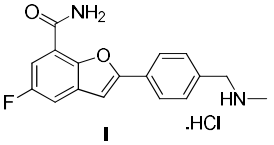
Claims

1. A polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride as shown in Formula I,



I

the polymorph is 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form A, 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form B or 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form C, wherein

the powder diffraction pattern of crystal form A comprises 10 or more 2θ values selected from the group consisting of: 6.49 ± 0.1 °, 12.625 ± 0.1 °, 15.271 ± 0.1 °, 20.727 ± 0.1 °, 22.933 ± 0.1 °, 23.913 ± 0.1 °, 25.139 ± 0.1 °, 25.618 ± 0.1 °, 26.082 ± 0.1 °, 27.084 ± 0.1 °, 27.406 ± 0.1 °, and 28.828 ± 0.1 °;

the powder diffraction pattern of crystal form B comprises 10 or more 2θ values selected from the group consisting of: 6.145 ± 0.1 °, 10.318 ± 0.1 °, 12.459 ± 0.1 °, 14.914 ± 0.1 °, 20.806 ± 0.1 °, 22.832 ± 0.1 °, 23.295 ± 0.1 °, 24.996 ± 0.1 °, 25.198 ± 0.1 °, 25.481 ± 0.1 °, 26.787 ± 0.1 °, 27.285 ± 0.1 °, 28.003 ± 0.1 °, and 29.59 ± 0.1 °;

the powder diffraction pattern of crystal form C comprises 10 or more 2θ values selected from the group consisting of: 10.306 ± 0.1 °, 12.666 ± 0.1 °, 15.312 ± 0.1 °, 17.436 ± 0.1 °, 18.918 ± 0.1 °, 20.748 ± 0.1 °, 22.974 ± 0.1 °, 24.553 ± 0.1 °, 25.238 ± 0.1 °, 26.241 ± 0.1 °, 29.336 ± 0.1 °, 32.739 ± 0.1 °, 33.738 ± 0.1 °, 34.118 ± 0.1 °, 35.204.

2. The polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to claim 1, wherein the crystal form A further has one or more characteristics selected from the group consisting of:

(1) the crystal form A has a DSC spectrum substantially as shown in Figure 1b;

(2) the crystal form A has an infrared spectrum substantially as shown in Figure 1c;

(3) the crystal form A has a TG spectrum substantially as shown in Figure 1d; and

(4) the crystal form A has a Raman spectrum substantially as shown in Figure 1e.

3. The polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to claim 1, wherein the crystal form B further has one or more characteristics selected from the group consisting of:

(1) the crystal form B has a DSC pattern substantially as shown in Figure 2b;

(2) the crystal form B has an infrared spectrum substantially as shown in Figure 2c;

(3) the crystal form B has a TG pattern substantially as shown in Figure 2d; and

(4) the crystal form B has a Raman spectrum substantially as shown in Figure 2e.

4. The polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to claim 1, wherein the crystal form C further has one or more characteristics selected from the group consisting of:

(1) the crystal form C has a DSC pattern substantially as shown in Figure 3b;

(2) the crystal form C has an infrared spectrum substantially as shown in Figure 3c;

(3) the crystal form C has a TG pattern substantially as shown in Figure 3d; and

(4) the crystal form C has a Raman spectrum substantially as shown in Figure 3e.

5. A method for preparing the polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to claim 1, comprising the steps of:

(i) dissolving 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form A in an alcohol at 0 ° C to 80 ° C to form an alcohol solution containing 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride;

(ii) adding an organic solvent dropwise to the alcohol solution of step i), stirring, standing, and precipitating crystals; and

(iii) isolating and drying the precipitated crystals to obtain 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form B;

wherein said alcohol is selected from the group consisting of: methanol, ethanol, propanol, tert-butanol, butanol, octanol, pentanol, hexanol, heptanol, decanol, or a combination thereof ; the organic solvent is selected from the group consisting of: butanone, methyl tert-butyl ether, isopropyl acetate, or a combination thereof;

or the preparation method includes the steps of:

(a) dissolving 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form A in an alcohol or an alcohol-water system at 0 ° C to 80 ° C to form an alcohol solution or an alcohol-water solution containing 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride;

(b) adjusting the pH of the alcohol solution or the alcohol-water solution of step a) to be acidic with hydrochloric acid, stirring at room temperature, standing, and precipitating crystals; and

(c) separating and drying the precipitated crystals to obtain 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride crystal form C;

wherein said alcohol-water system is selected from the group consisting of methanol-water, ethanol-water, propanol-water, tert-butanol-water, butanol-water, octanol-water, pentanol-water, hexanol-water, heptanol-water or decanol-water;

wherein the crystal form A is prepared as follows:

mefurapine in free form is dissolved in an organic solvent, HCl/organic solvent is slowly added dropwise at an equivalent ratio, stirred to precipitate solids, which are filtered and dried to obtain mefurapine hydrochloride crystal form A; wherein the organic solvent is one or more of methanol, ethanol, dichloromethane, ethyl acetate, tetrahydrofuran, and acetone.

6. A pharmaceutical composition, characterized in that the composition comprises a pharmaceutically effective dose of the polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to any one of claims 1 to 4, and a pharmaceutically acceptable excipient or carrier.

7. Use of the polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-7-carboxamide hydrochloride according to any one of claims 1 to 4 or the composition according to claim 6 for preparing a drug for treating and/or preventing diseases related to poly (ADP-ribose polymerase) (PARP);

wherein the diseases related to poly (ADP-ribose polymerase) (PARP) is selected from the group consisting of tumor, inflammation, cardiovascular disease, diabetes, rheumatoid arthritis, endotoxic shock, and stroke.

8. A method of treating and/or preventing a disease related to poly (ADP-ribose polymerase) (PARP) comprising the step of administering to a subject in need thereof an effective amount of a polymorph of 2-[4-(methylaminomethyl)phenyl]-5-fluoro-benzofuran-

7-carboxamide hydrochloride according to any one of claims 1 to 4 or the composition according to claim **6**;

wherein the disease related to poly (ADP-ribose polymerase) (PARP) is selected from the group consisting of tumor, inflammation, cardiovascular disease, diabetes, rheumatoid arthritis, endotoxic shock, and stroke**.**