SALT FORM AND CRYSTAL FORM OF PYRIDINE MULTI-SUBSTITUTED COMPOUND AND PREPARATION METHOD THEREFOR

[0001] This application claims the priority of:

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Application number: CN202311689614.0; Application date: December 8, 2023.

TECHNICAL FIELD

[0002] The present disclosure relates to a salt form and a crystal form of a multi-substituted pyridine compound and a preparation method thereof, in particular to a crystal form of a compound of formula (I) and a preparation method thereof and use thereof in the manufacuture of a medicament for treating related diseases.

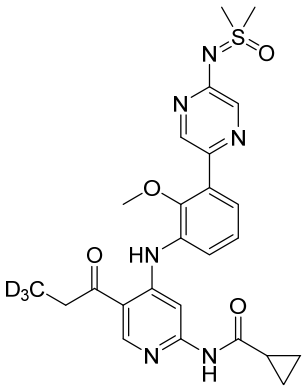
BACKGROUND

[0003] The family of Janus kinases (JAKs) of non-receptor tyrosine kinases is critical in mediating the signaling of numerous cytokines that cause inflammation. The JAK family includes JAK1, JAK2, JAK3, and TYK2. TYK2 and JAK1/2/3 usually work in pairs, or as "dimers," to transmit signals from extracellular cytokines to the cell nucleus. TYK2 selectively participates in the transmission of proinflammatory cytokines such as IL-23, IL-12, and type I IFN signals. Therefore, TYK2 inhibitors can be an effective treatment for a variety of severe inflammatory and autoimmune diseases.

[0004] JAK1, JAK2, JAK3 and TYK2 in the JAK protein family all have JAK homology domains (JH), of which the JH1 domain is also called the kinase domain and JH2 is a pseudokinase domain. Although the JH2 domain of TYK2 is very similar to the JH1 domain and contains an ATP binding site that is very similar to the JH1 domain, specific residue differences exclude the catalytic function of JH2. Although the specific mechanism by which TYK2 achieves allosteric inhibition through the JH2 domain has not been elucidated, there is evidence that small molecule ligands that bind to JH2 stabilize the autoinhibitory interaction between the JH2 domain and the JH1 active site. These interactions between JH2 and JH1 are believed to limit the conformational mobility of the JH1 active site required for phosphorus

CLAIMS

1. A compound of formula (I),



▪ HCl

(I) .

2. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern thereof has characteristic diffraction peaks at the following 2θ angles: 17.56±0.20°, 24.36±0.20°, 25.69±0.20°, and 27.37±0.20°.

3. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern of the crystal form A at least contains 6, 7 or 8 diffraction peaks expressed by 2θ angle selected from: 17.56±0.20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 24.36±0.20°, 25.69±0.20°, and 27.37±0.20°.

4. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern thereof has characteristic diffraction peaks at the following 2θ angles: 17.56±0.20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 24.36±0.20°, 25.69±0.20°, and 27.37±0.20°.

5. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern of the crystal form A at least contains 10, 11 or 12 diffraction peaks expressed by 2θ angle selected from: 8.70±0.20°, 10.05±0.20°, 15.56±0.20°, 17.56±0.20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 24.36±0.20°, 25.69±0.20°, 27.37±0.20°,

and 29.49±0.20°.

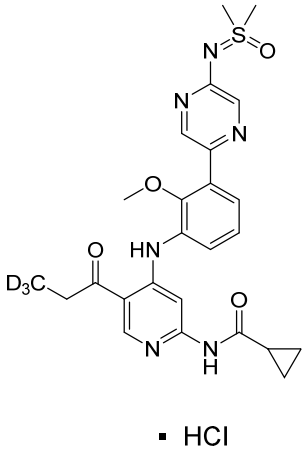
6. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern thereof has characteristic diffraction peaks at the following 2θ angles: 8.70±0.20°, 10.05±0.20°, 15.56±0.20°, 17.56±0.20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 24.36±0.20°, 25.69±0.20°, 27.37±0.20°, and 29.49±0.20°.

7. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern of the crystal form A at least contains 12, 13, 14, 15 or 16 diffraction peaks expressed by 2θ angle selected from: 8.70±0.20°, 10.05±0.20°, 12.08±0.20°, 15.56±0.20°, 17.56±0. 20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 23.77±0.20°, 24.36±0.20°, 25.69±0.20°, 26.33±0.20°, 27.37±0.20°, 27.83±0.20°, and 29.49±0.20°.

8. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction pattern thereof has characteristic diffraction peaks at the following 2θ angles: 8.70±0.20°, 10.05±0.20°, 12.08±0.20°, 15.56±0.20°, 17.56±0.20°, 18.76±0.20°, 19.63±0.20°, 20.44±0.20°, 22.89±0.20°, 23.77±0.20°, 24.36±0.20°, 25.69±0.20°, 26.33±0.20°, 27.37±0.20°, 27.83±0.20°, and 29.49±0.20°.

9. Crystal form A of the compound of formula (I) according to claim 1, wherein the X-ray powder diffraction peak spectrum thereof has characteristic diffraction peaks at the following 2θ angles: 17.56°±0.20°, 24.36°±0.20°, 27.37°±0.20°, and/or 8.70°±0.20°, and/or 10.05°±0.20°, and/or 12.08°±0.20°, and/or 14.63°±0.20°, and/or 15.56°±0.20°, and/or 16.39°±0.20°, and/or 18.76°±0.20°, and/or 19.35°±0.20°, and/or 19.63°±0.20°, and/or 20.44°±0.20°, and/or 21.94°±0.20°, and/or 22.53°±0.20°, and/or 22.89°±0.20°, and/or 23.23°±0.20°, and/or 23.77°±0.20°, and/or 24.51°±0.20°, and/or 25.69°±0.20°, and/or 26.33°±0.20°, and/or 26.73°±0.20°, and/or 27.83°±0.20°, and/or 28.58°±0.20°, and/or 29.49°±0.20°, and/or 30.42°±0.20°, and/or 31.13°±0.20°, and/or 32.29°±0.20°, and/or 32.88°±0.20°, and/or 34.04°±0.20°, and/or 35.19°±0.20°, and/or 36.30°±0.20°, and/or 38.89°±0.20°.

10. Crystal form A of the compound of formula (I),



(I)

wherein the XRPD pattern is shown in Fig. 1.

11. Crystal form A of the compound of formula (I) according to any one of claims 1 to 10, wherein the differential scanning calorimetry curve thereof has a starting point of an endothermic peak at 230.5°C±3.0°C.

12. The crystal form A of the compound of formula (I) according to claim 11, wherein the DSC spectrum thereof is shown in Fig. 2.

13. Crystal form A of the compound of formula (I) according to any one of claims 1 to 12, wherein the thermogravimetric analysis curve thereof shows a weight loss of up to 1.02%±0.20% at 175.0°C±3.0°C.

14. The crystal form A of the compound of formula (I) according to claim 13, wherein the TGA spectrum thereof is shown in Fig. 3.

15. Use of the compound according to claim 1 or the crystal form A of the compound of formula (I) according to any one of claims 2 to 14 in the manufacture of a medicament for treating Tyk2 JH2 related diseases.

16. The compound according to claim 1 or the crystal form A of the compound of formula (I) according to any one of claims 2 to 14, for use in therapy.

17. A medicament, comprising the compound according to claim 1 or the crystal form A of the compound of formula (I) according to any one of claims 2 to 14.