CRYSTAL FORM OF TETRAHYDROISOQUINOLINE COMPOUND AND USE THEREOF

TECHNICAL FIELD

[0001] The present disclosure relates to the field of medicinal chemistry, specifically to a tosylate salt and a mesylate salt of a compound of formula I: N-(4-(6-fluoro-3,4-dihydroisoquinolin-2(1H)-yl)-2,6-dimethylphenyl)-3,3-dimethylbutanamide, as well as to a tosylate salt crystal form A, a tosylate salt crystal form B, a tosylate salt crystal form E, and a mesylate salt crystal form A thereof, and a use thereof.

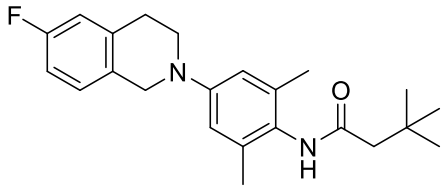
BACKGROUND

[0002] Voltage-gated potassium (Kv) channels are among the most important and critical channels in various physiological processes. The KCNQ family (Kv7 channels) consists of five members (KCNQ1–5). The Kv7 protein comprises six transmembrane segments, with S1 to S4 forming the voltage-sensing domain (VSD), S5 and S6 forming the pore domain (PD), and a short N-terminus and a long C-terminus present intracellularly. Throughout the body, Kv7 channels are not uniformly expressed. For instance, Kv7.1 expression is detected in vascular smooth muscle cells of many rodent and human arteries and in cardiac tissues. In central, peripheral, and sensory neurons, Kv7.2/7.3

channels are highly expressed and underlie the M-current, and mutations in the KCNQ2 or KCNQ3 gene lead to neuronal hyperexcitability, thereby causing epilepsy. Kv7.4 is expressed in the cochlea and is essential for normal hearing, and many cases of congenital deafness are caused by mutations in KCNQ4. In addition, Kv7.4 is a major functional regulator in many smooth muscle tissues. Kv7.5 is expressed in neurons, primarily involved in the delayed afterhyperpolarization, and is also located in skeletal muscle, blood vessels, and smooth muscle. And in arterial smooth muscle, Kv7.5 protein forms a complex with Kv7.4 protein.

[0003] *N*-(4-(6-fluoro-3,4-dihydroisoquinolin-2(1H)-yl)-2,6-dimethylphenyl)-3,3-dimethylbutanamide (structure shown below, hereinafter referred to as the compound of formula I) is a selective KCNQ potassium channel opener at the clinical trial stage. Relevant indications include epilepsy, major depressive disorder (MDD), and potentially other neurological disorders. Completed studies have shown that the activity of the compound of formula I is improved by approximately 20-fold relative to retigabine, which is also a KCNQ2/3 opener. The compound of formula I also exhibits relatively good KCNQ2/3 and KCNQ4/5 selectivity, and relatively good safety. Furthermore, preclinical *in vitro* and *in vivo* data show that the compound of formula I prevents MES-induced seizure behavior in ICR mice and 6-Hz-induced seizures in C57BL/6 mice in a dose-dependent manner.

[0004] The same compound may form different salts, and different salts may also have one or more crystal forms. Various salt forms and crystal forms of a drug molecule may exhibit specific physicochemical properties, including but not limited to melting point, solubility, dissolution rate, optical and mechanical properties, hygroscopicity, particle morphology, density, and flowability. These properties have a direct impact on the processability and manufacturability of drug molecules. Different crystal forms also exhibit different solid-state stability, chemical stability, and bioavailability. These factors will have a significant impact on the efficacy and toxicology of the drug. In the drug development stage, an inventor comprehensively evaluates the solid-state stability, chemical stability, solubility, and in vivo exposure of various salt forms and crystal forms, and selects the most suitable salt form and the corresponding crystal form.



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[0005] The invention of the salt forms and crystal forms of the compound of formula I is of great significance for the treatment of various neurological diseases. There are currently no relevant reports on salt forms of the above-mentioned compound of formula I and crystal forms of the salts thereof. The present disclosure provides salt forms of the compound of formula I and uses of the

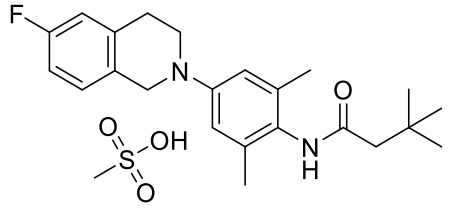
corresponding crystal forms, which can further optimize the druggability, safety, and efficacy of the compound.

SUMMARY

[0006] In view of the deficiencies of the free base of the existing compound of formula I in terms of solubility and druggability, the present disclosure provides a crystal form of the compound of formula I and a use thereof. The crystal form of the present disclosure has good crystallinity, solid-state stability, good solubility, and pharmacokinetic properties.

[0007] The present disclosure addresses the above technical problems through the following technical solutions.

[0008] The present disclosure provides a mesylate salt crystal form A of the compound of formula I,



[0009] structural formula of mesylate salt of compound of formula I

[0010] the mesylate salt crystal form A has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 5.60°±0.2°, 12.31°±0.2°, and

15.40°±0.2°.

[0011] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 9.47°±0.2°, 10.99°±0.2°, 17.57°±0.2°, and 19.15°±0.2°.

[0012] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 12.31°±0.2°, 15.40°±0.2°, 17.57°±0.2°, and 19.15°±0.2°.

[0013] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 14.86°±0.2°, 17.12°±0.2°, 18.33°±0.2°, 22.42°±0.2°, and 22.94°±0.2°.

[0014] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 12.31°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 22.42°±0.2°, and 22.94°±0.2°.

[0015] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 7.35°±0.2°, 11.36°±0.2°, 19.66°±0.2°,

20.10°±0.2°, 21.78°±0.2°, 26.69°±0.2°, and 28.95°±0.2°.

[0016] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 7.35°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 11.36°±0.2°, 12.31°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 19.66°±0.2°, 20.10°±0.2°, 21.78°±0.2°, 22.42°±0.2°, 22.94°±0.2°, 26.69°±0.2°, and 28.95°±0.2°.

[0017] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 7.35°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 11.36°±0.2°, 12.31°±0.2°, 13.48°±0.2°, 14.02°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 16.45°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 19.66°±0.2°, 20.10°±0.2°, 20.66°±0.2°, 21.78°±0.2°, 22.42°±0.2°, 22.94°±0.2°, 23.44°±0.2°, 26.69°±0.2°, 27.18°±0.2°, 28.95°±0.2°, 34.31°±0.2°, and 36.14°±0.2°.

[0018] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.60	15.76	100.00

7.35	12.02	5.52
9.47	9.34	15.75
10.99	8.05	15.18
11.36	7.78	5.25
12.31	7.18	30.38
13.48	6.56	2.22
14.02	6.31	2.03
14.86	5.96	7.19
15.40	5.75	42.13
16.45	5.39	2.22
17.12	5.18	6.96
17.57	5.04	12.61
18.33	4.84	8.44
19.15	4.63	13.26
19.66	4.51	4.53
20.10	4.41	5.51
20.66	4.29	2.95
21.78	4.08	3.66
22.42	3.96	9.95
22.94	3.87	7.28

23.44	3.79	2.46
26.69	3.34	3.46
27.18	3.28	2.42
28.95	3.08	3.45
34.31	2.61	2.69
36.14	2.48	1.33

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[0019] In one embodiment, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, is substantially as shown in FIG. 3.

[0020] In one embodiment, the mesylate salt crystal form A provides an X-ray powder diffraction pattern obtained with the following parameters:

Model	Malvern Panalytical Aeris model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)
X-ray emitter setting	The X-ray emitter was operated at a power of 300 W, a voltage of 40 kV, and a current of 7.5 mA. The test range is 3° to 40° (2θ), the scan speed is 0.14°/s, and the step size is 0.02° (2θ).

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[0021] In one embodiment, the mesylate salt crystal form A has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak

temperature of 213.85°C±3°C.

[0022] In one embodiment, the differential scanning calorimetry thermogram of the mesylate salt crystal form A comprises an endothermic peak at a peak temperature of 213.85°C±3°C, with a heat of fusion of 66.99 J/g.

[0023] In one embodiment, the differential scanning calorimetry thermogram of the mesylate salt crystal form A is as shown in FIG. 2.

[0024] In one embodiment, the mesylate salt crystal form A has a thermogravimetric analysis thermogram showing a weight loss of 0.85% upon heating to 180°C.

[0025] In one embodiment, the thermogravimetric analysis thermogram of the mesylate salt crystal form A is substantially as shown in FIG. 2.

[0026] In one embodiment, the mesylate salt crystal form A provides TGA and/or DSC thermograms obtained with the following parameters:

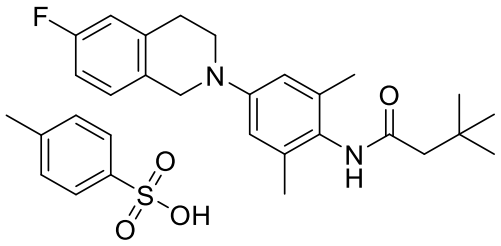
Parameters	TGA	DSC
Instrument	TGA550 thermogravimetric analyzer of TA Discovery series	Differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min

Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

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[0027] In one embodiment, the mesylate salt crystal form A is an anhydrous crystal form of a monomesylate salt.

[0028] The present disclosure provides a tosylate salt crystal form A of the compound of formula I;



[0029] structural formula of tosylate salt of compound of formula I

[0030] the tosylate salt crystal form A has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 5.17°±0.2°, 10.40°±0.2°, and 18.34°±0.2°.

[0031] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 8.55°±0.2° and 14.19°±0.2°.

[0032] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.17°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 14.19°±0.2°, and

18.34°±0.2°.

[0033] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 7.04°±0.2° and 17.56°±0.2°.

[0034] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.17°±0.2°, 7.04°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 14.19°±0.2°, 17.56°±0.2°, and 18.34°±0.2°.

[0035] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 11.16°±0.2°, 14.61°±0.2°, 15.14°±0.2°, 19.85°±0.2°, 21.01°±0.2°, 22.21°±0.2°, 22.58°±0.2°, and 24.65°±0.2°.

[0036] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.17°±0.2°, 7.04°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 11.16°±0.2°, 14.19°±0.2°, 14.61°±0.2°, 15.14°±0.2°, 17.56°±0.2°, 18.34°±0.2°, 19.85°±0.2°, 21.01°±0.2°, 22.21°±0.2°, 22.58°±0.2°, and 24.65°±0.2°.

[0037] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.17°±0.2°, 7.04°±0.2°, 7.98°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 11.16°±0.2°, 11.51°±0.2°, 13.15°±0.2°, 14.19°±0.2°, 14.61°±0.2°, 15.14°±0.2°,

16.15°±0.2°, 17.56°±0.2°, 18.34°±0.2°, 19.52°±0.2°, 19.85°±0.2°, 20.44°±0.2°, 21.01°±0.2°, 21.56°±0.2°, 22.21°±0.2°, 22.58°±0.2°, 23.75°±0.2°, 24.65°±0.2°, 25.38°±0.2°, 26.45°±0.2°, 26.96°±0.2°, 28.82°±0.2°, 30.53°±0.2°, 31.81°±0.2°, 35.27°±0.2°, and 37.51°±0.2°.

[0038] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.17	17.09	100.00
7.04	12.55	10.07
7.98	11.07	1.98
8.55	10.33	11.39
10.40	8.50	43.38
11.16	7.92	6.91
11.51	7.68	4.54
13.15	6.73	3.62
14.19	6.24	14.11
14.61	6.06	6.71
15.14	5.85	8.26

16.15	5.48	3.28
17.56	5.05	10.38
18.34	4.83	14.19
19.52	4.54	4.23
19.85	4.47	7.91
20.44	4.34	4.30
21.01	4.23	5.89
21.56	4.12	4.54
22.21	4.00	5.03
22.58	3.93	9.09
23.75	3.74	4.57
24.65	3.61	5.23
25.38	3.51	4.15
26.45	3.37	3.28
26.96	3.30	2.68
28.82	3.10	1.43
30.53	2.93	1.03
31.81	2.81	0.89
35.27	2.54	0.63
37.51	2.40	0.23

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[0039] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, is substantially as shown in FIG. 6.

[0040] In one embodiment, the tosylate salt crystal form A provides an XRPD pattern obtained with the following parameters:

Model	Rigaku Smartlab SE model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.544414 Å/1.540593 Å).
X-ray emitter setting	power: 1600 kW; voltage: 40 kV; current: 40 mA; incident slit: 0.5°; receiving slit: 20.0 mm; scan range: 3 to 40° (2θ), step speed: 8 °/min; step size: 0.01 ° (2θ).

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[0041] In one embodiment, the tosylate salt crystal form A has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak temperature of 223.99°C±3°C.

[0042] In one embodiment, the differential scanning calorimetry thermogram of the tosylate salt crystal form A comprises an endothermic peak at a peak temperature of 223.99°C±3°C, with a heat of fusion of 68.20 J/g.

[0043] In one embodiment, the differential scanning calorimetry thermogram of the tosylate salt crystal form A is as shown in FIG. 5.

[0044] In one embodiment, the tosylate salt crystal form A has a thermogravimetric analysis thermogram substantially as shown in FIG. 5.

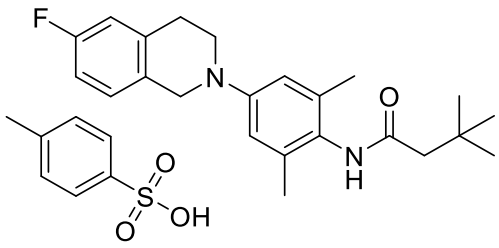
[0045] In one embodiment, the tosylate salt crystal form A provides TGA and/or DSC thermograms obtained with the following parameters:

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	Differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

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[0046] In one embodiment, the tosylate salt crystal form A is an anhydrous crystal form of a monotosylate salt.

[0047] The present disclosure provides a tosylate salt crystal form B of the compound of formula I;



[0048] structural formula of tosylate salt of compound of formula I

[0049] the tosylate salt crystal form B has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 13.44°±0.2°, 17.28°±0.2°, and 17.38°±0.2°.

[0050] In some embodiments, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 5.64°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 20.45°±0.2°, 21.15°±0.2°, and 22.15°±0.2°.

[0051] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.64°±0.2°, 13.44°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 20.45°±0.2°, 21.15°±0.2°, and 22.15°±0.2°.

[0052] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 7.84°±0.2°, 10.11°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.60°±0.2°, 18.58°±0.2°, and 23.97°±0.2°.

[0053] In one embodiment, the X-ray powder diffraction pattern of the tosylate

salt crystal form B, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.64°±0.2°, 7.84°±0.2°, 10.11°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 18.58°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, and 23.97°±0.2°.

[0054] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, further comprising diffraction peaks at one or more of the following positions: 5.09°±0.2°, 9.22°±0.2°, 10.87°±0.2°, 16.21°±0.2°, 19.55°±0.2°, 22.89°±0.2°, 25.03°±0.2°, and 27.08°±0.2°.

[0055] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.09°±0.2°, 5.64°±0.2°, 7.84°±0.2°, 9.22°±0.2°, 10.11°±0.2°, 10.87°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 16.21°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 18.58°±0.2°, 19.55°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, 22.89°±0.2°, 23.97°±0.2°, 25.03°±0.2°, and 27.08°±0.2°.

[0056] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.09°±0.2°, 5.64°±0.2°, 7.06°±0.2°, 7.84°±0.2°, 9.22°±0.2°, 10.11°±0.2°, 10.87°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 16.21°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 18.58°±0.2°,

19.55°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, 22.89°±0.2°, 23.97°±0.2°, 25.03°±0.2°, 27.08°±0.2°, 29.19°±0.2°, 30.07°±0.2°, 30.73°±0.2°, 31.60°±0.2°, 35.97°±0.2°, 37.84°±0.2°.

[0057] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.09	17.34	12.68
5.64	15.66	41.63
7.06	12.51	5.42
7.84	11.26	20.64
9.22	9.59	12.32
10.11	8.74	20.58
10.87	8.13	15.17
11.36	7.78	29.85
12.03	7.35	19.43
13.44	6.58	52.29
13.60	6.51	39.59
14.49	6.11	50.60

15.13	5.85	47.76
16.21	5.46	9.92
17.28	5.13	100.00
17.38	5.10	92.84
18.58	4.77	21.10
19.55	4.54	16.10
20.45	4.34	43.73
21.15	4.20	40.38
22.15	4.01	51.56
22.89	3.88	17.76
23.97	3.71	38.67
25.03	3.56	16.06
27.08	3.29	15.22
29.19	3.06	7.76
30.07	2.97	3.42
30.73	2.91	2.25
31.60	2.83	3.03
35.97	2.49	2.34
37.84	2.38	2.90

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[0058] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, is substantially as shown in FIG. 9.

[0059] In one embodiment, the tosylate salt crystal form B provides an XRPD pattern obtained with the following parameters:

Model	Bruker D2 model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)
X-ray emitter setting	power: 300 W; voltage: 30 kV; current: 10 mA; divergence slit: 0.6 mm; Soller slit: 4.0°; step speed: 0.15 s/step; step size: 0.02° (2θ); total number of steps: 1837 steps

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[0060] In one embodiment, the tosylate salt crystal form B has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak temperature of 222.98°C±3°C, with a heat of fusion of 54.52 J/g.

[0061] In one embodiment, the differential scanning calorimetry thermogram of the tosylate salt crystal form B is as shown in FIG. 8.

[0062] In one embodiment, the tosylate salt crystal form B has a thermogravimetric analysis thermogram substantially as shown in FIG. 8.

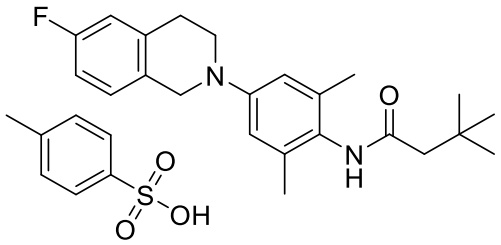
[0063] In one embodiment, the tosylate salt crystal form B provides TGA and/or DSC thermograms obtained with the following parameters:

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	Differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

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[0064] In one embodiment, the tosylate salt crystal form B is an anhydrous crystal form of a monotosylate salt.

[0065] The present disclosure provides a tosylate salt crystal form E of the compound of formula I;



[0066] structural formula of tosylate salt of compound of formula I

[0067] the tosylate salt crystal form E has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising

diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, and 17.33°±0.2°.

[0068] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 11.31°±0.2°, 13.89°±0.2°, and 19.88°±0.2°.

[0069] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 17.33°±0.2°, and 19.88°±0.2°.

[0070] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 9.85°±0.2°, 10.02°±0.2°, 18.83°±0.2°, and 20.23°±0.2°.

[0071] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 17.33°±0.2°, 18.83°±0.2°, 19.88°±0.2°, and 20.23°±0.2°.

[0072] In some embodiments, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, further comprises diffraction

peaks at one or more of the following positions: 14.15°±0.2°, 16.12°±0.2°, 17.88°±0.2°, 22.33°±0.2°, 25.51°±0.2°, and 27.23°±0.2°.

[0073] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 14.15°±0.2°, 16.12°±0.2°, 17.33°±0.2°, 17.88°±0.2°, 18.83°±0.2°, 19.88°±0.2°, 20.23°±0.2°, 22.33°±0.2°, 25.51°±0.2°, and 27.23°±0.2°.

[0074] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 3.34°±0.2°, 16.43°±0.2°, 21.72°±0.2°, 22.87°±0.2°, 23.17°±0.2°, 23.99°±0.2°, 24.51°±0.2°, 30.48°±0.2°, 33.75°±0.2°, and 34.38°±0.2°.

[0075] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks at the following positions: 3.34°±0.2°, 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 14.15°±0.2°, 16.12°±0.2°, 16.43°±0.2°, 17.33°±0.2°, 17.88°±0.2°, 18.83°±0.2°, 19.88°±0.2°, 20.23°±0.2°, 21.72°±0.2°, 22.33°±0.2°, 22.87°±0.2°, 23.17°±0.2°, 23.99°±0.2°, 24.51°±0.2°, 25.51°±0.2°, 27.23°±0.2°, 30.48°±0.2°, 33.75°±0.2°, and 34.38°±0.2°.

[0076] In one embodiment, the X-ray powder diffraction pattern of the tosylate

salt crystal form E, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
3.34	26.40	1.94
5.60	15.78	61.93
8.15	10.84	77.26
9.85	8.97	16.17
10.02	8.82	8.84
11.31	7.81	20.19
13.89	6.37	27.76
14.15	6.25	5.07
16.12	5.50	5.27
16.43	5.39	2.65
17.33	5.11	100.00
17.88	4.96	6.26
18.83	4.71	16.74
19.88	4.46	21.55
20.23	4.39	11.05

21.72	4.09	2.05
22.33	3.98	5.81
22.87	3.89	3.11
23.17	3.84	3.37
23.99	3.71	2.46
24.51	3.63	2.21
25.51	3.49	5.10
27.23	3.27	7.40
30.48	2.93	1.21
33.75	2.65	3.76
34.38	2.61	2.48

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[0077] In one embodiment, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, is substantially as shown in FIG. 10.

[0078] In one embodiment, the tosylate salt crystal form E provides an XRPD pattern obtained with the following parameters:

Model	Malvern Panalytical Aeris model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)
X-ray emitter setting	power: 300 W, voltage: 40 kV, current: 7.5 mA; test

	range: 3° to 40° (2θ), scan speed: 0.14°/s, step size: 0.02° (2θ)

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[0079] In one embodiment, the tosylate salt crystal form E has a differential scanning calorimetry thermogram comprising two endothermic peaks at peak temperatures of 180.26°C±3°C and 224.05°C±3°C.

[0080] In one embodiment, the differential scanning calorimetry thermogram of the tosylate salt crystal form E has an endothermic peak at a peak temperature of 180.26°C±3°C, with a heat of fusion of 26.13 J/g; and an endothermic peak at a peak temperature of 224.05°C±3°C, with a heat of fusion of 59.89 J/g.

[0081] In one embodiment, the differential scanning calorimetry thermogram of the tosylate salt crystal form E is as shown in FIG. 11.

[0082] In one embodiment, the tosylate salt crystal form E has a thermogravimetric analysis thermogram substantially as shown in FIG. 11.

[0083] In one embodiment, the tosylate salt crystal form E provides TGA and/or DSC thermograms obtained with the following parameters:

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	differential scanning calorimeter DSC2500 of TA Discovery series

Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

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[0084] In one embodiment, the tosylate salt crystal form E is an anhydrous crystal form of a monotosylate salt.

[0085] The present disclosure provides a pharmaceutical composition comprising the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, and tosylate salt crystal form E, and a pharmaceutical excipient.

[0086] The present disclosure further provides a use of the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, or the above-mentioned pharmaceutical composition in the preparation of a medicament for treating and/or preventing a disease or condition affected by voltage-gated potassium channels.

[0087] The present disclosure further provides a use of the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, or the above-mentioned pharmaceutical composition in the preparation of a medicament for treating and/or preventing

epilepsy.

[0088] The present disclosure further provides a use of the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, or the above-mentioned pharmaceutical composition in the preparation of a medicament for treating and/or preventing amyotrophic lateral sclerosis.

[0089] The present disclosure further provides a use of the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, or the above-mentioned pharmaceutical composition in the preparation of a medicament for treating and/or preventing depression.

[0090] The present disclosure further provides a use of the above-mentioned mesylate salt crystal form A, tosylate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, or the above-mentioned pharmaceutical composition in the preparation of a medicament for treating and/or preventing pain.

[0091] The positive and progressive effects of the present disclosure are:

[0092] (1) the crystal form of the present disclosure has advantages such as high purity, high stability, high solubility, reproducible preparation, and excellent properties.

[0093] (2) the solubility of the crystal form of the present disclosure in water,

fasted-state simulated intestinal fluid, and simulated gastric fluid is significantly higher than that of the free base.

[0094] (3) in a pharmacokinetic study in rats, the systemic exposure of the crystal forms of the present disclosure is significantly superior to that of the free base, and the overall pharmacokinetic properties are unexpectedly improved.

[0095] In summary, the salt forms and crystal forms of the present disclosure exhibit superior solubility and better *in vivo* exposure, significantly improving the druggability.

BRIEF DESCRIPTION OF THE DRAWINGS

[0096] FIG. 1 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the mesylate salt crystal form A of the compound of formula I.

[0097] FIG. 2 shows TGA/DSC thermograms of the mesylate salt crystal form A of the compound of formula I.

[0098] FIG. 3 shows an XRPD pattern of the mesylate salt crystal form A of the compound of formula I.

[0099] FIG. 4 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the tosylate salt crystal form A of the compound of formula I.

[0100] FIG. 5 shows TGA/DSC thermograms of the tosylate salt crystal form A of the compound of formula I.

[0101] FIG. 6 shows an XRPD pattern of the tosylate salt crystal form A of the

compound of formula I.

[0102] FIG. 7 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the tosylate salt crystal form B of the compound of formula I.

[0103] FIG. 8 shows TGA/DSC thermograms of the tosylate salt crystal form B of the compound of formula I.

[0104] FIG. 9 shows an XRPD pattern of the tosylate salt crystal form B of the compound of formula I.

[0105] FIG. 10 shows an XRPD pattern of the tosylate salt crystal form E of the compound of formula I.

[0106] FIG. 11 shows TGA/DSC thermograms of the tosylate salt crystal form E of the compound of formula I.

[0107] FIG. 12 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the tosylate salt crystal form E of the compound of formula I.

[0108] FIG. 13 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the tosylate salt crystal form C of the compound of formula I.

[0109] FIG. 14 shows TGA/DSC thermograms of the tosylate salt crystal form C of the compound of formula I.

[0110] FIG. 15 shows an XRPD pattern of the tosylate salt crystal form C of the compound of formula I.

[0111] FIG. 16 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the hydrochloride salt crystal form B of the compound of formula I.

[0112] FIG. 17 shows an XRPD pattern of the hydrochloride salt crystal form B of the compound of formula I.

[0113] FIG. 18 shows TGA/DSC thermograms of the hydrochloride salt crystal form B of the compound of formula I.

[0114] FIG. 19 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the sulfate salt crystal form A of the compound of formula I.

[0115] FIG. 20 shows TGA/DSC thermograms of the sulfate salt crystal form A of the compound of formula I.

[0116] FIG. 21 shows an XRPD pattern of the sulfate salt crystal form A of the compound of formula I.

[0117] FIG. 22 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the benzenesulfonate salt crystal form A of the compound of formula I.

[0118] FIG. 23 shows TGA/DSC thermograms of the benzenesulfonate salt crystal form A of the compound of formula I.

[0119] FIG. 24 shows an XRPD pattern of the benzenesulfonate salt crystal form A of the compound of formula I.

[0120] FIG. 25 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the benzenesulfonate salt crystal form B of the compound of formula I.

[0121] FIG. 26 shows TGA/DSC thermograms of the benzenesulfonate salt crystal form B of the compound of formula I.

[0122] FIG. 27 shows an XRPD pattern of the benzenesulfonate salt crystal form

B of the compound of formula I.

[0123] FIG. 28 shows an XRPD pattern of the benzenesulfonate salt crystal form B heated to 120°C.

[0124] FIG. 29 shows TGA/DSC thermograms of the benzenesulfonate salt crystal form B heated to 120°C.

[0125] FIG. 30 shows a ^{1}H NMR spectrum of the benzenesulfonate salt crystal form B heated to 120°C.

[0126] FIG. 31 shows an XRPD pattern of the naphthoate salt crystal form B of the compound of formula I.

[0127] FIG. 32 shows a ^{1}H NMR spectrum (deuterated DMSO, 400 MHz) of the maleate salt crystal form A of the compound of formula I.

[0128] FIG. 33 shows TGA/DSC thermograms of the maleate salt crystal form A of the compound of formula I.

[0129] FIG. 34 shows an XRPD pattern of the maleate salt crystal form A of the compound of formula I.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0130] The present disclosure is further illustrated by the examples below, but is not intended to be limited to the scope of the described examples. The experimental methods in the following examples, where specific conditions are not indicated, were performed according to conventional methods and conditions,

or selected according to the manufacturer's instructions.

[0131] Instruments and analytical methods

[0132] X-ray powder diffraction (XRPD)

[0133] The X-ray powder diffraction (XRPD) method used in the present disclosure is as follows:

[0134] The X-ray powder diffraction data of the sample were collected using a Bruker D2 X-ray powder diffractometer under ambient conditions. About 2 mg of a sample was taken, spread flat on a high-purity silicon sample stage, flattened using a glass slide with weighing paper interposed therebetween, and then loaded for detection. An X-ray tube employing a Cu target (Kα) was used, with a Kα2/Kα1 intensity ratio of 0.50 (1.54439 Å/1.5406 Å), and the X-ray generator was operated at a power of 300 W, a voltage of 30 kV, and a current of 10 mA. The divergence slit was 0.6 mm, and the Soller slit was 4.0°. The step speed was 0.15 s/step, the step size was 0.02° (2θ), and the total number of steps was 1837 steps.

[0135] The X-ray powder diffraction data of the sample are collected under ambient conditions using a Rigaku Smartlab SE X-ray powder diffractometer. About 2 mg of a sample is taken, spread flat on a high-purity silicon sample stage, flattened using a glass slide with weighing paper interposed therebetween, and then loaded for detection. An X-ray tube employing a Cu target (Kα) is used, with a Kα2/Kα1 intensity ratio of 0.50 (1.544414 Å/1.540593 Å), and the X-ray

generator is operated at a power of 1600 kW, a voltage of 40 kV, and a current of 40 mA. The incident slit was 0.5°, and the receiving slit was 20.0 mm. The system employed a test range of 3 to 40° (2θ), a step speed of 8°/min, and a step size of 0.01° (2θ).

[0136] The X-ray powder diffraction data of the sample were collected using a Malvern Panalytical Aeris model X-ray powder diffractometer under ambient conditions. A several-milligram sample was taken, spread flat on a zero-background silicon sample pan, flattened using a glass slide with weighing paper interposed therebetween, and then loaded for detection. An X-ray tube employing a Cu target (Kα) was used, with a Kα2/Kα1 intensity ratio of 0.50 (1.54439 Å/1.5406 Å), and the X-ray generator was operated at a power of 300 W, a voltage of 40 kV, and a current of 7.5 mA. The test range was 3° to 40° (2θ), the scan speed was 0.14°/s, and the step size was 0.02° (2θ).

[0137] Thermogravimetric analyzer (TGA)

[0138] Thermogravimetric Analysis (TGA) curves involved in the present disclosure were obtained by collecting thermogravimetric data of samples using a TA Discovery series TGA550 thermogravimetric analyzer, specifically as follows:

[0139] A several-milligram sample was placed into a Tzero aluminum pan (automatically weighed by the instrument during testing) and heated from room temperature to a target temperature under N_2 atmosphere, using a N_2 flow rate of

60 mL/min and a heating rate of 10 °C/min.

[0140] Differential scanning calorimeter (DSC)

[0141] Differential scanning calorimetry (DSC) curves involved in the present disclosure were obtained by collecting thermal data of the sample using a TA Discovery series differential scanning calorimeter DSC2500, specifically as follows:

[0142] A several-milligram sample was weighed into a Tzero aluminum pan and sealed with a Tzero hermetic lid. The sample was heated to a target temperature (prior to the decomposition temperature) under N_2 atmosphere, with an N_2 flow rate of 50 mL/min and a heating rate of 10°C/min.

[0143] ^{1}H Nuclear magnetic resonance (^{1}H NMR)

[0144] The Nuclear Magnetic Resonance (NMR) spectra involved in the present disclosure were acquired using a Bruker AVANCE NEO 400 MHz NMR spectrometer, utilizing DMSO-d6 as the NMR solvent.

[0145] High-performance liquid chromatography (HPLC)

[0146] The purity/content of the samples involved in the present disclosure were acquired by high-performance liquid chromatography on an Agilent 1260 II model or an equivalent high-performance liquid chromatography instrument. Specific instruments and test parameters are as follows:

Item	**Parameters**	
Instrument	Agilent 1260 II HPLC or equivalent	
Chromatographic column	ACE Excel 3 C18-PFP 150×4.6 mm, 3 μm (PN: EXL-1110-1546U)	
Mobile phase	A: 0.01 mol/L potassium dihydrogen phosphate (pH 3.0) (e.g., obtained by accurately weighing 1.36 g of potassium dihydrogen phosphate into 1000 mL of ultrapure water, with pH adjusted to 3.0 with phosphoric acid)	B: acetonitrile:methanol=85:15 (v/v)
Detector	UV 240 nm (if DAD, bandwidth 4 nm; reference-off)	
Chromatographic column temperature	30°C	
Sample chamber temperature	Room temperature	

Item	**Parameters**		
Flow rate	1.0 mL/min		
Injection volume	5 μL		
Needle wash solvent	ACN		
Diluent	50% ACN		
Run time	51 min		
Sample purity test Elution procedure	Time (min)	%A	%B
	0	75	25
	3	65	35
	13	55	45
	20	55	45
	32	35	65
	37	15	85
	44	15	85
	44.1	75	25
	51	75	25

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[0147] Ion chromatography test (IC)

[0148] The contents of chloride ions and sulfate ions involved in the present

disclosure were tested using ion chromatography (IC), and the specific instrument and test parameters of the test method are as follows:

[0149] Test method for chloride ion content:

[0150]

Instrument model	DIONEX ICS-6000^{+} DP
Chromatographic column	Dionex IonPac AS11-HC (4×250 mm, P/N: 052960)
Guard column	Dionex IonPac AG11-HC (4×50 mm, P/N: 052962)
Suppressor	Dionex ADRS 600 4 mm, P/N: 088666
Detector	Conductivity detector
Mobile phase A	A: ultrapure water Isocratic: 20 mM KOH
Needle wash solvent	Water
Eluent generator	EGC 500 KOH, PN: 075778
Run time	25 minutes
Column temperature	30°C
Sample cell temperature	35.0°C

<table>
<tr><td>Instrument model</td><td>DIONEX ICS-6000^{+} DP</td></tr>
<tr><td>Autosampler temperature</td><td>Room temperature</td></tr>
<tr><td>Flow rate</td><td>1.0 mL/min</td></tr>
<tr><td>Injection volume</td><td>25 μL</td></tr>
<tr><td>Elution procedure</td><td><table><tr><td>Time (min)</td><td>Concentration (mM)</td></tr><tr><td>0.0</td><td>20</td></tr><tr><td>10.5</td><td>20</td></tr><tr><td>12.5</td><td>40</td></tr><tr><td>18.5</td><td>40</td></tr><tr><td>20.5</td><td>20</td></tr><tr><td>25.0</td><td>20</td></tr></table></td></tr>
<tr><td>Solvent</td><td>4-Methyl-2-pentanone, purified water</td></tr>
<tr><td>Standard solution (0.010 mg/mL, Cl^{-})</td><td>A volume of 0.1 mL of a 1000 μg/mL chloride ion standard solution was pipetted into a 25 mL volumetric flask containing 10 mL of methyl isobutyl ketone (MIBK). Subsequently, 9.9 mL of purified water was added. The resulting mixture was shaken for 30 seconds and allowed to stand for 5 minutes, and the lower aqueous phase was then collected.</td></tr>
</table>

Instrument model	DIONEX ICS-6000^{+} DP
Sample solution (0.1 mg/mL)	Approximately 2 mg of the sample (weighed to an accuracy of 0.01 mg) was placed into a 50 mL volumetric flask. 20 mL of MIBK was added, and dissolution was assisted by ultrasonication. Following dissolution, 20 mL of purified water was added. The mixture was shaken for 30 seconds and allowed to stand for 5 minutes, and the lower aqueous phase was then collected.
Calculation	The chloride ion content (%) for each injection of Sample 1 (SPL1) and Sample 2 (SPL2) was determined using the calculation formula derived from the Standard (STD) solution. $\mathrm{RF} = \frac{A_{RS}}{C_{RS}}$ $\mathrm{Assay}(\%) = \frac{A_{SPL}}{C_{SPL} \times RF} \times 100$ wherein: RF : Response Factor of chloride ions in the control solution; C_{RS}: concentration of chloride ions in the control solution; A_{RS}: average peak area of chloride ions in the control solution;

Instrument model	DIONEX ICS-6000^{+} DP
	A_{SPL}: peak area of chloride ions in the sample solution; C_{SPL}: concentration of the sample solution, mg/mL; Assay(%): content of chloride ions in the sample solution; Results assessment: where all test results fall within the range specified in the standard, the results are reported as the mean value of two parallel results. Note: Blank integration was subtracted.

[0151] Test method for sulfate content

Instrument model	DIONEX ICS-6000^{+} DP
Chromatographic column	Dionex IonPac AS11-HC (4×250 mm, P/N: 052960)
Guard column	Dionex IonPac AG11-HC (4×50 mm, P/N: 052962)
Suppressor	Dionex ADRS 600 4 mm, P/N: 088666
Detector	Conductivity detector
Mobile phase A	A: ultrapure water Isocratic: 20 mM KOH
Needle wash solvent	Water

<table>
<tr><td>Instrument model</td><td>DIONEX ICS-6000^{+} DP</td></tr>
<tr><td>Eluent generator</td><td>EGC 500 KOH, PN: 075778</td></tr>
<tr><td>Run time</td><td>25 minutes</td></tr>
<tr><td>Column temperature</td><td>30°C</td></tr>
<tr><td>Sample cell temperature</td><td>35.0°C</td></tr>
<tr><td>Autosampler temperature</td><td>Room temperature</td></tr>
<tr><td>Flow rate</td><td>1.0 mL/min</td></tr>
<tr><td>Injection volume</td><td>25 μL</td></tr>
<tr><td>Elution procedure</td><td>
<table>
<tr><td>Time (min)</td><td>Concentration (mM)</td></tr>
<tr><td>0.0</td><td>20</td></tr>
<tr><td>10.5</td><td>20</td></tr>
<tr><td>12.5</td><td>40</td></tr>
<tr><td>18.5</td><td>40</td></tr>
<tr><td>20.5</td><td>20</td></tr>
<tr><td>25.0</td><td>20</td></tr>
</table>
</td></tr>
<tr><td>Solvent</td><td>4-Methyl-2-pentanone, purified water</td></tr>
</table>

Instrument model	DIONEX ICS-6000^{+} DP
Standard solution (0.020 mg/mL, sulfate)	A volume of 0.2 mL of a 1000 μg/mL sulfate ion standard solution was pipetted into a 25 mL volumetric flask containing 10 mL of methyl isobutyl ketone (MIBK). Subsequently, 9.8 mL of purified water was added. The resulting mixture was shaken for 30 seconds and allowed to stand for 5 minutes, and the lower aqueous phase was then collected.
Sample solution (0.1 mg/mL)	Approximately 2 mg of the sample (weighed to an accuracy of 0.01 mg) was placed into a 50 mL volumetric flask. 20 mL of MIBK was added, and dissolution was assisted by ultrasonication. Following dissolution, 20 mL of purified water was added. The mixture was shaken for 30 seconds and allowed to stand for 5 minutes, and the lower aqueous phase was then collected.
Calculation	The sulfate content (%) for each injection of Sample 1 (SPL1) and Sample 2 (SPL2) was determined using the calculation formula derived from the Standard (STD) solution. $$\mathrm{RF} = \frac{A_{RS}}{C_{RS}}$$

Instrument model	DIONEX ICS-6000^{+} DP
	$\text{Assay}(\%) = \frac{A_{SPL}}{C_{SPL} \times RF} \times 100$ wherein: RF: Response Factor of sulfate in the control solution; C_{RS}: concentration of sulfate in the control solution; A_{RS}: average peak area of sulfate in the control solution; A_{SPL}: peak area of sulfate in the sample solution; C_{SPL}: concentration of the sample solution, mg/mL; $\text{Assay}(\%)$: content of sulfate ions in the sample solution; Results assessment: where all test results fall within the range specified in the standard, the results are reported as the mean value of two parallel results. Note: Blank integration was subtracted.

[0152] Dynamic solubility evaluation (water, SGF, FaSSIF)

[0153] Biological vehicles (SGF, FaSSIF) or water were separately added to the samples (loading concentration of 1 mg/mL, calculated as the free base of the compound of formula I). After shaking or ultrasonicating for approximately 2 mins, the turbid samples were transferred to a shaker (37°C, 100 rpm/min). After shaking for a corresponding period of time, the samples were filtered using a filter membrane (nylon membrane, pore size 0.22 μm), and the solubility of the filtrate was tested. Therein, the SGF system was shaken for 1 hour, and the water

and FaSSIF systems were shaken for 4 hours.

[0154] The specific preparation process for the biological vehicles used to assess the dynamic solubility of the samples is shown in the table below:

Biological vehicle	**Preparation method**
Simulated gastric fluid SGF	1. 1005.90 mg of NaCl was weighed into a 500 ml beaker, and 450 ml of deionized water was added to dissolve the NaCl. 2. The pH was adjusted to 1.660 using 1N HCl; the solution was diluted to volume (500 ml) with deionized water to obtain an SGF dissolution solution. 3. 80 ml of the above buffer solution was taken into a 100 ml volumetric flask. 6 mg of SIF powder was weighed and added to the above SGF dissolution solution, and the mixture was stirred until completely dissolved; the mixture was diluted to a volume of 100 ml with the SGF dissolution solution to prepare the SGF vehicle. 4. The vehicle was allowed to stand at room temperature for 2 hours before use.
Fasted state	1. 210.01 mg of NaOH, 2248.38 mg of $NaH_2PO_4 \cdot 2H_2O$,

Biological vehicle	**Preparation method**
simulated intestinal fluid (FaSSIF)	and 3103.28 mg of NaCl were weighed into a 500 ml beaker, and 450 ml of deionized water was added to dissolve the components. 2. The pH was adjusted to 6.560 using 1N HCl; the solution was diluted to volume (500 ml) with deionized water to obtain a FaSSIF dissolution solution. 3. 80 ml of the above buffer solution was taken into a 100 ml volumetric flask. 224.47 mg of SIF powder was weighed and added to the above FaSSIF dissolution solution, and the mixture was stirred until completely dissolved; the mixture was diluted to a volume of 100 ml with the FaSSIF dissolution solution to prepare the FaSSIF vehicle. 4. The vehicle was allowed to stand at room temperature for 2 hours before use.

[0155] Table of English/Abbreviation to Chinese equivalents for solvents involved in the present disclosure

English/Abbreviations	Full name
1,4-Dioxane	1,4-dioxane

2-Butanol	*sec*-butanol
2-MeTHF	2-methyltetrahydrofuran
AC	acetone
ACN	acetonitrile
AUC	area under the drug concentration-time curve
°C	degrees Celsius
$CHCl_3$	trichloromethane
Cmax	peak drug concentration
CPME	cyclopentyl methyl ether
DCM	dichloromethane
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DSC	differential scanning calorimetry
eq.	equivalent
EtOAc	ethyl acetate
EtOH	ethanol
g	gram
h	hour
H_2O	Water

HPLC	high-performance liquid chromatography
IC	ion chromatography
IPA	isopropyl alcohol
IPAC	isopropyl acetate
kg	kilogram
KOH	potassium hydroxide
L	liter
Me	methyl
MEK	methyl ethyl ketone
MeOH	methanol
mg	milligram
MIBK	methyl isobutyl ketone
min	minute
mL	milliliter
mM	millimole
mol	mole
MTBE	methyl tert-butyl ether
NaOH	sodium hydroxide
n-Heptane	n-heptane

TGA	thermogravimetric analysis
THF	tetrahydrofuran
Toluene	toluene
XRPD	X-ray powder diffraction
μg	microgram
$Pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium
DavePhos	2-dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl
mpk	milligrams per kilogram of body weight
HPMC E5	hydroxypropyl methylcellulose E5

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[0156] Starting Materials Preparation Example

[0157] The free base 1 of the compound of formula I was obtained by referring to the preparation method for crystal form 1 of compound A in Example 6.2.1 A of Patent Application CN 115190874A.

[0158] The free base 4 of the compound of formula I was obtained by referring to the preparation method for crystal form 4 of compound A in Example 6.2.4 D of Patent Application CN 115190874A.

[0159] In the following Examples, Effect Examples, and Comparative Examples, all references to "free base" refer to free base 1, with the exception of Example 4.

[0160] Salt Forms Preparation Example

[0161] Example 1: Preparation and characterization of mesylate salt crystal form A of the compound of formula I

[0162] 602.46 mg of the free base of the compound of formula I was weighed into a 20 mL glass vial, and 7 mL of MTBE was added to obtain a suspension. 151.55 mg of methanesulfonic acid was diluted with 2.5 mL of MTBE and then slowly added to the suspension of the free base. Residual acidic solution was rinsed with 4 mL of MTBE and then added to the suspension. The molar ratio of the reactants was 1/1 (acid/free base). Magnetic stirring was performed at 5°C while the vial was wrapped in aluminum foil to protect the mixture from light.

[0163] After magnetic stirring was conducted for 2 days, the solid was isolated from the sample and dried under vacuum at 30°C. The dried sample was transferred to a 20 mL glass vial, and 5 mL of toluene was added to perform slurring at room temperature for 1 hour while the vial was wrapped in aluminum foil to protect the mixture from light. The solid was then isolated by centrifugation and dried under vacuum at 30°C for 7 hours to obtain 550.88 mg of a sample of the mesylate salt crystal form A of the compound of formula I as an off-white solid, with a yield of 71% and a purity of 97.7%.

[0164] The mesylate salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 1; the DSC/TGA are shown in FIG. 2; and the XRPD

pattern is shown in FIG. 3.

[0165] The ^{1}H NMR results of the mesylate salt crystal form A of the compound of formula I show that the molar ratio of acid to base is 1.0. The TGA/DSC thermograms thereof show that the weight loss before 180°C was relatively small, with a weight loss of 0.85%; there was a minor endothermic peak at approximately 174.14°C (peak value) and a sharp endothermic peak at 213.85°C (peak value) with an enthalpy value of 66.99 J/g. Relevant characterization data indicate that the mesylate salt crystal form A is an anhydrous crystal form of a mono salt.

[0166] The characteristic peak data of the XRPD (Malvern Panalytical Aeris model) are shown in the table below:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.60	15.76	100.00
7.35	12.02	5.52
9.47	9.34	15.75
10.99	8.05	15.18
11.36	7.78	5.25
12.31	7.18	30.38
13.48	6.56	2.22

14.02	6.31	2.03
14.86	5.96	7.19
15.40	5.75	42.13
16.45	5.39	2.22
17.12	5.18	6.96
17.57	5.04	12.61
18.33	4.84	8.44
19.15	4.63	13.26
19.66	4.51	4.53
20.10	4.41	5.51
20.66	4.29	2.95
21.78	4.08	3.66
22.42	3.96	9.95
22.94	3.87	7.28
23.44	3.79	2.46
26.69	3.34	3.46
27.18	3.28	2.42
28.95	3.08	3.45
34.31	2.61	2.69
36.14	2.48	1.33

[0167] Example 2: Preparation and characterization of tosylate salt crystal form A of the compound of formula I

[0168] 20 mg of the free base of the compound of formula I was weighed into an HPLC vial, and 0.3 mL of EtOAc and an equimolar ratio of p-toluenesulfonic acid were added thereto. Magnetic stirring was performed at room temperature. After magnetic stirring was conducted at room temperature (approximately 20°C) for 2 to 3 days, the mixture was isolated by centrifugation. After drying under vacuum at 30°C for 5 hours, the tosylate salt crystal form A of the compound of formula I was obtained with an HPLC purity of 92.7%.

[0169] The tosylate salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 4; the DSC/TGA thermograms are shown in FIG. 5; and the XRPD pattern is shown in FIG. 6.

[0170] The TGA results show that the sample had no significant weight loss before decomposition. The DSC results show that the sample had minor endothermic peaks at 113.26°C and 178.05°C (peak values), and an endothermic peak at 223.99°C (peak value) with a heat of fusion of 68.20 J/g. The ^{1}H NMR results show that the sample contained 1.0 equivalent of p-toluenesulfonic acid. The tosylate salt crystal form A is an anhydrous crystal form of a monotosylate salt.

[0171] The characteristic peak data of the XRPD (Rigaku Smartlab SE model)

are shown in the table below:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.17	17.09	100.00
7.04	12.55	10.07
7.98	11.07	1.98
8.55	10.33	11.39
10.40	8.50	43.38
11.16	7.92	6.91
11.51	7.68	4.54
13.15	6.73	3.62
14.19	6.24	14.11
14.61	6.06	6.71
15.14	5.85	8.26
16.15	5.48	3.28
17.56	5.05	10.38
18.34	4.83	14.19
19.52	4.54	4.23
19.85	4.47	7.91
20.44	4.34	4.30
21.01	4.23	5.89

21.56	4.12	4.54
22.21	4.00	5.03
22.58	3.93	9.09
23.75	3.74	4.57
24.65	3.61	5.23
25.38	3.51	4.15
26.45	3.37	3.28
26.96	3.30	2.68
28.82	3.10	1.43
30.53	2.93	1.03
31.81	2.81	0.89
35.27	2.54	0.63
37.51	2.40	0.23

[0172] Example 3: Preparation and characterization of tosylate salt crystal form B of the compound of formula I

[0173] 500.3 mg of the free base of the compound of formula I was weighed into a 20-mL glass vial, and 7.5 mL of toluene was added to obtain a suspension. 253.71 mg of p-toluenesulfonic acid monohydrate was weighed and added to the suspension. The molar ratio of the reactants was 1/1 (acid/free base). A small amount of seed crystals was then added, and magnetic stirring was performed at room temperature. After stirring was conducted for a period of time, an

additional 1 mL of toluene was added. The system was continued to be magnetically stirred at room temperature for 2 days, after which it became a light yellow suspension. The solid was isolated by centrifugation. The obtained solid was dried under vacuum at 30°C overnight to obtain 601.8 mg of a sample, with a yield of approximately 79.3%.

[0174] 100 mg of the sample dried under vacuum at 30°C was taken and slurred in 2 mL of 2-MeTHF at room temperature while protected from light. After slurring overnight, a small sample was taken and subjected to suction filtration to obtain a filter cake. The filter cake was dried under vacuum at room temperature overnight, and then further dried under vacuum in an oven at room temperature overnight to obtain 437.3 mg of the tosylate salt crystal form B, with an HPLC purity of 96.8%.

[0175] Preparation method for seed crystals: 100.57 mg of the free base of the compound of formula I was weighed into an HPLC vial, and 1.5 mL of toluene was added to obtain a suspension. 50.69 mg of p-toluenesulfonic acid monohydrate was added thereto (acid/base loading ratio was 1/1). Magnetic stirring was performed overnight at room temperature while the mixture was protected from light, and the solid was then isolated by centrifugation and dried under vacuum at 30°C overnight to obtain the seed crystals.

[0176] The tosylate salt crystal form B of the compound of formula I was characterized by ^{1}H NMR, XRPD, and TGA, respectively. The ^{1}H NMR

spectrum is shown in FIG. 7; the TGA/DSC thermograms are shown in FIG. 8; and the XRPD pattern is shown in FIG. 9.

[0177] The ^{1}H NMR results show that the tosylate salt crystal form B of the compound of formula I contained 1.0 equivalent of p-toluenesulfonic acid. The TGA results show that the sample had no significant weight loss before decomposition. The DSC results show that the sample had endothermic peaks at 180.9°C and 223.0°C (peak values), and the heat of fusion of the endothermic peak at 223.0°C was 54.52 J/g. Relevant characterization data indicate that the tosylate salt crystal form B is an anhydrous crystal form of a monotosylate salt.

[0178] The characteristic peak data of the XRPD (Bruker D2 model) of the tosylate salt crystal form B are shown in the table below:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.09	17.34	12.68
5.64	15.66	41.63
7.06	12.51	5.42
7.84	11.26	20.64
9.22	9.59	12.32
10.11	8.74	20.58
10.87	8.13	15.17

11.36	7.78	29.85
12.03	7.35	19.43
13.44	6.58	52.29
13.60	6.51	39.59
14.49	6.11	50.60
15.13	5.85	47.76
16.21	5.46	9.92
17.28	5.13	100.00
17.38	5.10	92.84
18.58	4.77	21.10
19.55	4.54	16.10
20.45	4.34	43.73
21.15	4.20	40.38
22.15	4.01	51.56
22.89	3.88	17.76
23.97	3.71	38.67
25.03	3.56	16.06
27.08	3.29	15.22
29.19	3.06	7.76
30.07	2.97	3.42

30.73	2.91	2.25
31.60	2.83	3.03
35.97	2.49	2.34
37.84	2.38	2.90

[0179] Example 4: Preparation and characterization of tosylate salt crystal form E of the compound of formula I

[0180] Preparation method: 499.94 mg of free base 4 (i.e., crystal form 4 of the free base) of the compound of formula I was weighed into a 20 mL vial. 7.5 mL of ethyl acetate and an equimolar ratio (254.19 mg) of p-toluenesulfonic acid monohydrate were added thereto (acid/base loading ratio was 1/1). Magnetic stirring was performed overnight at room temperature while the mixture was protected from light. After stirring overnight, the solid was isolated by centrifugation and dried under vacuum at 30°C for 4 hours to obtain the tosylate salt crystal form E of the compound of formula I, with a purity of 98.6%.

[0181] The tosylate salt crystal form E of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The XRPD pattern is shown in FIG. 10; the TGA/DSC thermograms are shown in FIG. 11; and the ^{1}H NMR spectrum is shown in FIG. 12.

[0182] The TGA results show that the sample had no significant weight loss before decomposition. The DSC results show that the sample had an endothermic peak at 180.26°C with a heat of fusion of 26.13 J/g, and an

endothermic peak at 224.05°C (peak value) with a heat of fusion of 59.89 J/g. The 1H NMR results show that the sample contained 1.0 equivalent of p-toluenesulfonic acid. Relevant characterization data indicate that the tosylate salt crystal form E is an anhydrous crystal form of a monotosylate salt. The characteristic peak data of the XRPD (Malvern Panalytical Aeris model) are shown in the table below:

Pos.[°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
3.3440	32.24	0.4330	26.40016	1.94
5.5976	1027.33	0.0866	15.77559	61.93
8.1505	1281.59	0.0866	10.83911	77.26
9.8512	268.16	0.0866	8.97135	16.17
10.0185	146.62	0.0649	8.82191	8.84
11.3137	334.85	0.1082	7.81471	20.19
13.8880	460.50	0.1082	6.37143	27.76
14.1506	84.07	0.0866	6.25376	5.07
16.1162	87.36	0.1299	5.49518	5.27
16.4309	43.89	0.1299	5.39062	2.65
17.3320	1658.75	0.1299	5.11234	100.00
17.8765	103.81	0.1732	4.95783	6.26
18.8287	277.66	0.1082	4.70920	16.74

19.8833	357.46	0.1082	4.46176	21.55
20.2254	183.24	0.0866	4.38704	11.05
21.7187	34.01	0.1732	4.08867	2.05
22.3279	96.34	0.1082	3.97847	5.81
22.8657	51.57	0.0866	3.88609	3.11
23.1659	55.92	0.1732	3.83642	3.37
23.9893	40.80	0.5196	3.70656	2.46
24.5103	36.67	0.1299	3.62894	2.21
25.5081	84.56	0.1299	3.48920	5.10
27.2253	122.82	0.1082	3.27289	7.40
30.4799	20.01	0.5196	2.93043	1.21
33.7537	62.39	0.0866	2.65331	3.76
34.3805	41.11	0.1299	2.60636	2.48

[0183] Example 5: Preparation and characterization of tosylate salt crystal form C of the compound of formula I

[0184] 20 mg of the free base of the compound of formula I was weighed into an HPLC vial, and 0.3 mL of MTBE and an equimolar ratio of p-toluenesulfonic acid were added thereto. Magnetic stirring was performed at room temperature. After magnetic stirring was conducted at room temperature (approximately 20°C) for 2 to 3 days, the mixture was isolated by centrifugation. After drying under vacuum at 30°C for 5 hours, the tosylate salt crystal form C of the compound of

formula I was obtained with an HPLC purity of 95.9%.

[0185] The tosylate salt crystal form C of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 13; the TGA/DSC thermograms are shown in FIG. 14; and the XRPD pattern is shown in FIG. 15.

[0186] The TGA results show that the weight loss of the sample before 150°C was 4.973%. The DSC results show that the sample had endothermic peaks at 128.1°C and 224.2°C (peak values), with the enthalpy value of the endothermic peak at 224.2°C being 60.17 J/g, and an exothermic peak was present at 143.0°C (peak value). The ^{1}H NMR results show that the sample contained 1.0 equivalent of p-toluenesulfonic acid. The tosylate salt crystal form C is a hydrate of the monotosylate salt.

[0187] The characteristic peak data of the XRPD (Rigaku Smartlab SE model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
4.9196	3013.62	0.0689	17.94808	100.00
7.6211	56.49	0.0787	11.59076	1.87
8.7276	17.54	0.2362	10.12370	0.58
9.8818	111.90	0.2362	8.94366	3.71

10.3286	37.67	0.1181	8.55772	1.25
12.2660	27.38	0.2362	7.21006	0.91
14.6923	81.70	0.1378	6.02440	2.71
16.8544	99.30	0.1378	5.25613	3.29
17.7818	85.12	0.1378	4.98404	2.82
18.8413	58.81	0.3149	4.70609	1.95
20.2883	22.66	0.3936	4.37358	0.75
21.4070	49.90	0.1968	4.14749	1.66
21.8678	54.50	0.1574	4.06113	1.81
23.0371	27.95	0.3149	3.85756	0.93

[0188] Example 6: Preparation and characterization of hydrochloride salt crystal form B of the compound of formula I

[0189] 19.99 mg of the starting free base was weighed into an HPLC vial, and 0.3 mL of MTBE was added to obtain a suspension. 4.4 μL of hydrochloric acid was added to the suspension of the free base (acid/base loading ratio of 1/1), and magnetic stirring was performed at room temperature (17°C to 21°C). At the beginning of the reaction, an additional 0.2 mL of MTBE was added. After magnetic stirring was continued at room temperature for 2 days, the system became a white suspension. The solid was isolated by centrifugation and dried under vacuum at 30°C for 5 hours to obtain the crystal form B of the hydrochloride of the compound of formula I, with an HPLC purity of 93.6%.

[0190] The hydrochloride salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 16; the XRPD pattern is shown in FIG. 17; and the TGA/DSC thermograms are shown in FIG. 18.

[0191] The TGA results show that the sample had a weight loss of 0.2099% before 120°C and a weight loss of 8.859% between 120°C and 190°C. The DSC results showed that the sample had endothermic peaks at 173.0°C and 197.7°C (peak values).

[0192] A sample was re-prepared using the above method under light-protected conditions and dried under vacuum at 40°C for 4 hours to obtain a sample with an HPLC purity of 94.6%, which was used for the collection of molar ratio data. Therein, the free base content was measured by HPLC to be 85.5%, and the Cl- content was measured by IC to be 5.8%; the calculated molar ratio of acid to base was 0.7. The hydrochloride salt crystal form B is an anhydrous crystal form.

[0193] The characteristic peak data of the XRPD (Bruker D2 model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
5.7481	514.07	0.1181	15.36288	100.00
10.1230	74.29	0.2755	8.73108	14.45

11.4009	208.24	0.1968	7.75515	40.51
13.1890	44.92	0.2362	6.70748	8.74
14.6758	114.27	0.1181	6.03112	22.23
15.5483	57.25	0.2362	5.69459	11.14
17.8756	93.52	0.3149	4.95808	18.19
19.8665	69.82	0.3149	4.46549	13.58
22.0152	50.56	0.4723	4.03426	9.83
23.1468	47.34	0.3936	3.83954	9.21
31.2174	12.61	0.9446	2.86286	2.45

[0194] Example 7: Preparation and characterization of sulfate salt crystal form A of the compound of formula I

[0195] 20 mg of the free base of the compound of formula I was weighed into an HPLC vial, and 0.3 mL of IPA and an equimolar ratio of sulfuric acid were added thereto. Magnetic stirring was performed at room temperature. After magnetic stirring was conducted at room temperature (approximately 20°C) for 2 to 3 days, the mixture was isolated by centrifugation. After drying under vacuum at 30°C for 5 hours, the sulfate salt crystal form A of the compound of formula I was obtained with an HPLC purity of 98.2%.

[0196] The sulfate salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 19; the TGA/DSC thermograms are shown in FIG. 20;

and the XRPD pattern is shown in FIG. 21.

[0197] The TGA results show that the weight loss of the sample before 170°C was 10.82%. The DSC results show that the sample had an endothermic peak at 139.0°C (peak value) with an enthalpy value of 114.9 J/g.

[0198] A sample was re-prepared using the above method under light-protected conditions and dried under vacuum at 40°C for 4 hours to obtain a sample with an HPLC purity of 98.4%, which was used for the collection of molar ratio data. The free base content was measured by HPLC to be 85.5%, and the sulfate content was measured by IC to be 17.0%; the calculated molar ratio of acid to base was 1.0. The sulfate salt crystal form A is a hydrate crystal form of the monosulfate salt.

[0199] The characteristic peak data of the XRPD (Rigaku Smartlab SE model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
5.4511	1789.24	0.0590	16.19901	100.00
8.4856	46.16	0.1574	10.41181	2.58
10.1354	10.10	0.3936	8.72045	0.56
10.9300	27.73	0.1181	8.08821	1.55
11.6459	88.09	0.0984	7.59252	4.92
12.3506	109.78	0.1181	7.16087	6.14

13.3414	20.50	0.1574	6.63122	1.15
14.0532	126.26	0.0984	6.29690	7.06
14.5162	46.96	0.1181	6.09706	2.62
15.0232	52.60	0.0984	5.89241	2.94
17.3767	21.28	0.2362	5.09931	1.19
18.0539	103.76	0.0984	4.90953	5.80
20.0113	57.83	0.1968	4.43349	3.23
20.5813	162.35	0.1181	4.31198	9.07
21.3848	56.52	0.1181	4.15174	3.16
21.7914	137.38	0.1181	4.07519	7.68
22.0613	105.40	0.1181	4.02595	5.89

[0200] Example 8: Preparation and characterization of benzenesulfonate salt crystal form A of the compound of formula I

[0201] 29.91 mg of the starting free base and 12.39 mg of benzenesulfonic acid were weighed into an HPLC vial (acid/base loading ratio of 1/1). 0.65 mL of MTBE was added, and magnetic stirring was performed at room temperature (14°C to 23°C) while protected from light. The system solidified at the beginning of the reaction, and an additional 0.2 mL of MTBE was added. After magnetic stirring was continued overnight at room temperature, the system became a white suspension. After reacting for 3 days, the solid was isolated by centrifugation and dried under vacuum at 40°C for 4 hours to obtain the

benzenesulfonate salt crystal form A of the compound of formula I, with an HPLC purity of 96.0%.

[0202] The benzenesulfonate salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 22; the TGA/DSC thermograms are shown in FIG. 23; and the XRPD pattern is shown in FIG. 24.

[0203] The TGA results show that the sample had no weight loss before decomposition. The DSC results show that the sample had an endothermic peak at 207.7°C (peak value) with an enthalpy value of 58.34 J/g. The ^{1}H NMR results show that the sample contained 1.0 equivalent of benzenesulfonic acid. The benzenesulfonate salt crystal form A is an anhydrous crystal form of a monobenzenesulfonate salt.

[0204] The characteristic peak data of the XRPD (Bruker D2 model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
5.1602	129.91	0.2755	17.11178	69.60
8.4602	96.58	0.1574	10.44307	51.74
9.5232	53.39	0.2362	9.27961	28.60
10.4003	186.66	0.3149	8.49888	100.00
12.3995	57.93	0.1574	7.13271	31.03

14.6948	113.92	0.2362	6.02337	61.03
15.7166	62.44	0.3936	5.63397	33.45
16.9731	60.54	0.4723	5.21964	32.43
17.8415	144.20	0.2362	4.96750	77.25
18.4888	129.35	0.2755	4.79501	69.30
19.2929	33.39	0.2362	4.59693	17.89
21.0141	44.01	0.3149	4.22414	23.58
22.5264	122.97	0.1574	3.94386	65.88
23.2543	86.45	0.3149	3.82202	46.32
29.2833	10.32	0.9446	3.04740	5.53

[0205] Example 9: Preparation and characterization of benzenesulfonate salt crystal form B of the compound of formula I

[0206] 100.32 mg of the starting free base and 62.14 mg of benzenesulfonic acid (acid/base loading ratio of 1/1) were weighed into a 4 mL glass vial. 2 mL of MTBE was added, and magnetic stirring was performed at room temperature (approximately 15°C) while the mixture was protected from light. At the beginning of the reaction, about 2 mg of seed crystals of the benzenesulfonate salt crystal form A was added. After reacting for 2 days at room temperature, the solid was isolated by centrifugation and dried under vacuum at 30°C overnight to obtain the benzenesulfonate salt crystal form B of the compound of formula I, with an HPLC purity of 97.7%.

[0207] Preparation method for seed crystals: 29.91 mg of the free base of the compound of formula I was weighed into an HPLC vial, and 0.65 mL of MTBE was added to obtain a suspension. Upon the addition of 12.39 mg of benzenesulfonic acid (acid/base loading ratio of 1/1), the system solidified. An additional 0.2 mL of solvent was added to obtain a white suspension. After magnetic stirring was conducted for around 3 days at room temperature while the mixture was protected from light, the solid was isolated by centrifugation and dried under vacuum at 40°C for 4 hours.

[0208] The benzoate salt crystal form B of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 25; the TGA/DSC thermograms are shown in FIG. 26; and the XRPD pattern is shown in FIG. 27.

[0209] The TGA results show that the weight loss of the sample before 120°C was 1.3%. The DSC results show that the sample had endothermic peaks at 86.0°C and 200.7°C (peak values). The ^{1}H NMR results show that the sample contained 1.2 equivalents of benzenesulfonic acid.

[0210] The sample was heated to 120°C and returned to room temperature for XRPD testing, which show that the crystal form of the sample remained unchanged, although some peaks were shifted (FIG. 28). TGA/DSC results show that the weight loss of the sample before 120°C was 0.4%, and DSC results show that the sample had endothermic peaks at 71.0°C and 204.3°C (peak values)

(FIG. 29). The ^{1}H NMR results show that the sample contained 1.2 equivalents of benzenesulfonic acid (FIG. 30). The above data indicate that benzenesulfonate salt crystal form B is a hydrate of a monobenzenesulfonate salt.

[0211] The characteristic peak data of the XRPD (Bruker D2 model) (before heating) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
3.3325	0.13	0.6298	26.49159	0.03
5.0341	183.96	0.1574	17.54000	41.16
5.2552	216.24	0.1181	16.80258	48.39
8.3379	243.98	0.1968	10.59596	54.59
9.6912	169.97	0.2362	9.11912	38.03
10.2742	402.44	0.1771	8.60288	90.05
10.6773	222.47	0.0984	8.27906	49.78
12.1113	307.61	0.0984	7.30180	68.83
12.3157	286.43	0.1181	7.18105	64.09
13.2997	313.24	0.1181	6.65190	70.09
14.4162	193.23	0.1968	6.13912	43.24
15.0588	128.24	0.2362	5.87858	28.70
16.9198	302.50	0.1574	5.23596	67.69
17.4980	343.11	0.1574	5.06423	76.77

19.6233	364.45	0.1181	4.52027	81.55
20.0526	144.89	0.1574	4.42446	32.42
20.6290	169.55	0.1574	4.30211	37.94
21.6014	446.90	0.0984	4.11059	100.00
24.6140	59.63	0.1574	3.61389	13.34
29.0273	52.83	0.4723	3.07369	11.82
31.5213	21.26	0.4723	2.83595	4.76
34.5722	28.06	0.4723	2.59235	6.28

[0212] Example 10: Preparation and characterization of naphthoate salt crystal form B of the compound of formula I

[0213] 29.75 mg of the starting free base and 21.29 mg of 2-naphthalenesulfonic acid (acid/base loading ratio of 1.3/1) were weighed into an HPLC vial. 0.45 mL of EtOAc was added thereto, and magnetic stirring was performed at room temperature (14°C to 23°C) while protected from light. After reacting for 3 days, the solid was isolated by centrifugation and dried under vacuum at 40°C for 4 hours to obtain the naphthoate salt crystal form B of the compound of formula I, with an HPLC purity of 80.0%.

[0214] The naphthoate salt crystal form B of the compound of formula I was characterized by XRPD. The XRPD pattern is as shown in FIG. 31.

[0215] The characteristic peak data of the XRPD (Bruker D2 model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
4.4768	129.03	0.1574	19.72199	55.90
4.9816	78.95	0.1574	17.72471	34.20
9.2819	203.22	0.1574	9.52025	88.04
10.1017	115.13	0.1968	8.74947	49.88
10.9215	121.27	0.1574	8.09443	52.54
13.7421	124.67	0.1574	6.43874	54.01
14.6486	76.17	0.1574	6.04226	33.00
15.1605	66.39	0.1574	5.83938	28.76
17.3033	118.97	0.1968	5.12076	51.54
18.4536	230.83	0.0984	4.80408	100.00
19.5296	84.04	0.1181	4.54175	36.41
20.3946	74.31	0.3936	4.35103	32.19
21.4420	89.37	0.4723	4.14080	38.72
23.1624	114.29	0.0787	3.83699	49.51

[0216] Example 11: Preparation and characterization of maleate salt crystal form A of the compound of formula I

[0217] 29.99 mg of the starting free base and 9.14 mg of maleic acid were weighed into an HPLC vial (acid/base loading ratio of 1/1). 0.65 mL of MTBE was added, and magnetic stirring was performed at room temperature (14°C to

23°C) while protected from light. The system solidified at the beginning of the reaction, and an additional 0.2 mL of MTBE was added. After magnetic stirring was continued overnight at room temperature, the system became a white suspension. The solid was isolated by centrifugation and dried under vacuum at 30°C overnight to obtain the maleate salt crystal form A of the compound of formula I, with an HPLC purity of 96.9%.

[0218] The maleate salt crystal form A of the compound of formula I was characterized by ^{1}H NMR, XRPD, DSC, and TGA, respectively. The ^{1}H NMR spectrum is shown in FIG. 32; the TGA/DSC thermograms are shown in FIG. 33; and the XRPD pattern is shown in FIG. 34.

[0219] The TGA results show that the weight loss of the sample before 120°C was 0.5%. The DSC results show that the sample had an endothermic peak at 127.8°C (peak value) with an enthalpy value of 73.43 J/g. The ^{1}H NMR results show that the sample contained 1.0 equivalent of maleic acid. The maleate salt crystal form A is an anhydrous crystal form of a monomaleate salt.

[0220] The characteristic peak data of the XRPD (Bruker D2 model) are shown in the table below:

Pos. [°2θ]	Height [cts]	FWHM Left [°2θ]	d-Spacing [Å]	Rel. Int. [%]
5.0525	24.18	0.2362	17.47616	1.81
8.1617	319.21	0.2362	10.82430	23.85

9.6419	80.22	0.1574	9.16562	5.99
10.1913	138.27	0.1378	8.67268	10.33
10.9507	95.14	0.2362	8.07294	7.11
12.3188	1274.10	0.1574	7.17926	95.21
14.7302	143.40	0.2362	6.00897	10.72
15.9526	226.97	0.1574	5.55118	16.96
16.4790	436.62	0.1378	5.37502	32.63
17.6825	167.81	0.1968	5.01178	12.54
18.5818	102.34	0.2362	4.77121	7.65
19.1817	170.54	0.1574	4.62333	12.74
20.6530	1338.26	0.1968	4.29718	100.00
22.6499	181.50	0.2362	3.92263	13.56
23.7438	86.00	0.2362	3.74433	6.43
24.8556	364.81	0.1968	3.57930	27.26
26.4115	112.21	0.1574	3.37187	8.38
27.2460	159.54	0.2362	3.27046	11.92
29.0556	196.89	0.2362	3.07075	14.71
31.2983	60.50	0.1574	2.85565	4.52
33.4219	80.96	0.1968	2.67889	6.05
36.6501	19.10	0.4723	2.45000	1.43

38.7310	31.39	0.4723	2.32302	2.35

[0221] Effect example 1: Solubility testing of high-purity salt form samples of the compound of formula I

[0222] Solubility testing was performed in biological media and water for the following four salt form samples: tosylate salt crystal forms A, B, and E, and mesylate salt crystal form A. The specific steps were as follows: Water or biological vehicles were separately added to the samples (loading concentration of 1 mg/mL, calculated as the free base of the compound of formula I). After shaking or ultrasonicating for approximately 2 mins, the turbid samples were transferred to a shaker (37°C, 100 rpm/min). After shaking for a corresponding period of time, the samples were filtered using a filter membrane (nylon membrane, pore size 0.22 μm), and the solubility of the filtrate was tested. Therein, the SGF system was shaken for 1 hour, and the water and FaSSIF systems were shaken for 4 hours.

[0223] The results show that, compared with the free base, all salt forms have a certain improvement in solubility (mg/mL) in water/FaSSIF/SGF, being 0.008-0.05 vs. <LOQ, 0.002-0.004 vs. 0.001, and 0.22-0.24 vs. 0.11, respectively. The solubility in simulated gastric fluid (SGF) was 2 to 2.18 times that of the free base; the solubility in fasted state simulated intestinal fluid (FaSSIF) was 2 to 4 times that of the free base; and the solubility in water was more than 100 to 800 times that of the free base, respectively.

[0224] Table 1.: Summary of solubilities of four salt forms and the free base

Salt form	**H_2O (RT/4h) mg/ml**	**FaSSIF (37°C/4h) mg/ml**	**SGF (37°C/1h) mg/ml**
tosylate salt crystal form A	0.008	0.002	0.23
tosylate salt crystal form B	0.009	0.002	0.22
tosylate salt crystal form E	0.0498	0.004	0.24
Mesylate salt crystal form A	0.012	0.003	0.22
Free base	<LOD	0.001	0.11

Solubility unit (based on free base): mg/mL; LOD=0.06 μg/mL, LOQ=0.18 μg/mL.

[0225] Effect example 2: Solid-state stability evaluation of high-purity salt form samples of the compound of formula I

[0226] Evaluation was performed on the following six samples: sulfate salt crystal form A, tosylate salt crystal form B, tosylate salt crystal form E, mesylate salt crystal form A, benzenesulfonate salt crystal form B, and maleate salt crystal form A. Specifically, 4 to 11 mg of each sample was weighed into amber HPLC

vials and placed open under three conditions: 1) 25°C/60% RH, 2) 40°C/75% RH, and 3) 60°C. Purity testing (HPLC) and crystal form detection (XRPD) were conducted on the initial samples and the samples stored for 1 and 2 weeks.

[0227] The experimental results are shown in the table below. 1) In terms of crystal form: the tosylate salt crystal form B/mesylate salt crystal form A/tosylate salt crystal form E remained unchanged in crystal form after storage for two weeks under various conditions; the other salt forms underwent deliquescence or decrease in crystallinity after storage; 2) In terms of purity: after storage for 2 weeks, the purity of mesylate salt crystal form A under conditions of 25°C/60% RH and 60°C, and that of tosylate salt crystal form B under the condition of 25°C/60% RH remained essentially unchanged or slightly decreased; the purity of tosylate salt crystal form E remained essentially unchanged or slightly decreased under all three investigated conditions. All other samples exhibited a significant reduction in purity under different conditions.

[0228] Table 2.: Summary of 2-week solid-state stability study data for six salt forms and free base crystal form A

Starting sample (batch number)		**Condition**	**1 week**		**2 week**	
Salt form	**Purity (Area %)**		**Purity (Area %)**	**Crystal form Variation**	**Purity (Area %)**	**Crystal form Variation**
Sulfate salt crystal form A	97.9	25°C/60RH%	98.0^	crystallinity decreases	96.0*	crystallinity decreases
		40°C/75RH%	NA	deliquescence	NA	deliquescence
		60°C	95.7	substantially amorphous	87.7	substantially amorphous
Tosylate salt crystal form B	97.2	25°C/60RH%	97.1^	unchanged	96.2*	unchanged
		40°C/75RH%	92.0^		72.4	
		60°C	95.5		93.6	
Tosylate salt	97.7	25°C/60R	97.6	unchange	97.0	unchange

Starting sample (batch number)		**Condition**	**1 week**		**2 week**	
Salt form	**Purity (Area %)**		**Purity (Area %)**	**Crystal form Variation**	**Purity (Area %)**	**Crystal form Variation**
crystal form E		H% 40°C/75RH% 60°C	97.4 97.3	d	96.7 96.8	d
Mesylate salt crystal form A	97.8	25°C/60RH%	97.5^	unchanged	97.2*	unchanged
		40°C/75RH%	97.3		95.8	
		60°C	97.5		97.3	
Benzenesulfonate salt crystal form B	97.7	25°C/60RH%	83.8^	unchanged	67.6*	unchanged
		40°C/75RH%	NA	deliquescence	NA	deliquescence
		60°C	97.6	unchanged	96.8	unchanged

Starting sample (batch number)		**Condition**	**1 week**		**2 week**	
Salt form	**Purity (Area %)**		**Purity (Area %)**	**Crystal form Variation**	**Purity (Area %)**	**Crystal form Variation**
Maleate salt crystal form A	96.5	25°C/60RH%	96.0^	unchanged	94.7*	unchanged
		40°C/75RH%	84.5		60.7	
		60°C	90.4		87.0	New peaks appeared, and crystallinity decreased.

[0229] All samples were freshly prepared and immediately injected. NA: Sample deliquesced and was not analyzed.

[0230] ^: Samples with this notation were sampled and tested on Day 6; others were tested at 1 week.

[0231] *: Samples with this notation were sampled and tested on Day 13; others were tested at 2 weeks.

[0232] Effect example 3: Comparison of pharmacokinetic properties of the mesylate salt crystal form A, tosylate salt crystal forms B and E, and the free base of the compound of formula I in rats

[0233] 1) Research objective: To obtain the pharmacokinetic profiles of the free base, tosylate salt crystal form B, tosylate salt crystal form E, and mesylate salt crystal form A of the compound of formula I in male SD rats.

[0234] 2) Experimental content

[0235] Healthy male SD rats (3 animals/group) were selected and fasted for at least 12 hours. The animals were administered a dose of 10 mg per kg of body weight. At 0.25, 0.5, 1, 2, 4, 6, 8, and 24 hours after administration, whole blood samples (approximately 0.2 mL) were collected via the jugular vein into anticoagulant tubes containing EDTA-K2. Within 1 hour after collection, the plasma was separated by centrifugation and stored at -80°C for future use. The plasma concentrations in the resulting samples were determined using an LC-MS/MS method.

[0236] Experimental results: Based on the obtained plasma concentration data, the pharmacokinetic parameters after administration were calculated using the non-compartmental model in WinNonlin® 7.0 software (Pharsight, USA).

[0237] Table 3.: PK parameters of the free base, tosylate salt crystal form B,

tosylate salt crystal form E, and mesylate salt crystal form A of the compound of formula I in male SD rats after a single dose (10 mg/kg)

Parameters	Unit		Plasma		
		free base	tosylate salt crystal form B	tosylate salt crystal form E	mesylate salt crystal form A
$T_{1/2}$	h	4.56	5.71	5.29	4.70
T_{max}	h	2.00	2.67	2.75	3.33
C_{max}	ng/mL	331.25	647.78	835.77	938.72
AUC_{last}	hr*ng/mL	3500.00	7543.52	10296.17	8569.96
AUC_{Inf}	hr*ng/mL	3604.19	7962.79	10800.66	8831.15

[0238] As can be seen from the table above, tosylate salt crystal form B, tosylate salt crystal form E, and mesylate salt crystal form A involved in the present disclosure all exhibit significant improvements in PK properties compared to the free base.

[0239] The C_{max} and $AUC_{(0-t)}$ (0-24 hours) of tosylate salt crystal form B were 647.78 ng/mL and 7543.52 h·ng/mL, respectively. Compared to 331.25 ng/mL and 3500.00 h·ng/mL for the free base, both indicators showed an increase of nearly two-fold, representing a significant improvement in performance.

[0240] The C_{max} and $AUC_{(0-t)}$ (0-24 hours) of tosylate salt crystal form E were 835.77 ng/mL and 10296.17 h·ng/mL, respectively. Compared to the free base,

there was a nearly 2.5-fold increase in C_{max} and a 2.9-fold increase in $AUC_{(0-t)}$ (0-24 hours), demonstrating excellent performance.

[0241] The C_{max} and $AUC_{(0-t)}$ (0-24 hours) of mesylate salt crystal form A were 938.72 ng/mL and 8569.96 h·ng/mL, respectively. Compared to the free base, there was a nearly 2.8-fold increase in C_{max} and a 2.4-fold increase in $AUC_{(0-t)}$ (0-24 hours), also demonstrating excellent performance.

[0242] Comparative example: Summary of preparation results for various salt forms under non-light-protected conditions

[0243] Based on the pKa of the free base of the compound of formula I (acidic: 14.6 and basic: 5.6; calculated using ACD/Labs software), 50 salt/cocrystal experiments were set up using 10 acids in 5 solvent systems. Conventional experimental operations were employed without shielding from light, and all loadings were performed at an equimolar ratio of acid to base. The specific experimental steps were as follows: approximately 20 mg of the free base synthesized according to the Raw Material Preparation Example and an equimolar ratio of the ligand were weighed into an HPLC vial, and then 0.3 mL of the corresponding solvent was added (for liquid ligands, the free base was weighed and added, followed by the addition of the solvent and, finally, the ligand). Magnetic stirring was performed at room temperature. After magnetic stirring at room temperature (approximately 20°C) for 2 to 3 days, samples that were clear or had a small amount of solid were transferred to 5°C for stirring and then to

about 20°C for standing. If the samples remained clear, attempts were made using open evaporation at room temperature or the addition of an anti-solvent. The solids were then isolated by centrifugation and dried under vacuum at 30°C for 5 hours for characterization.

[0244] Relevant experimental results indicate that the salt form of the compound of formula I that is relatively stable and of higher purity is difficult to obtain.

[0245] Table 4: Summary of preparation results of salt forms of the compound of formula I

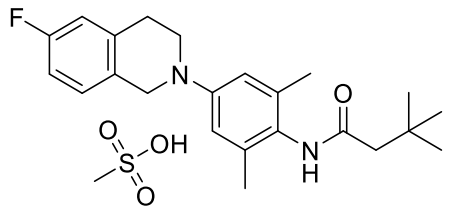
Solvent / **Result** / **Ligand**		IPA A	Toluene B	EtOAc C	MTBE D	ACN/H_2O (9/1, v/v) E
0	blank	free base	free base	free base	free base	free base
1	phosphoric acid	free base	free base	free base	free base + multiple peaks	free base
2	oxalic acid	free base	free base	free base	free base	free base
3	gentisic acid	free base	free base	free base	free base	free base
4	L-tartaric acid	free base	free base + ligand	free base	free base + ligand	free base

Result / **Solvent** **Ligand**		IPA A	Toluene B	EtOAc C	MTBE D	ACN/H_2O (9/1, v/v) E
5	citric acid	free base	free base + ligand	free base + ligand	free base + ligand	free base
6	L-pyroglutamic acid	free base	free base + ligand	free base + ligand	free base + ligand	free base + ligand
7	L-malic acid	free base	free base	adhesive	free base	free base
8	hippuric acid	free base + ligand	free base + ligand	free base + ligand	free base + ligand	free base
9	fumaric acid	free base	free base	free base	free base + ligand	free base + ligand
10	pyruvic acid	free base	adhesive	free base	free base	free base

[0246] Gel: A gel formed after 2 to 3 days of reaction at room temperature. Based on the XRPD results, if diffraction peaks of the acid ligand involved in the experiment were detected, the sample was labeled as “free base + ligand”; if only diffraction peaks of the free base were observed, the sample was recorded as “free base”.

CLAIMS

1. A mesylate salt crystal form A of a compound of formula I, wherein the mesylate salt crystal form A has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 5.60°±0.2°, 12.31°±0.2°, and 15.40°±0.2°;



structural formula of mesylate salt of compound of formula I.

2. The mesylate salt crystal form A according to claim 1, wherein the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 9.47°±0.2°, 10.99°±0.2°, 17.57°±0.2°, and 19.15°±0.2°;

preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 14.86°±0.2°, 17.12°±0.2°, 18.33°±0.2°, 22.42°±0.2°, and 22.94°±0.2°;

more preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 7.35°±0.2°, 11.36°±0.2°, 19.66°±0.2°, 20.10°±0.2°, 21.78°±0.2°, 26.69°±0.2°, and 28.95°±0.2°.

3. The mesylate salt crystal form A according to claim 1, wherein the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 12.31°±0.2°, 15.40°±0.2°, 17.57°±0.2°, and 19.15°±0.2°;

preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.60°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 12.31°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 22.42°±0.2°, and 22.94°±0.2°;

more preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.60°±0.2°, 7.35°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 11.36°±0.2°, 12.31°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 19.66°±0.2°, 20.10°±0.2°, 21.78°±0.2°, 22.42°±0.2°, 22.94°±0.2°, 26.69°±0.2°, and 28.95°±0.2°;

further preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.60°±0.2°, 7.35°±0.2°, 9.47°±0.2°, 10.99°±0.2°, 11.36°±0.2°, 12.31°±0.2°, 13.48°±0.2°, 14.02°±0.2°, 14.86°±0.2°, 15.40°±0.2°, 16.45°±0.2°, 17.12°±0.2°, 17.57°±0.2°, 18.33°±0.2°, 19.15°±0.2°, 19.66°±0.2°, 20.10°±0.2°, 20.66°±0.2°, 21.78°±0.2°, 22.42°±0.2°, 22.94°±0.2°, 23.44°±0.2°, 26.69°±0.2°, 27.18°±0.2°, 28.95°±0.2°, 34.31°±0.2°, and 36.14°±0.2°.

4. The mesylate salt crystal form A according to claim 3, wherein the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.60	15.76	100.00
7.35	12.02	5.52
9.47	9.34	15.75
10.99	8.05	15.18
11.36	7.78	5.25
12.31	7.18	30.38
13.48	6.56	2.22
14.02	6.31	2.03
14.86	5.96	7.19
15.40	5.75	42.13
16.45	5.39	2.22
17.12	5.18	6.96
17.57	5.04	12.61
18.33	4.84	8.44

19.15	4.63	13.26
19.66	4.51	4.53
20.10	4.41	5.51
20.66	4.29	2.95
21.78	4.08	3.66
22.42	3.96	9.95
22.94	3.87	7.28
23.44	3.79	2.46
26.69	3.34	3.46
27.18	3.28	2.42
28.95	3.08	3.45
34.31	2.61	2.69
36.14	2.48	1.33

;

preferably, the X-ray powder diffraction pattern of the mesylate salt crystal form A, expressed in 2θ angles, is substantially as shown in FIG. 3.

5. The mesylate salt crystal form A according to any one of claims 1 to 4, wherein one or more of the following conditions are met:

(1) the mesylate salt crystal form A has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak temperature of

213.85°C±3°C;

preferably, the differential scanning calorimetry thermogram of the mesylate salt crystal form A comprises an endothermic peak at a peak temperature of 213.85°C±3°C, with a heat of fusion of 66.99 J/g;

more preferably, the differential scanning calorimetry thermogram of the mesylate salt crystal form A is substantially as shown in FIG. 2;

(2) the mesylate salt crystal form A has a thermogravimetric analysis thermogram showing a weight loss of 0.85% upon heating to 180°C;

preferably, the thermogravimetric analysis thermogram of the mesylate salt crystal form A is substantially as shown in FIG. 2;

(3) the mesylate salt crystal form A is an anhydrous crystal form of a monomesylate salt.

6. The mesylate salt crystal form A according to claim 5, wherein one or more of the following conditions are met:

(1) the mesylate salt crystal form A provides an X-ray powder diffraction pattern obtained with the following parameters:

Model	Malvern Panalytical Aeris model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)

X-ray emitter setting	X-ray generator power: 300 W; voltage: 40 kV; current: 7.5 mA; test range: 3 to 40° (2θ); scan speed: 0.14°/s; step size: 0.02° (2θ)

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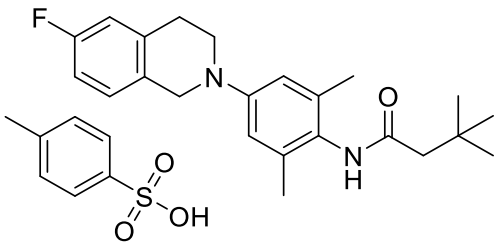
(2) the mesylate salt crystal form A provides TGA and/or DSC thermograms obtained with the following parameters:

Parameters	TGA	DSC
Instrument	TGA550 thermogravimetric analyzer of TA Discovery series	differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

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7. A tosylate salt crystal form A of a compound of formula I, wherein the tosylate salt crystal form A has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 5.17°±0.2°, 10.40°±0.2°, and 18.34°±0.2°;



structural formula of tosylate salt of compound of formula I.

8. The tosylate salt crystal form A according to claim 7, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 8.55°±0.2° and 14.19°±0.2°;

preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 7.04°±0.2° and 17.56°±0.2°;

more preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 11.16°±0.2°, 14.61°±0.2°, 15.14°±0.2°, 19.85°±0.2°, 21.01°±0.2°, 22.21°±0.2°, 22.58°±0.2°, and 24.65°±0.2°.

9. The tosylate salt crystal form A according to claim 7, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.17°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 14.19°±0.2°, and 18.34°±0.2°;

preferably, the X-ray powder diffraction pattern comprises diffraction peaks

at the following positions: 5.17°±0.2°, 7.04°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 14.19°±0.2°, 17.56°±0.2°, and 18.34°±0.2°;

more preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.17°±0.2°, 7.04°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 11.16°±0.2°, 14.19°±0.2°, 14.61°±0.2°, 15.14°±0.2°, 17.56°±0.2°, 18.34°±0.2°, 19.85°±0.2°, 21.01°±0.2°, 22.21°±0.2°, 22.58°±0.2°, and 24.65°±0.2°;

further preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.17°±0.2°, 7.04°±0.2°, 7.98°±0.2°, 8.55°±0.2°, 10.40°±0.2°, 11.16°±0.2°, 11.51°±0.2°, 13.15°±0.2°, 14.19°±0.2°, 14.61°±0.2°, 15.14°±0.2°, 16.15°±0.2°, 17.56°±0.2°, 18.34°±0.2°, 19.52°±0.2°, 19.85°±0.2°, 20.44°±0.2°, 21.01°±0.2°, 21.56°±0.2°, 22.21°±0.2°, 22.58°±0.2°, 23.75°±0.2°, 24.65°±0.2°, 25.38°±0.2°, 26.45°±0.2°, 26.96°±0.2°, 28.82°±0.2°, 30.53°±0.2°, 31.81°±0.2°, 35.27°±0.2°, and 37.51°±0.2°.

10. The tosylate salt crystal form A according to claim 9, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
5.17	17.09	100.00

7.04	12.55	10.07
7.98	11.07	1.98
8.55	10.33	11.39
10.40	8.50	43.38
11.16	7.92	6.91
11.51	7.68	4.54
13.15	6.73	3.62
14.19	6.24	14.11
14.61	6.06	6.71
15.14	5.85	8.26
16.15	5.48	3.28
17.56	5.05	10.38
18.34	4.83	14.19
19.52	4.54	4.23
19.85	4.47	7.91
20.44	4.34	4.30
21.01	4.23	5.89
21.56	4.12	4.54
22.21	4.00	5.03
22.58	3.93	9.09

23.75	3.74	4.57
24.65	3.61	5.23
25.38	3.51	4.15
26.45	3.37	3.28
26.96	3.30	2.68
28.82	3.10	1.43
30.53	2.93	1.03
31.81	2.81	0.89
35.27	2.54	0.63
37.51	2.40	0.23

;

preferably, the X-ray powder diffraction pattern of the tosylate salt crystal form A, expressed in 2θ angles, is substantially as shown in FIG. 6.

11. The tosylate salt crystal form A according to any one of claims 7 to 10, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form A has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak temperature of 223.99°C±3°C;

preferably, the differential scanning calorimetry thermogram of the tosylate salt crystal form A comprises an endothermic peak at a peak temperature of

223.99°C±3°C, with a heat of fusion of 68.20 J/g;

further preferably, the differential scanning calorimetry thermogram of the tosylate salt crystal form A is substantially as shown in FIG. 5;

(2) the tosylate salt crystal form A has a thermogravimetric analysis thermogram substantially as shown in FIG. 5;

(3) the tosylate salt crystal form A is an anhydrous crystal form of a monotosylate salt.

12. The tosylate salt crystal form A according to claim 11, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form A provides an XRPD pattern obtained with the following parameters:

Model	Rigaku Smartlab SE model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.544414 Å/1.540593 Å).
X-ray emitter setting	power: 1600 kW; voltage: 40 kV; current: 40 mA; incident slit: 0.5°; receiving slit: 20.0 mm; scan range: 3 to 40° (2θ), step speed: 8 °/min; step size: 0.01 ° (2θ).

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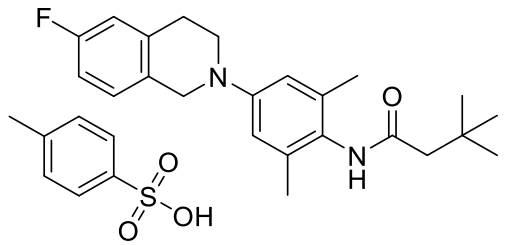
(2) the tosylate salt crystal form A provides TGA and/or DSC thermograms

obtained with the following parameters;

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

.

13. A tosylate salt crystal form B of a compound of formula I, wherein the tosylate salt crystal form B has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 13.44°±0.2°, 17.28°±0.2°, and 17.38°±0.2°;



structural formula of tosylate salt of compound of formula I.

14. The tosylate salt crystal form B according to claim 13, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 5.64°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 20.45°±0.2°, 21.15°±0.2°, and 22.15°±0.2°;

preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 7.84°±0.2°, 10.11°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.60°±0.2°, 18.58°±0.2°, and 23.97°±0.2°;

more preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 5.09°±0.2°, 9.22°±0.2°, 10.87°±0.2°, 16.21°±0.2°, 19.55°±0.2°, 22.89°±0.2°, 25.03°±0.2°, and 27.08°±0.2°.

15. The tosylate salt crystal form B according to claim 13, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.64°±0.2°, 13.44°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 20.45°±0.2°, 21.15°±0.2°, and 22.15°±0.2°;

preferably, 5.64°±0.2°, 7.84°±0.2°, 10.11°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 17.28°±0.2°, 17.38°±0.2°,

18.58°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, and 23.97°±0.2°;

more preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.09°±0.2°, 5.64°±0.2°, 7.84°±0.2°, 9.22°±0.2°, 10.11°±0.2°, 10.87°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 16.21°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 18.58°±0.2°, 19.55°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, 22.89°±0.2°, 23.97°±0.2°, 25.03°±0.2°, and 27.08°±0.2°;

further preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.09°±0.2°, 5.64°±0.2°, 7.06°±0.2°, 7.84°±0.2°, 9.22°±0.2°, 10.11°±0.2°, 10.87°±0.2°, 11.36°±0.2°, 12.03°±0.2°, 13.44°±0.2°, 13.60°±0.2°, 14.49°±0.2°, 15.13°±0.2°, 16.21°±0.2°, 17.28°±0.2°, 17.38°±0.2°, 18.58°±0.2°, 19.55°±0.2°, 20.45°±0.2°, 21.15°±0.2°, 22.15°±0.2°, 22.89°±0.2°, 23.97°±0.2°, 25.03°±0.2°, 27.08°±0.2°, 29.19°±0.2°, 30.07°±0.2°, 30.73°±0.2°, 31.60°±0.2°, 35.97°±0.2°, and 37.84°±0.2°.

16. The tosylate salt crystal form B according to claim 15, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]

5.09	17.34	12.68
5.64	15.66	41.63
7.06	12.51	5.42
7.84	11.26	20.64
9.22	9.59	12.32
10.11	8.74	20.58
10.87	8.13	15.17
11.36	7.78	29.85
12.03	7.35	19.43
13.44	6.58	52.29
13.60	6.51	39.59
14.49	6.11	50.60
15.13	5.85	47.76
16.21	5.46	9.92
17.28	5.13	100.00
17.38	5.10	92.84
18.58	4.77	21.10
19.55	4.54	16.10
20.45	4.34	43.73
21.15	4.20	40.38

22.15	4.01	51.56
22.89	3.88	17.76
23.97	3.71	38.67
25.03	3.56	16.06
27.08	3.29	15.22
29.19	3.06	7.76
30.07	2.97	3.42
30.73	2.91	2.25
31.60	2.83	3.03
35.97	2.49	2.34
37.84	2.38	2.90

;

preferably, the X-ray powder diffraction pattern of the tosylate salt crystal form B, expressed in 2θ angles, is substantially as shown in FIG. 9.

17. The tosylate salt crystal form B according to claim 13, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form B has a differential scanning calorimetry thermogram comprising an endothermic peak at a peak temperature of 222.98°C±3°C, with a heat of fusion of 54.52 J/g;

preferably, the differential scanning calorimetry thermogram of the tosylate

salt crystal form B is substantially as shown in FIG. 8;

(2) the tosylate salt crystal form B has a thermogravimetric analysis thermogram substantially as shown in FIG. 8;

(3) the tosylate salt crystal form B is an anhydrous crystal form of a monotosylate salt.

18. The tosylate salt crystal form B according to claim 17, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form B provides an XRPD pattern obtained with the following parameters:

Model	Bruker D2 model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)
X-ray emitter setting	power: 300 W; voltage: 30 kV; current: 10 mA; divergence slit: 0.6 mm; Soller slit: 4.0°; step speed: 0.15 s/step; step size: 0.02° (2θ); total number of steps: 1837 steps

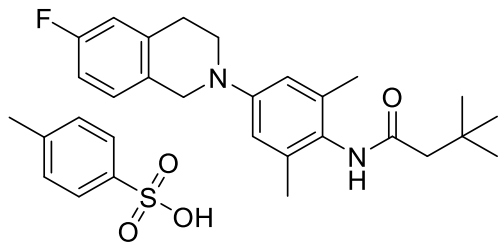
;

(2) the tosylate salt crystal form B provides TGA and/or DSC thermograms obtained with the following parameters;

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

.

19. A tosylate salt crystal form E of a compound of formula I, wherein the tosylate salt crystal form E has an X-ray powder diffraction pattern, obtained using Cu-Kα radiation and expressed in 2θ angles, comprising diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, and 17.33°±0.2°;



structural formula of tosylate salt of compound of formula I.

20. The tosylate salt crystal form E according to claim 19, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, further comprises diffraction peaks at one or more of the following positions: 11.31°±0.2°, 13.89°±0.2°, and 19.88°±0.2°;

preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 9.85°±0.2°, 10.02°±0.2°, 18.83°±0.2°, and 20.23°±0.2°;

more preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 14.15°±0.2°, 16.12°±0.2°, 17.88°±0.2°, 22.33°±0.2°, 25.51°±0.2°, and 27.23°±0.2°;

further preferably, the X-ray powder diffraction pattern further comprises diffraction peaks at one or more of the following positions: 3.34°±0.2°, 16.43°±0.2°, 21.72°±0.2°, 22.87°±0.2°, 23.17°±0.2°, 23.99°±0.2°, 24.51°±0.2°, 30.48°±0.2°, 33.75°±0.2°, and 34.38°±0.2°.

21. The tosylate salt crystal form E according to claim 19, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 17.33°±0.2°, and 19.88°±0.2°;

preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 17.33°±0.2°, 18.83°±0.2°, 19.88°±0.2°, and 20.23°±0.2°;

more preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 14.15°±0.2°, 16.12°±0.2°, 17.33°±0.2°, 17.88°±0.2°, 18.83°±0.2°, 19.88°±0.2°, 20.23°±0.2°, 22.33°±0.2°, 25.51°±0.2°, and 27.23°±0.2°;

further preferably, the X-ray powder diffraction pattern comprises diffraction peaks at the following positions: 3.34°±0.2°, 5.60°±0.2°, 8.15°±0.2°, 9.85°±0.2°, 10.02°±0.2°, 11.31°±0.2°, 13.89°±0.2°, 14.15°±0.2°, 16.12°±0.2°, 16.43°±0.2°, 17.33°±0.2°, 17.88°±0.2°, 18.83°±0.2°, 19.88°±0.2°, 20.23°±0.2°, 21.72°±0.2°, 22.33°±0.2°, 22.87°±0.2°, 23.17°±0.2°, 23.99°±0.2°, 24.51°±0.2°, 25.51°±0.2°, 27.23°±0.2°, 30.48°±0.2°, 33.75°±0.2°, and 34.38°±0.2°.

22. The tosylate salt crystal form E according to claim 21, wherein the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, comprises diffraction peaks as shown in the following table:

Diffraction angle [°2θ]	d-Spacing [Å]	Relative intensity [%]
3.34	26.40	1.94
5.60	15.78	61.93
8.15	10.84	77.26
9.85	8.97	16.17
10.02	8.82	8.84
11.31	7.81	20.19
13.89	6.37	27.76
14.15	6.25	5.07
16.12	5.50	5.27
16.43	5.39	2.65
17.33	5.11	100.00
17.88	4.96	6.26
18.83	4.71	16.74
19.88	4.46	21.55
20.23	4.39	11.05
21.72	4.09	2.05
22.33	3.98	5.81
22.87	3.89	3.11

23.17	3.84	3.37
23.99	3.71	2.46
24.51	3.63	2.21
25.51	3.49	5.10
27.23	3.27	7.40
30.48	2.93	1.21
33.75	2.65	3.76
34.38	2.61	2.48

;

preferably, the X-ray powder diffraction pattern of the tosylate salt crystal form E, expressed in 2θ angles, is substantially as shown in FIG. 10.

23. The tosylate salt crystal form E according to any one of claims 19 to 22, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form E has a differential scanning calorimetry thermogram comprising two endothermic peaks at peak temperatures of 180.26°C±3°C and 224.05°C±3°C;

preferably, the differential scanning calorimetry thermogram of the tosylate salt crystal form E has an endothermic peak at a peak temperature of 180.26°C±3°C, with a heat of fusion of 26.13 J/g; and an endothermic peak at a peak temperature of 224.05°C±3°C, with a heat of fusion of 59.89 J/g;

further preferably, the differential scanning calorimetry thermogram of the tosylate salt crystal form E is substantially as shown in FIG. 11;

(2) the tosylate salt crystal form E has a thermogravimetric analysis thermogram substantially as shown in FIG. 11;

(3) the tosylate salt crystal form E is an anhydrous crystal form of a monotosylate salt.

24. The tosylate salt crystal form E according to claim 23, wherein one or more of the following conditions are met:

(1) the tosylate salt crystal form E provides an XRPD pattern obtained with the following parameters:

Model	Malvern Panalytical Aeris model
X-ray	Cu target (Kα)
X-ray tube setting	Kα2/Kα1 intensity ratio: 0.50 (1.54439 Å/1.5406 Å)
X-ray emitter setting	power: 300 W; voltage: 40 kV; current: 7.5 mA; test range: 3 to 40° (2θ); scan speed: 0.14°/s; step size: 0.02° (2θ)

;

(2) the tosylate salt crystal form E provides TGA and/or DSC thermograms obtained with the following parameters;

Parameters	TGA	DSC
Method	TGA550 thermogravimetric analyzer of TA Discovery series	Differential scanning calorimeter DSC2500 of TA Discovery series
Sample pan	Tzero aluminum pan	Tzero aluminum pan
Temperature range	RT to 350°C	RT to 350°C
Scan rate (°C/min)	10°C/min	10°C/min
Protective gas	N_2	N_2
Gas flow rate	60 mL/min	50 mL/min

.

25. A pharmaceutical composition comprising the mesylate salt crystal form A according to any one of claims 1 to 6, the tosylate salt crystal form A according to any one of claims 7 to 12, the tosylate salt crystal form B according to any one of claims 13 to 18, or the tosylate salt crystal form E according to any one of claims 19 to 24,

and a pharmaceutical excipient.

26. Use of the mesylate salt crystal form A according to any one of claims 1

to 6, the tosylate salt crystal form A according to any one of claims 7 to 12, the tosylate salt crystal form B according to any one of claims 13 to 18, the tosylate salt crystal form E according to any one of claims 19 to 24, or the pharmaceutical composition according to claim 25 in the manufacture of a medicament,

the medicament is for use in treating and/or preventing a disease or condition affected by voltage-gated potassium channels.

27. Use of the mesylate salt crystal form A according to any one of claims 1 to 6, the tosylate salt crystal form A according to any one of claims 7 to 12, the tosylate salt crystal form B according to any one of claims 13 to 18, the tosylate salt crystal form E according to any one of claims 19 to 24, or the pharmaceutical composition according to claim 25 in the manufacture of a medicament,

the medicament is for use in treating and/or preventing one or more of the following diseases or conditions: epilepsy, amyotrophic lateral sclerosis, depression, and pain.