SSTR4 AGONIST SALTS

The present invention relates to novel SSTR4 agonist salts, to pharmaceutical compositions comprising the salts, to methods of using the salts to treat physiological disorders, and to intermediates useful in the synthesis of the salts.

Somatostatin, or somatotropin-release inhibitory factor (SRIF), is a cyclic peptide found in humans. It is produced widely in the human body and acts both systemically and locally to inhibit the secretion of various hormones, growth factors and neurotransmitters. The effects of somatostatin are mediated by a family of G protein-coupled receptors, of which five subtypes are known. These subtypes are divided into two subfamilies, the first comprising SSTR2, SSTR3 and SSTR5 and the second SSTR1 and SSTR4.

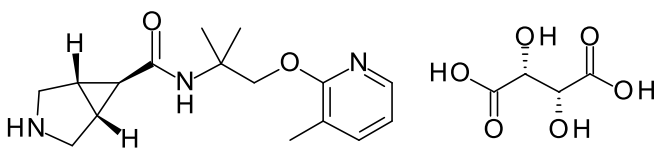
Somatostatin is involved in the regulation of processes such as for example cellular proliferation, glucose homeostasis, inflammation, and pain. In this aspect, somatostatin or other members of the somatostatin peptide family are believed to inhibit nociceptive and inflammatory processes via the SSTR4 pathway. A number of further therapeutic areas for SSTR4 agonists have been discussed (for examples see Crider, A; *Mini Rev. Med. Chem.* 2002, 7, 213 and references therein; WO 2010/059922 and references therein).

WO 2014/184275 discloses certain 3-azabicyclo[3.1.0]hexane-6-carboxamide derivatives which are SSTR4 agonists, and which are useful for preventing or treating medical disorders related to SSTR4.

There is a need for alternative solid-state forms of selective SSTR4 agonists with improved stability in excipients and favorable flow and bulk properties for the manufacturing of the active pharmaceutical product and drug products.

Summary

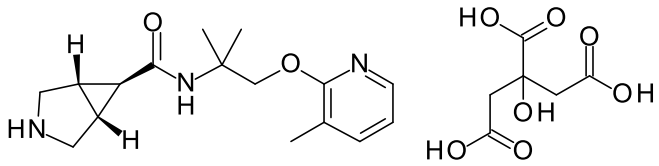
In a first aspect of the present disclosure, there is provided a compound of the formula:



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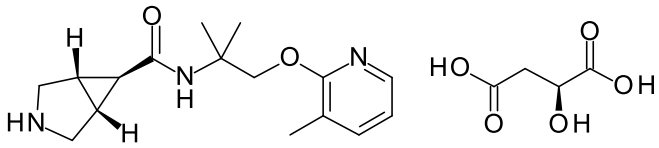
or a hydrate thereof.

In another aspect of the present disclosure, there is provided a compound of the formula:



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In yet another aspect of the present disclosure, there is provided a compound of the formula:



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In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as disclosed herein with one or more pharmaceutically acceptable carriers, diluents, or excipients.

In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating pain in a patient.

In yet another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating chronic back pain in a patient.

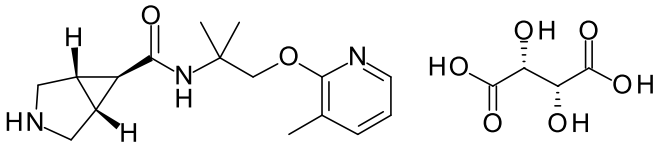
In a further aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating neuropathic pain in a patient.

In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating pain associated with osteoarthritis in a patient.

In yet another aspect of the present disclosure, there is provided a compound as disclosed herein, or a pharmaceutical composition as disclosed herein, for use in therapy.

Description

Accordingly, the present invention provides a compound of Formula I:

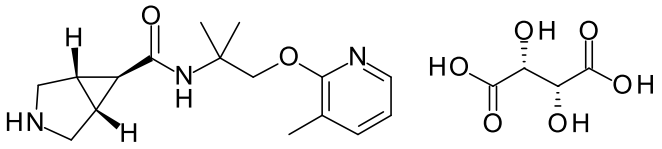


Formula I

or a hydrate thereof.

WE CLAIM:

1. A compound of the formula:

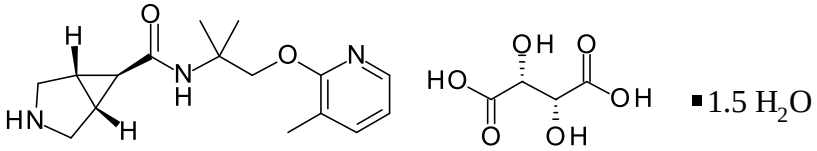


or a hydrate thereof.

2. The compound according to claim 1, which is a hydrate.

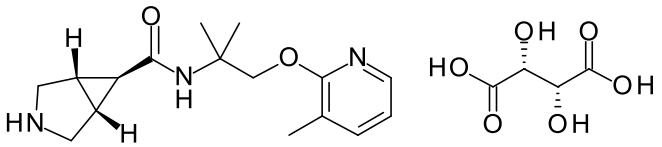
3. The compound according to claim 1 or claim 2, which is a hydrate, wherein the water content at ambient temperature is in the range of 3% to 9% by weight.

4. The compound according to any one of claims 1 to 3, which is:

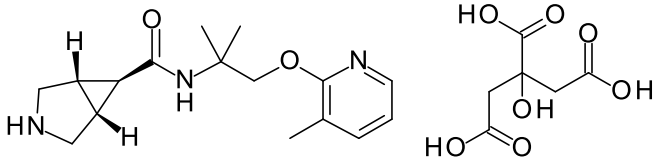


5. The compound according to claim 4, which is crystalline.

6. The compound according to claim 1, which is:

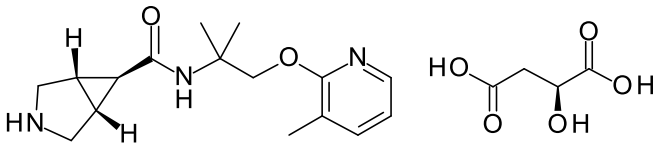


7. A compound of the formula:



8. The compound according to claim 7, which is crystalline.

9. A compound of the formula:



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10. The compound according to claim 9, which is crystalline.

11. The compound according to claim 4, which is crystalline, and which is characterized by an X-ray powder diffraction patter using CuKα radiation comprising a peak at diffraction angle 2-theta of 15.2º, and one or more peaks at 10.6º or 21.9º (±0.2º respectively).

12. The compound according to claim 7, which is crystalline, and which is characterized by an X-ray powder diffraction patter using CuKα radiation comprising a peak at diffraction angle 2-theta of 20.8º, and one or more peaks selected at 10.3º, 16.2º or 5.4º (±0.2º respectively).

13. The compound according to claim 9, which is crystalline, and which is characterized by an X-ray powder diffraction patter using CuKα radiation comprising a peak at diffraction angle 2-theta of 18.1º, and one or more peaks at 4.9º or 17.3º (±0.2º respectively).

14. A pharmaceutical composition comprising a compound according to any one of claims 1 to 13 with one or more pharmaceutically acceptable carriers, diluents, or excipients.

15. Use of a compound according to any one of claims 1 to 13, or the pharmaceutical composition according to claim 14, in the manufacture of a medicament for treating pain in a patient.

16. Use of a compound according any one of claims 1 to 13, or the pharmaceutical composition according to claim 14, in the manufacture of a medicament for treating chronic back pain in a patient.

17. Use of a compound according any one of claims 1 to 13, or the pharmaceutical composition according to claim 14, in the manufacture of a medicament for treating neuropathic pain in a patient.

18. The use according to claim 17, wherein the neuropathic pain is diabetic peripheral neuropathic pain.

19. Use of a compound according to any one of claims 1 to 13, or the pharmaceutical composition according to claim 14, in the manufacture of a medicament for treating pain associated with osteoarthritis in a patient.

20. A compound according to any one of claims 1 to 13, or a pharmaceutical composition according to claim 14, for use in therapy.