

ORGANIC ACID SALT OF NICOTINAMIDE RIBOSE, CRYSTAL FORM, AND PREPARATION METHOD THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to the patent application filed on December 22, 2023, with application number 202311781327.2, entitled “Organic Acid Salts of Nicotinamide Riboside, Crystalline Forms, and Preparation Methods Thereof”.

TECHNICAL FIELD

[0002] The present disclosure relates to the field of chemical raw materials, and in particular to organic acid salts of nicotinamide riboside, crystalline forms and preparation methods thereof.

BACKGROUND

[0003] Nicotinamide riboside (NR) is a derivative of vitamin B3 (also known as niacin). Extensive studies have shown that NR has effects such as enhancing metabolism, preventing stem cell aging, and maintaining stem cell function. In liver cancer research, results indicate that dietary supplementation of NR can inhibit the development of liver cancer in mice, induce tumor regression, and no side effects have been observed even at high doses. In addition, β -nicotinamide mononucleotide (β -NMN), obtained by phosphorylation of β -nicotinamide riboside (β -NR), is a synthetic substrate for coenzyme I in organisms. Studies have shown that β -NMN exhibits activities such as anti-aging, regulation of insulin secretion, and influence on mRNA expression levels. Therefore, β -NR and β -NMN have become hotspot compounds in drug development, regenerative medicine, and skincare fields, with enormous market demand prospects.

[0004] The free form of nicotinamide riboside exists as a cation and is inherently unstable; it requires pairing with anions to form an ion pair for stability.

[0005] However, currently reported NR forms, such as chloride salts and other organic acid salts, generally suffer from issues such as poor stability requiring refrigeration, high hygroscopicity, poor flowability making formulation process development difficult, and high usage costs. Apart from chloride salts, many organic acids also present these issues as pharmaceutically unacceptable salt forms, which may be toxic or otherwise biologically intolerable. These problems generally limit their processing and application in downstream fields. Therefore, developing NR organic acid salts that are more stable to water and the environment, safe, and low-cost is of significant importance.

SUMMARY

[0006] In view of the drawbacks of the prior art described above, an objective of the present application is to provide organic acid salts of nicotinamide riboside, crystalline forms, and preparation methods thereof.

[0007] A first aspect of the present disclosure provides an organic acid salt of nicotinamide riboside, wherein the organic acid is selected from acetic acid, citric acid, or fumaric acid; and the molar ratio of nicotinamide riboside to the organic acid is 1:1-1.5.

[0008] In some embodiments of the present disclosure, the molar ratio of nicotinamide riboside to the organic acid is 1:1.

[0009] A second aspect of the present disclosure provides a preparation method for the organic acid salt of nicotinamide riboside according to the first aspect of the present disclosure, wherein the preparation method comprises the following steps:

- 1) Providing multiple resin columns connected in series, each filled with anion resin;
- 2) Washing the anion resin with an organic acid salt solution, followed by washing the anion resin with water until the pH of the effluent is 7-8;
- 3) Passing an aqueous solution of nicotinamide riboside chloride through the anion resin, the anion resin with water, collecting and combining the eluate, and lyophilizing to obtain the organic acid salts of nicotinamide riboside.

[0010] A third aspect of the present disclosure further provides a crystalline form of an organic acid salt of nicotinamide ribose, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide ribose is Form A of nicotinamide riboside hydrogen fumarate. Form A exhibits characteristic peaks in X-ray powder diffraction at 2θ values of at least one of the following positions: $17.59^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $22.31^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, or $29.17^\circ \pm 0.2^\circ$.

[0011] A fourth aspect of the present disclosure provides another crystalline form of an organic acid salt of nicotinamide riboside, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide riboside is Form B of nicotinamide riboside hydrogen fumarate; Form B exhibits characteristic peaks in at least one of the following 2θ values as determined by X-ray powder diffraction: $13.57^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, or $24.44^\circ \pm 0.2^\circ$.

[0012] A fifth aspect of the present disclosure provides a preparation method for the crystalline form of the organic acid salt of nicotinamide riboside according to the third aspect and the fourth aspect of the present disclosure, the preparation method comprising: dissolving the organic acid salt of nicotinamide riboside in water to obtain a clear solution, adding an organic solvent at room temperature, stirring at low temperature to obtain a white suspension, centrifuging, performing

solid-liquid separation, and drying to obtain the crystalline form of the organic acid salt of nicotinamide riboside, wherein the organic acid salt of nicotinamide riboside is nicotinamide riboside hydrogen fumarate.

[0013] The beneficial effects of the present disclosure are as follows: The present disclosure discloses organic acid salts of nicotinamide riboside, wherein the organic acid is acetic acid, citric acid, or fumaric acid, and the molar ratio of nicotinamide riboside to the organic acid is 1:1-1.5, preferably 1:1; the present disclosure also discloses preparation methods for nicotinamide riboside acetate, nicotinamide riboside dihydrogen citrate, and nicotinamide riboside hydrogen fumarate; the present disclosure further discloses two crystalline forms of nicotinamide riboside hydrogen fumarate, designated as Form A and Form B. Both crystalline forms of nicotinamide riboside hydrogen fumarate exhibit the following advantages: 1) Excellent flowability, specifically reflected in high tap density (≥ 0.8 g/mL) and small angle of repose ($30-35^\circ$); 2) Superior stability, as long-term stability and accelerated stability data indicate that both Form B and Form A of nicotinamide riboside hydrogen fumarate currently demonstrate the highest stability among known salt forms of NR; 3) High purity and content, with purity reaching 99.5% and content 99.0%. Additionally, these forms exhibit the following characteristics: low hygroscopicity, excellent color stability, solid-state integrity, and low effective concentration, thereby lowering application costs, as well as enhanced suitability for large-scale production and broader application potential.

BRIEF DESCRIPTION OF DRAWINGS

[0014] FIG. 1 shows the XRPD spectrum of the acetate salt of nicotinamide riboside according to Example 1 of the present disclosure.

[0015] FIG. 2 shows the XRPD spectrum of the dihydrogen citrate salt of nicotinamide riboside according to Example 2 of the present disclosure.

[0016] FIG. 3 shows the XRPD spectrum of the hydrogen fumarate salt of nicotinamide riboside according to Example 3 of the present disclosure.

[0017] FIG. 4 shows the XRPD spectrum of Form A of the hydrogen fumarate salt of nicotinamide riboside according to Example 4 of the present disclosure.

[0018] FIG. 5 shows the XRPD spectrum of Form B of the hydrogen fumarate salt of nicotinamide riboside according to Example 7 of the present disclosure.

[0019] FIG. 6 shows the DSC spectrum of Form A of the hydrogen fumarate salt of nicotinamide riboside according to Example 4 of the present disclosure.

[0020] FIG. 7 shows the DSC spectrum of Form B of the hydrogen fumarate salt of nicotinamide riboside according to Example 7 of the present disclosure.

[0021] FIG. 8 shows the NMR spectrum of Form A of the hydrogen fumarate salt of nicotinamide riboside according to Example 4 of the present disclosure and Form B of the hydrogen fumarate salt according to Example 7.

[0022] FIG. 9 shows the cell proliferation experimental results in Example 14 of the present disclosure.

[0023] FIG. 10 shows the quantitative measurement results of NAD⁺ concentration by high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) in Example 14 of the present disclosure.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0024] The following describes in detail the embodiments of the specifically disclosed organic acid salts of nicotinamide riboside, crystalline forms thereof, and preparation methods thereof.

[0025] The “range” disclosed in this application is defined in the form of a lower limit and an upper limit. A given range is defined by selecting a lower limit and an upper limit, and the selected lower and upper limits define the boundaries of the particular range. Ranges defined in this manner may be inclusive or exclusive of the endpoints and may be arbitrarily combined, meaning any lower limit may be combined with any upper limit to form a range. For example, if ranges of 60-120 and 80-110 are listed for a particular parameter, it is to be understood that ranges of 60-110 and 80-120 are also contemplated. Furthermore, if the minimum range values 1 and 2 are listed, and if the maximum range values 3, 4, and 5 are listed, then all of the following ranges are contemplated: 1-3, 1-4, 1-5, 2-3, 2-4, and 2-5. In this application, unless otherwise stated, the numerical range “a-b” is an abbreviated representation of any combination of real numbers between a and b, where both a and b are real numbers. For example, the numerical range “0-5” indicates that all real numbers between “0-5” have been fully enumerated herein, and “0-5” is merely an abbreviated representation of these numerical combinations. Additionally, when a parameter is expressed as an integer ≥ 2 , it is equivalent to disclosing that the parameter is, for example, the integers 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, etc.

[0026] Unless otherwise specified, all embodiments and optional embodiments of this application may be combined with each other to form new technical solutions.

[0027] Unless otherwise specified, all technical features and optional technical features of this application may be combined with each other to form new technical solutions.

[0028] Through extensive exploratory experiments, the inventors of the present application have successfully obtained nicotinamide riboside (NR) acetate, nicotinamide riboside dihydrogen citrate, and nicotinamide riboside hydrogen fumarate. The present disclosure discloses the

corresponding preparation methods for these compounds, and has yielded two crystalline forms of nicotinamide riboside hydrogen fumarate, designated as Form A and Form B. Both crystalline forms of nicotinamide riboside hydrogen fumarate exhibit the following advantages: 1) Excellent flowability, specifically reflected in high tap density (≥ 0.8 g/mL) and small angle of repose (30-35°); 2) Superior stability, as long-term stability and accelerated stability data indicate that both Form B and Form A of nicotinamide riboside hydrogen fumarate currently demonstrate the highest stability among known salt forms of NR; 3) High purity and content, with purity reaching 99.5% and content 99.0%. Additionally, these forms exhibit the following characteristics: low hygroscopicity, excellent color stability and solid-state integrity; low effective concentration that enables superior efficacy even at reduced dosage levels, thereby lowering application costs; as well as enhanced suitability for large-scale production and broader application potential. The present disclosure is implemented on this basis.

[0029] Organic Acid Salts of Nicotinamide Riboside

[0030] A first aspect of the present disclosure provides an organic acid salt of nicotinamide riboside, wherein the organic acid is selected from acetic acid, citric acid, or fumaric acid; and the molar ratio of nicotinamide riboside to the organic acid is 1:1-1.5. Optionally, it may be 1:1-1.3, 1:1.3-1.5, 1:1-1.1, 1:1.1-1.2, 1:1.2-1.3, 1:1.3-1.4, or 1:1.4-1.5. The molar ratio of nicotinamide riboside to the organic acid anion is 1:1-1.5. Optionally, it may be 1:1-1.3, 1:1.3-1.5, 1:1-1.1, 1:1.1-1.2, 1:1.2-1.3, 1:1.3-1.4, or 1:1.4-1.5. For example, the molar ratio of nicotinamide riboside to acetate is 1:1-1.5. Optionally, it may be 1:1-1.3, 1:1.3-1.5, 1:1-1.1, 1:1.1-1.2, 1:1.2-1.3, 1:1.3-1.4, or 1:1.4-1.5. The molar ratio of nicotinamide riboside to citrate is 1:1-1.5. Optionally, it may be 1:1-1.3, 1:1.3-1.5, 1:1-1.1, 1:1.1-1.2, 1:1.2-1.3, 1:1.3-1.4, or 1:1.4-1.5. The molar ratio of nicotinamide riboside to fumarate is 1:1-1.5. Optionally, it may be 1:1-1.3, 1:1.3-1.5, 1:1-1.1, 1:1.1-1.2, 1:1.2-1.3, 1:1.3-1.4, or 1:1.4-1.5.

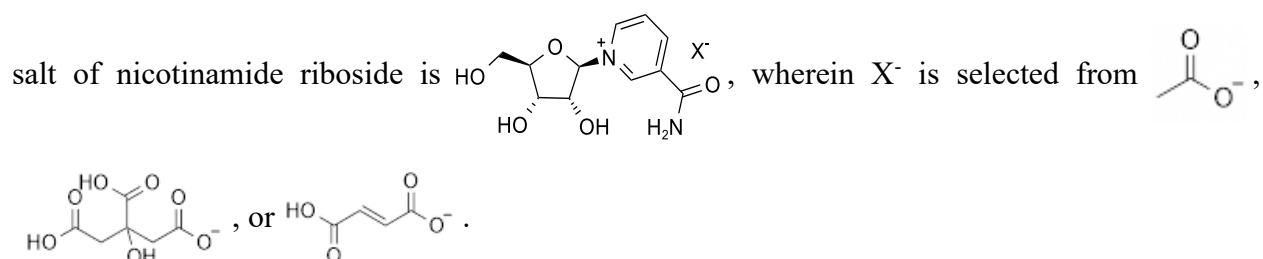
[0031] In some embodiments of the present disclosure, in the organic acid salt of nicotinamide riboside, the organic acid is selected from acetic acid, citric acid, or fumaric acid; and the molar ratio of nicotinamide riboside to the organic acid is 1:1. The molar ratio of nicotinamide riboside to the organic acid anion is 1:1. Further optionally, the molar ratio of nicotinamide riboside to acetate is 1:1. The molar ratio of nicotinamide riboside to citrate is 1:1. The molar ratio of nicotinamide riboside to fumarate is 1:1.

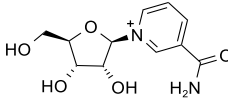
[0032] When the organic acid is acetic acid, the organic acid salt of nicotinamide riboside is nicotinamide riboside acetate.

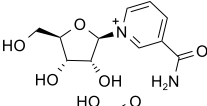
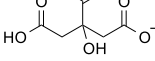
[0033] When the organic acid is citric acid, the organic acid salt of nicotinamide riboside is nicotinamide riboside dihydrogen citrate.

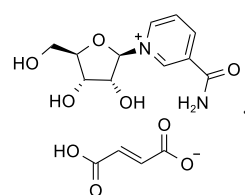
[0034] When the organic acid is fumaric acid, the organic acid salt of nicotinamide riboside is nicotinamide riboside hydrogen fumarate. Fumaric acid is the simplest unsaturated dicarboxylic acid. It was first discovered in *Corydalis Rhizoma*, and is also found in various mushrooms and fresh beef. Fumaric acid is a commonly used medicinal acid radical, and can also be used as an acidity regulator, acidulant, antioxidant aid, curing accelerator, and flavoring agent in the food industry. European Commission, ESIS; IUCLID Dataset, Fumaric acid (110-17-8) p.39 (2000 CD-ROM edition) records: 75 hospitalized patients (42 females, 33 males, aged 20-91 years) took 500 mg of fumaric acid daily for one year. No effects on various blood and urine parameters were observed, and no changes in liver function were noted. Therefore, due to its safety profile, fumaric acid is highly suitable as an anion for NR.

[0035] In some embodiments of the present disclosure, the structural formula of the organic acid salt of nicotinamide riboside is



[0036] Specifically: the acetate of nicotinamide riboside is ; the citrate of nicotinamide riboside is .

nicotinamide riboside is ; the hydrogen fumarate of nicotinamide riboside is .



[0037] Preparation Method for Organic Acid Salts of Nicotinamide Riboside

[0038] A second aspect of the present disclosure provides a preparation method for the organic acid salt of nicotinamide riboside according to the first aspect of the present disclosure, wherein the preparation method comprises the following steps:

- 1) Providing multiple resin columns connected in series, each filled with anion resin;
- 2) Washing the anion resin with an organic acid salt solution, followed by washing the anion resin with water until the pH of the effluent is 7-8;

3) Passing an aqueous solution of nicotinamide riboside chloride through the anion resin, the anion resin with water, collecting and combining the eluate, and lyophilizing to obtain the organic acid salts of nicotinamide riboside.

[0039] In the preparation method of the organic acid salts of nicotinamide riboside provided by the present disclosure, step 1) is providing multiple resin columns connected in series, each filled with anion resin. Specifically:

[0040] In step 1) of the present disclosure, the anion resin is anion resin D301.

[0041] In the preparation method of the organic acid salts of nicotinamide riboside provided by the present disclosure, step 2) is washing the anion resin with an organic acid salt solution, followed by washing the anion resin with water until the pH of the effluent is 7-8. Specifically:

[0042] In step 2) of the present disclosure, the organic acid salt solution is selected from an aqueous solution of sodium acetate, an aqueous solution of monosodium citrate, or an aqueous solution of monosodium fumarate.

[0043] In step 2) of the present disclosure, the concentration of the organic acid salt solution is 3%-5%. Optionally, the concentration of the organic acid salt solution is 3%-4% or 4%-5%, etc.

[0044] In step 2) of the present disclosure, the amount of the organic acid salt solution is 380-420 mL. Optionally, the amount of the organic acid salt solution is 380-400 mL or 400-420 mL, etc.

[0045] In step 2) of the present disclosure, the organic acid salt solution is used to wash the anion resin at a flow rate of 95-105 mL/h. Optionally, the flow rate is 95-100 mL/h or 100-105 mL/h, etc.

[0046] In step 2) of the present disclosure, the water washing of the anion resin is performed at a flow rate of 95-105 mL/h. Optionally, the flow rate is 95-100 mL/h or 100-105 mL/h, etc.

[0047] In step 2) of the present disclosure, the amount of water is 380-420 mL. Optionally, the amount of water is 380-400 mL or 400-420 mL, etc.

[0048] In step 2) of the present disclosure, the water is deionized water.

[0049] In the preparation method of the organic acid salts of nicotinamide riboside provided by the present disclosure, step 3) involves passing an aqueous solution of nicotinamide riboside chloride through the anion resin, the anion resin with water, collecting and combining the eluate, and lyophilizing to obtain the organic acid salts of nicotinamide riboside.

[0050] In step 3) of the present disclosure, the mass of the aqueous solution of nicotinamide riboside chloride is 190-210 g.

[0051] In step 3) of the present disclosure, the mass concentration of the aqueous solution of nicotinamide riboside chloride is 1%-2%.

[0052] In step 3) of the present disclosure, the water washing of the anion resin is performed at a flow rate of 95-105 mL/h to wash the anion resin. Optionally, the flow rate is 95-100 mL/h or 100-105 mL/h, etc.

[0053] In step 3) of the present disclosure, the amount of water is 190-210 mL. Optionally, the amount of water is 190-200 mL or 200-210 mL, etc.

[0054] In step 3) of the present disclosure, the water is deionized water.

[0055] Crystalline form of the organic acid salt of nicotinamide riboside (Form A of nicotinamide riboside hydrogen fumarate)

[0056] The present disclosure further provides a crystalline form of an organic acid salt of nicotinamide riboside, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide riboside is Form A of nicotinamide riboside hydrogen fumarate; Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of $17.59^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $22.31^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, or $29.17^\circ \pm 0.2^\circ$. “At least one” means including one, two, three, ..., or all of the positions. The explanation regarding “at least one” is the same as above and will not be repeated.

[0057] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values selected from $17.59^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $22.31^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, and $29.17^\circ \pm 0.2^\circ$.

[0058] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of $12.8^\circ \pm 0.2^\circ$, $17.46^\circ \pm 0.2^\circ$, $17.59^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $22.30^\circ \pm 0.2^\circ$, $23.36^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, $26.04^\circ \pm 0.2^\circ$, $28.29^\circ \pm 0.2^\circ$, or $29.17^\circ \pm 0.2^\circ$.

[0059] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at $12.8^\circ \pm 0.2^\circ$, $17.46^\circ \pm 0.2^\circ$, $17.59^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $22.30^\circ \pm 0.2^\circ$, $23.36^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, $26.04^\circ \pm 0.2^\circ$, $28.29^\circ \pm 0.2^\circ$, and $29.17^\circ \pm 0.2^\circ$.

[0060] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of $11.25^\circ \pm 0.2^\circ$, $12.8^\circ \pm 0.2^\circ$, $12.19^\circ \pm 0.2^\circ$, $14.08^\circ \pm 0.2^\circ$, $16.47^\circ \pm 0.2^\circ$, $17.46^\circ \pm 0.2^\circ$, $17.59^\circ \pm 0.2^\circ$, $20.50^\circ \pm 0.2^\circ$, $21.32^\circ \pm 0.2^\circ$, $21.52^\circ \pm 0.2^\circ$, $21.50^\circ \pm 0.2^\circ$, $22.31^\circ \pm 0.2^\circ$, $22.56^\circ \pm 0.2^\circ$, $23.36^\circ \pm 0.2^\circ$, $24.50^\circ \pm 0.2^\circ$, $25.46^\circ \pm 0.2^\circ$, $25.7^\circ \pm 0.2^\circ$, $26.04^\circ \pm 0.2^\circ$, $26.19^\circ \pm 0.2^\circ$, $26.39^\circ \pm 0.2^\circ$, $27.30^\circ \pm 0.2^\circ$, $28.29^\circ \pm 0.2^\circ$, $29.17^\circ \pm 0.2^\circ$, $31.10^\circ \pm 0.2^\circ$, $35.54^\circ \pm 0.2^\circ$, or $37.89^\circ \pm 0.2^\circ$.

[0061] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at $11.25^\circ \pm 0.2^\circ$, $12.8^\circ \pm 0.2^\circ$, $12.19^\circ \pm 0.2^\circ$,

14.08°±0.2°, 16.47°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 20.50°±0.2°, 21.32°±0.2°, 21.52°±0.2°, 22.31°±0.2°, 22.56°±0.2°, 23.36°±0.2°, 24.50°±0.2°, 25.46°±0.2°, 25.7°±0.2°, 26.04°±0.2°, 26.19°±0.2°, 26.39°±0.2°, 27.30°±0.2°, 28.29°±0.2°, 29.17°±0.2°, 31.10°±0.2°, 35.54°±0.2°, and 37.89°±0.2°.

[0062] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of 5.10°±0.2°, 11.25°±0.2°, 12.19°±0.2°, 12.8°±0.2°, 13.80°±0.2°, 14.08°±0.2°, 15.66°±0.2°, 16.47°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 18.51°±0.2°, 20.50°±0.2°, 21.32°±0.2°, 21.52°±0.2°, 21.95°±0.2°, 22.31°±0.2°, 22.56°±0.2°, 23.36°±0.2°, 24.50°±0.2°, 24.65°±0.2°, 25.11°±0.2°, 25.46°±0.2°, 25.7°±0.2°, 26.04°±0.2°, 26.19°±0.2°, 26.39°±0.2°, 27.09°±0.2°, 27.30°±0.2°, 27.54°±0.2°, 27.66°±0.2°, 28.01°±0.2°, 28.29°±0.2°, 28.50°±0.2°, 29.17°±0.2°, 29.65°±0.2°, 31.10°±0.2°, 32.82°±0.2°, 32.96°±0.2°, 35.47°±0.2°, 35.54°±0.2°, 35.80°±0.2°, 36.39°±0.2°, 37.71°±0.2°, 37.90°±0.2°, 38.15°±0.2°, 38.44°±0.2°, 38.56°±0.2°, 39.05°±0.2°, 39.32°±0.2°, 41.57°±0.2°, 42.18°±0.2°, 43.81°±0.2°, 45.06°±0.2°, 45.23°±0.2°, or 47.53°±0.2°.

[0063] In some embodiments of the present disclosure, Form A, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at 11.25°±0.2°, 12.19°±0.2°, 12.8°±0.2°, 13.80°±0.2°, 14.08°±0.2°, 15.66°±0.2°, 16.47°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 18.51°±0.2°, 20.50°±0.2°, 21.32°±0.2°, 21.52°±0.2°, 21.95°±0.2°, 22.31°±0.2°, 22.56°±0.2°, 23.36°±0.2°, 24.50°±0.2°, 24.65°±0.2°, 25.11°±0.2°, 25.46°±0.2°, 25.7°±0.2°, 26.04°±0.2°, 26.19°±0.2°, 26.39°±0.2°, 27.09°±0.2°, 27.30°±0.2°, 27.54°±0.2°, 27.66°±0.2°, 28.01°±0.2°, 28.29°±0.2°, 28.50°±0.2°, 29.17°±0.2°, 29.65°±0.2°, 31.10°±0.2°, 32.82°±0.2°, 32.96°±0.2°, 35.47°±0.2°, 35.54°±0.2°, 35.80°±0.2°, 36.39°±0.2°, 37.71°±0.2°, 37.90°±0.2°, 38.15°±0.2°, 38.44°±0.2°, 38.56°±0.2°, 39.05°±0.2°, 39.32°±0.2°, 41.57°±0.2°, 42.18°±0.2°, 43.81°±0.2°, 45.06°±0.2°, 45.23°±0.2°, and 47.53°±0.2°.

[0064] In some embodiments of the present disclosure, Form A is further determined by differential scanning calorimetry (DSC), and exhibits an endothermic peak at least at 113-118°C as determined by DSC.

[0065] In a preferred embodiment, the DSC curve of Form A exhibits an endothermic peak near 118°C, and the curve is substantially as characterized in FIG. 6.

[0066] In some embodiments of the present disclosure, Form A exhibits decomposition at 165-200°C as determined by DSC.

[0067] Crystalline Form of Organic Acid Salt of Nicotinamide Riboside (Form B of Nicotinamide Riboside Hydrogen Fumarate)

[0068] The present disclosure further provides another crystalline form of an organic acid salt of nicotinamide riboside, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide riboside is Form B of nicotinamide riboside hydrogen fumarate; Form B exhibits characteristic peaks in at least one of the following 2θ values as determined by X-ray powder diffraction: $13.57^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, or $24.44^\circ \pm 0.2^\circ$.

[0069] In some embodiments of the present disclosure, Form B, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at $13.57^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, and $24.44^\circ \pm 0.2^\circ$.

[0070] In some embodiments of the present disclosure, Form B, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of $13.42^\circ \pm 0.2^\circ$, $13.57^\circ \pm 0.2^\circ$, $19.15^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, $24.44^\circ \pm 0.2^\circ$, $25.85^\circ \pm 0.2^\circ$, or $29.47^\circ \pm 0.2^\circ$.

[0071] In some embodiments of the present disclosure, Form B, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at $13.42^\circ \pm 0.2^\circ$, $13.57^\circ \pm 0.2^\circ$, $19.15^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, $24.44^\circ \pm 0.2^\circ$, $25.85^\circ \pm 0.2^\circ$, and $29.47^\circ \pm 0.2^\circ$.

[0072] In some embodiments of the present disclosure, Form B, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at least at one of $10.52^\circ \pm 0.2^\circ$, $10.63^\circ \pm 0.2^\circ$, $12.81^\circ \pm 0.2^\circ$, $13.42^\circ \pm 0.2^\circ$, $13.57^\circ \pm 0.2^\circ$, $13.78^\circ \pm 0.2^\circ$, $15.19^\circ \pm 0.2^\circ$, $15.48^\circ \pm 0.2^\circ$, $17.64^\circ \pm 0.2^\circ$, $17.80^\circ \pm 0.2^\circ$, $17.97^\circ \pm 0.2^\circ$, $19.15^\circ \pm 0.2^\circ$, $19.86^\circ \pm 0.2^\circ$, $21.02^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, $23.05^\circ \pm 0.2^\circ$, $24.44^\circ \pm 0.2^\circ$, $24.85^\circ \pm 0.2^\circ$, $25.85^\circ \pm 0.2^\circ$, $26.17^\circ \pm 0.2^\circ$, $27.12^\circ \pm 0.2^\circ$, $27.56^\circ \pm 0.2^\circ$, $27.99^\circ \pm 0.2^\circ$, $29.47^\circ \pm 0.2^\circ$, $29.70^\circ \pm 0.2^\circ$, $30.85^\circ \pm 0.2^\circ$, $30.94^\circ \pm 0.2^\circ$, $31.42^\circ \pm 0.2^\circ$, $31.83^\circ \pm 0.2^\circ$, $32.17^\circ \pm 0.2^\circ$, $32.47^\circ \pm 0.2^\circ$, $34.61^\circ \pm 0.2^\circ$, $35.29^\circ \pm 0.2^\circ$, $35.89^\circ \pm 0.2^\circ$, $36.72^\circ \pm 0.2^\circ$, $37.48^\circ \pm 0.2^\circ$, $37.69^\circ \pm 0.2^\circ$, $38.96^\circ \pm 0.2^\circ$, $40.45^\circ \pm 0.2^\circ$, $45.73^\circ \pm 0.2^\circ$, $46.29^\circ \pm 0.2^\circ$, or $46.45^\circ \pm 0.2^\circ$.

[0073] In some embodiments of the present disclosure, Form B, as determined by X-ray powder diffraction, exhibits characteristic peaks at 2θ values at $10.52^\circ \pm 0.2^\circ$, $10.63^\circ \pm 0.2^\circ$, $12.81^\circ \pm 0.2^\circ$, $13.42^\circ \pm 0.2^\circ$, $13.57^\circ \pm 0.2^\circ$, $13.78^\circ \pm 0.2^\circ$, $15.19^\circ \pm 0.2^\circ$, $15.48^\circ \pm 0.2^\circ$, $17.64^\circ \pm 0.2^\circ$, $17.80^\circ \pm 0.2^\circ$, $17.97^\circ \pm 0.2^\circ$, $19.15^\circ \pm 0.2^\circ$, $19.86^\circ \pm 0.2^\circ$, $21.02^\circ \pm 0.2^\circ$, $21.40^\circ \pm 0.2^\circ$, $22.64^\circ \pm 0.2^\circ$, $23.05^\circ \pm 0.2^\circ$, $24.44^\circ \pm 0.2^\circ$, $24.85^\circ \pm 0.2^\circ$, $25.85^\circ \pm 0.2^\circ$, $26.17^\circ \pm 0.2^\circ$, $27.12^\circ \pm 0.2^\circ$, $27.56^\circ \pm 0.2^\circ$, $27.99^\circ \pm 0.2^\circ$, $29.47^\circ \pm 0.2^\circ$, $29.70^\circ \pm 0.2^\circ$, $30.85^\circ \pm 0.2^\circ$, $30.94^\circ \pm 0.2^\circ$, $31.42^\circ \pm 0.2^\circ$, $31.83^\circ \pm 0.2^\circ$, $32.17^\circ \pm 0.2^\circ$, $32.47^\circ \pm 0.2^\circ$, $34.61^\circ \pm 0.2^\circ$, $35.29^\circ \pm 0.2^\circ$, $35.89^\circ \pm 0.2^\circ$, $36.72^\circ \pm 0.2^\circ$, $37.48^\circ \pm 0.2^\circ$, $37.69^\circ \pm 0.2^\circ$, $38.96^\circ \pm 0.2^\circ$, $40.45^\circ \pm 0.2^\circ$, $45.73^\circ \pm 0.2^\circ$, $46.29^\circ \pm 0.2^\circ$, and $46.45^\circ \pm 0.2^\circ$.

[0074] In some embodiments of the present disclosure, Form B is further determined by differential scanning calorimetry (DSC), and Form B, as determined by DSC, exhibits an endothermic peak at least at 110-117°C.

[0075] In a preferred embodiment, Form B exhibits an endothermic peak near 117°C in the DSC

spectrum, and the spectrum is substantially as characterized in FIG. 7.

[0076] In some embodiments of the present disclosure, Form B exhibits decomposition at 165-185°C as measured by DSC.

[0077] Preparation Method of Crystalline Form of Organic Acid Salt of Nicotinamide Riboside

[0078] The present disclosure further provides a preparation method for the crystalline form of the organic acid salt of nicotinamide riboside according to the third aspect and the fourth aspect of the present disclosure, the preparation method comprising: dissolving the organic acid salt of nicotinamide riboside in water to obtain a clear solution, adding an organic solvent at room temperature, stirring at low temperature to obtain a white suspension, centrifuging, performing solid-liquid separation, and drying to obtain the crystalline form of the organic acid salt of nicotinamide riboside, wherein the organic acid salt of nicotinamide riboside is nicotinamide riboside hydrogen fumarate.

[0079] In some embodiments of the present disclosure, when the organic solvent is selected from alcoholic solvents, Form A of the organic acid salt of nicotinamide riboside is obtained. Optionally, when the organic solvent is selected from methanol and/or ethanol, Form A of the organic acid salt of nicotinamide riboside is obtained.

[0080] In some embodiments of the present disclosure, when the organic solvent is selected from one or more of acetone, acetonitrile, and ethyl acetate, Form B of the organic acid salt of nicotinamide riboside is obtained. Optionally, when the organic solvent is selected from one of acetone, acetonitrile, and ethyl acetate, Form B of the organic acid salt of nicotinamide riboside is obtained.

[0081] In some embodiments of the present disclosure, the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to water is 1.0-1.2 g: 4.8-5.3 mL. Optionally, the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to water may be, for example, 1.0-1.2 g: 4.8-5.0 mL, 1.0-1.2 g: 5.0-5.3 mL, 1.0-1.1 g: 4.8-5.3 mL, or 1.1-1.2 g: 4.8-5.3 mL, etc.

[0082] In some embodiments of the present disclosure, the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to the organic solvent is 1.0-1.2 g: 13.3-14.7 mL. Optionally, the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to the organic solvent may be, for example, 1.0-1.2 g: 13.3-14.0 mL, 1.0-1.2 g: 14.0-14.7 mL, 1.0-1.1 g: 13.3-14.7 mL, or 1.1-1.2 g: 13.3-14.7 mL, etc.

[0083] In some embodiments of the present disclosure, the low-temperature stirring temperature is 5-10°C. Optionally, the low-temperature stirring temperature is 5-8°C or 8-10°C, etc.

[0084] In some embodiments of the present disclosure, the low-temperature stirring time is 10-

12 h. Optionally, the low-temperature stirring time is 10-11 h or 11-12 h, etc.

[0085] In some embodiments of the present disclosure, the drying temperature is 40-45°C. Optionally, the drying temperature may be, for example, 40-43°C or 43-45°C, etc.

[0086] Specific embodiments of the present disclosure are described with reference to the following examples, which are provided to illustrate the disclosure and are not intended to limit the disclosure in any way. The raw materials, unless otherwise specified, are all obtainable from publicly available commercial sources. The instruments involved in the implementation of this application, unless otherwise specified, are all common instruments routinely used in the field.

[0087] The XRPD (X-ray powder diffraction) pattern measurement method described in the present disclosure: samples were collected on a Bruker D2 PHASER X-ray powder diffractometer; X-ray source: Cu (1.54184 Å); voltage: 40 kV; current: 40 mA; scanning range: 3.0°-50°; scanning step size: 0.02°; scanning speed: 6°/min.

[0088] DSC (differential scanning calorimetry) pattern measurement method: samples were collected on a DSC-25 instrument from TA Instruments, USA; scanning speed: 10°C/min; protective gas: nitrogen, nitrogen flow rate: 50 mL/min; temperature range: room temperature to 330°C.

[0089] Example 1: Preparation method of nicotinamide riboside acetate (molar ratio of nicotinamide riboside to acetate in the product is 1:1)

[0090] 200 g of anion resin D301 was packed into two 100 mL resin columns, with the two resin columns connected in series. The resin was washed with a 3% by mass aqueous sodium acetate solution at a flow rate of 100 mL/h, consuming a total of 400 mL. Then the resin was washed with deionized water at a flow rate of 100 mL/h until the pH of the effluent is 7-8, consuming a total of 400 mL of deionized water. 200 g of a 1% aqueous nicotinamide riboside chloride solution by mass was passed through the resin at a flow rate of 100 mL/h, then washed with deionized water at a flow rate of 100 mL/h, consuming 200 g of deionized water, and the eluate was collected based on HPLC results. The eluate was combined and lyophilized to obtain nicotinamide riboside acetate as a powdered solid. The XRPD spectrum of the nicotinamide riboside acetate is shown in FIG. 1.

[0091] Example 2: Preparation method of nicotinamide riboside dihydrogen citrate (molar ratio of nicotinamide riboside to citrate in the product is 1:1)

[0092] 200 g of anion resin D301 was packed into two 100 mL resin columns, with the two resin columns connected in series. The resin was washed with a 3% aqueous monosodium citrate solution by mass at a flow rate of 100 mL/h, consuming a total of 400 mL. Then the resin was

washed with deionized water at a flow rate of 100 mL/h until the pH of the effluent is 7-8, consuming a total of 400 mL of deionized water. 200 g of a 1% aqueous nicotinamide riboside chloride solution by mass was passed through the resin at a flow rate of 100 mL/h, then washed with deionized water at a flow rate of 100 mL/h, consuming 200 g of deionized water, and the eluate was collected based on HPLC results. The eluate was combined and lyophilized to obtain nicotinamide riboside dihydrogen citrate as a powdered solid. The XRPD spectrum of the nicotinamide riboside dihydrogen citrate is shown in FIG. 2.

[0093] Example 3: Preparation method of nicotinamide riboside hydrogen fumarate (molar ratio of nicotinamide riboside to fumarate in the product is 1:1)

[0094] 200 g of anion resin D301 was packed into two 100 mL resin columns, with the two resin columns connected in series. The resin was washed with a 3% aqueous monosodium fumarate solution by mass at a flow rate of 100 mL/h, consuming a total of 400 mL. Then the resin was washed with deionized water at a flow rate of 100 mL/h until the pH of the effluent is 7-8, consuming a total of 400 mL of deionized water. 200 g of a 1% aqueous nicotinamide riboside chloride solution by mass was passed through the resin at a flow rate of 100 mL/h, then washed with deionized water at a flow rate of 100 mL/h, consuming 200 g of deionized water, and the eluate was collected based on HPLC results. The eluate was combined and lyophilized to obtain nicotinamide riboside hydrogen fumarate as a powdered solid. The XRPD spectrum of the nicotinamide riboside hydrogen fumarate is shown in FIG. 3.

[0095] Example 4: Preparation method of Form A of nicotinamide riboside hydrogen fumarate

[0096] 100 mg of the powdered solid of nicotinamide riboside hydrogen fumarate (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 3 mL glass vial. 0.5 mL of pure water was added, and a polytetrafluoroethylene stir bar was added. The mixture was stirred at 35°C for 1 h to obtain a clear solution. 1.4 mL of methanol was slowly added dropwise at room temperature, and then the mixture was transferred to a biochemical incubator at 5°C and stirred at low temperature for an additional 10 h to obtain a white suspension. The suspension was transferred to a centrifuge tube and centrifuged. After solid-liquid separation, the solid was vacuum-dried at 40°C for 4 h to obtain a solid, which was subjected to XRPD testing. The XRPD results indicated that it was nicotinamide riboside hydrogen fumarate Form A. The XRPD pattern of the nicotinamide riboside hydrogen fumarate Form A is substantially as characterized in FIG. 4. The DSC pattern of the nicotinamide riboside hydrogen fumarate Form A exhibits an endothermic peak near 118°C, and the pattern is substantially as characterized in FIG. 6. The NMR spectrum

of the nicotinamide riboside hydrogen fumarate Form A is shown in FIG. 8.

[0097] Using Cu-K α radiation, the X-ray powder diffraction data of the nicotinamide riboside hydrogen fumarate Form A at 2 θ values are shown in Table 1:

[0098] Table 1

2-Theta	d(A)	Height	I%	Area	I%
5.095	17.3308	74	3.6	395	1.8
11.246	7.8617	271	13.2	2358	10.7
12.19	7.2545	237	11.5	1927	8.8
12.8	6.9103	444	21.6	4575	20.8
13.795	6.414	54	2.6	493	2.2
14.08	6.2846	132	6.4	1466	6.7
15.661	5.6537	79	3.8	437	2
16.469	5.3781	158	7.7	1155	5.3
17.458	5.0757	543	26.4	9169	41.7
17.592	5.0372	567	27.6	9471	43.1
18.506	4.7904	105	5.1	656	3
20.495	4.3299	274	13.3	2090	9.5
21.324	4.1632	265	12.9	4499	20.5
21.519	4.1261	699	34	9637	43.9
21.951	4.0457	174	8.5	2578	11.7
22.307	3.9821	2053	100	21965	100
22.556	3.9387	125	6.1	3433	15.6
23.358	3.8052	285	13.9	2181	9.9
24.495	3.6311	195	9.5	1966	9
24.653	3.6082	114	5.6	1452	6.6
25.11	3.5435	80	3.9	1329	6.1
25.461	3.4955	990	48.2	12243	55.7
25.7	3.4636	124	6	1642	7.5
26.035	3.4197	305	14.9	4377	19.9
26.193	3.3994	189	9.2	3619	16.5
26.394	3.374	127	6.2	715	3.3
27.086	3.2894	73	3.6	448	2
27.297	3.2644	245	11.9	2871	13.1

27.539	3.2362	61	3	302	1.4
27.657	3.2227	65	3.2	344	1.6
28.006	3.1834	113	5.5	1171	5.3
28.285	3.1526	457	22.3	5927	27
28.496	3.1297	77	3.8	1220	5.6
29.171	3.0588	644	31.4	8425	38.4
29.649	3.0106	89	4.3	464	2.1
31.096	2.8737	126	6.1	1058	4.8
32.815	2.727	79	3.8	527	2.4
32.958	2.7154	58	2.8	205	0.9
35.465	2.5291	86	4.2	1188	5.4
35.538	2.524	123	6	1291	5.9
35.801	2.5061	103	5	455	2.1
36.387	2.4671	93	4.5	313	1.4
37.714	2.3832	52	2.5	285	1.3
37.894	2.3723	166	8.1	1047	4.8
38.145	2.3573	61	3	499	2.3
38.444	2.3397	80	3.9	567	2.6
38.561	2.3328	68	3.3	247	1.1
39.048	2.3048	52	2.5	457	2.1
39.321	2.2894	49	2.4	208	0.9
41.574	2.1705	71	3.5	341	1.6
42.175	2.1409	62	3	331	1.5
43.809	2.0647	49	2.4	255	1.2
45.064	2.0101	106	5.2	1050	4.8
45.228	2.0032	51	2.5	162	0.7
47.531	1.9114	70	3.4	896	4.1

[0099] Example 5: Preparation method of Form A of nicotinamide riboside hydrogen fumarate

[0100] 100 mg of the powdered solid of nicotinamide riboside hydrogen fumarate (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 3 mL glass vial, 0.5 mL of pure water was added, and a polytetrafluoroethylene stir bar was added. The mixture was stirred at 35°C for 1 h to obtain a clear solution. 1.4 mL of ethanol was slowly added dropwise at room

temperature, and then the mixture was transferred to a biochemical incubator at 5°C and stirred at low temperature for an additional 10 h to obtain a white suspension. The suspension was transferred to a centrifuge tube and centrifuged. After solid-liquid separation, the solid was vacuum-dried at 40°C for 4 h to obtain a solid, which was subjected to XRPD testing. The XRPD results indicated that it was nicotinamide riboside hydrogen fumarate Form A.

[0101] Example 6: Preparation method of Form A of nicotinamide riboside hydrogen fumarate (1.0 kg)

1.0 kg of the nicotinamide riboside hydrogen fumarate powdered solid (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 20 L jacketed reactor. 5.0 L of pure water was added, heated to 35°C, and mechanically stirred for 1 h to obtain a clear solution. 14 L of methanol was slowly added dropwise at room temperature, then cooled to 5°C and stirred for 10 h to obtain a white suspension. The suspension was filtered to separate the solid and liquid phases. The solid was vacuum-dried at 40 °C for 16 hours to obtain a solid product. XRPD testing was performed on the obtained solid, and the XRPD results indicated that it was the nicotinamide riboside hydrogen fumarate Form A.

[0102] Example 7: Preparation method of Form B of nicotinamide riboside hydrogen fumarate

[0103] 100 mg of the powdered solid of nicotinamide riboside hydrogen fumarate (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 3 mL glass vial, 0.5 mL of pure water was added, and a polytetrafluoroethylene stir bar was added. The mixture was stirred at 35°C for 1 h to obtain a clear solution. 1.2 mL of acetone was slowly added dropwise at room temperature, and then the mixture was transferred to a biochemical incubator at 5°C and stirred at low temperature for an additional 10 h to obtain a white suspension. The suspension was transferred to a centrifuge tube and centrifuged. After solid-liquid separation, the solid was vacuum-dried at 40°C for 4 h to obtain a solid, which was subjected to XRPD testing. The XRPD results indicated that it was Form B. The XRPD pattern of the nicotinamide riboside hydrogen fumarate Form B is substantially as characterized in FIG. 5. The DSC curve of the nicotinamide riboside hydrogen fumarate Form B exhibits an endothermic peak near 117°C, and the pattern is substantially as characterized in FIG. 7. The NMR spectrum of the nicotinamide riboside hydrogen fumarate Form B is shown in FIG. 8.

[0104] Using Cu-K α radiation, the X-ray powder diffraction data of the nicotinamide riboside hydrogen fumarate Form B at 2 θ values are shown in Table 2:

[0105] Table 2

2-Theta	d(A)	Height	I%	Area	I%
10.517	8.4046	80	6.8	912	5
10.634	8.3127	101	8.6	1465	8.1
12.806	6.907	115	9.7	1179	6.5
13.416	6.5944	341	28.9	17013	93.8
13.572	6.5191	641	54.3	9090	50.1
13.777	6.4224	57	4.8	2110	11.6
15.189	5.8284	73	6.2	1298	7.2
15.484	5.7179	75	6.4	1477	8.1
17.635	5.025	71	6	1624	9
17.798	4.9793	153	13	4838	26.7
17.968	4.9328	176	14.9	4319	23.8
19.153	4.6301	288	24.4	2645	14.6
19.861	4.4665	224	19	2480	13.7
21.018	4.2233	55	4.7	521	2.9
21.401	4.1485	531	45	6840	37.7
22.644	3.9235	465	39.4	5140	28.3
23.054	3.8546	216	18.3	2623	14.5
24.439	3.6393	1181	100	18137	100
24.854	3.5794	132	11.2	2230	12.3
25.854	3.4432	294	24.9	3663	20.2
26.172	3.4021	81	6.9	442	2.4
27.119	3.2854	228	19.3	3349	18.5
27.563	3.2335	50	4.2	310	1.7
27.991	3.185	77	6.5	585	3.2
29.465	3.029	293	24.8	3555	19.6
29.695	3.006	54	4.6	242	1.3
30.845	2.8965	127	10.8	1209	6.7
30.944	2.8875	98	8.3	1350	7.4
31.419	2.8449	261	22.1	3899	21.5
31.829	2.8091	176	14.9	2563	14.1
32.165	2.7806	72	6.1	519	2.9
32.465	2.7555	134	11.3	1898	10.5

34.605	2.5899	60	5.1	394	2.2
35.288	2.5413	72	6.1	772	4.3
35.894	2.4998	220	18.6	2361	13
36.724	2.4452	75	6.4	441	2.4
37.478	2.3977	64	5.4	1022	5.6
37.687	2.3849	56	4.7	1482	8.2
38.955	2.3101	62	5.2	439	2.4
40.454	2.2279	52	4.4	423	2.3
45.725	1.9826	60	5.1	522	2.9
46.286	1.9599	52	4.4	479	2.6
46.449	1.9534	64	5.4	645	3.6

[0106] Example 8: Preparation method of Form B of nicotinamide riboside hydrogen fumarate

[0107] 100 mg of the powdered solid of nicotinamide riboside hydrogen fumarate (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 3 mL glass vial. 0.5 mL of pure water was added, and a polytetrafluoroethylene stir bar was added. The mixture was stirred at 35°C for 1 h to obtain a clear solution. 1.2 mL of acetonitrile was slowly added dropwise at room temperature, and then the mixture was transferred to a biochemical incubator at 5°C and stirred at low temperature for an additional 10 h to obtain a white suspension. The suspension was transferred to a centrifuge tube and centrifuged. After solid-liquid separation, the solid was vacuum-dried at 40°C for 4 h to obtain a solid, which was subjected to XRPD testing. The XRPD results indicated that it was nicotinamide riboside hydrogen fumarate Form B.

[0108] Example 9: Preparation method of Form B of nicotinamide riboside hydrogen fumarate

[0109] 100 mg of the powdered solid of nicotinamide riboside hydrogen fumarate (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 3 mL glass vial, 0.5 mL of pure water was added, and a polytetrafluoroethylene stir bar was added. The mixture was stirred at 35°C for 1 h to obtain a clear solution. 1.2 mL of ethyl acetate was slowly added dropwise at room temperature, and then the mixture was transferred to a biochemical incubator at 5°C and stirred at low temperature for an additional 10 h to obtain a white suspension. The suspension was transferred to a centrifuge tube and centrifuged. After solid-liquid separation, the solid was vacuum-dried at 40°C for 4 h to obtain a solid, which was subjected to XRPD testing. The XRPD results indicated that it was nicotinamide riboside hydrogen fumarate Form B.

[0110] Example 10: Preparation method of Form B of nicotinamide riboside hydrogen fumarate (1.0 kg)

[0111] 1.0 kg of the nicotinamide riboside hydrogen fumarate powdered solid (amorphous solid of hydrogen fumarate) prepared in Example 3 above was placed in a 20 L jacketed reactor, 5.0 L of pure water was added, heated to 35°C, and stirred for 1 h to obtain a clear solution. 12 L of acetone was slowly added dropwise at room temperature, then cooled to 5°C and stirred for 10 h to obtain a white suspension. The suspension was filtered to separate the solid and liquid phases. The solid was vacuum-dried at 40°C for 16 hours to obtain a solid product. XRPD testing was performed on the obtained solid, and the XRPD results indicated that it was Form B.

[0112] Example 11: Flowability experiment

[0113] The flowability indicators of Form A of nicotinamide riboside hydrogen fumarate (NR-hydrogen fumarate Form A) prepared in Example 4, Form B of nicotinamide riboside hydrogen fumarate (NR-hydrogen fumarate Form B) prepared in Example 7, NR chloride Crystalline Form II (purchased from Hunan Xin'an Biotechnology Co., Ltd., batch number NB240101B, crystallized with a substrate:water:ethanol volume ratio of 1:1:10), and NR succinate crystals (self-prepared, preparation method: first prepare a succinate-type anion resin, then pass the NR chloride purchased from Hunan Xin'an Biotechnology Co., Ltd., batch number NB240101B, through the anion resin, and after concentrating the column eluate, crystallize with a substrate:water:ethanol volume ratio of 1:3:10) are as follows:

[0114] Mainly including tapped density and angle of repose data:

[0115] Tapped density test method: Precisely weigh approximately 20 g of sample using an analytical balance, transfer it to a 50 mL graduated cylinder, then place the cylinder into the tapped density tester. Set the number of taps (Traptimes) to 2400 and the speed control to 80, and press the “start” key to begin. After tapping is completed, read the sample volume and calculate the tapped density.

[0116] Angle of repose test method: Take approximately 20 g of sample and slowly add it from the top of the funnel device. The material leaking from the bottom of the funnel forms a conical pile on the horizontal material tray. When the horizontal material tray is fully covered, use a protractor to measure the acute angle between the inclined surface of the sample pile and the bottom horizontal plane, which is the angle of repose.

[0117] Table 3

	NR-Hydrogen Fumarate Form A	NR-Hydrogen Fumarate Form B	NR Chloride Crystalline Form	NR Succinate Crystal
--	--------------------------------	--------------------------------	---------------------------------	-------------------------

			II	
Tapped Density (g/mL)	0.8126	0.8319	0.6360	0.6613
Angle of Repose (°)	34	33	45	42

[0118] Example 12 Stability Test

(I) Short-term stability test method: Using the acetate prepared in Example 1 [NR-acetate (amorphous)], the dihydrogen citrate of nicotinamide riboside from Example 2 [NR-dihydrogen citrate (amorphous)], the hydrogen fumarate of nicotinamide riboside from Example 3 [NR-hydrogen fumarate (amorphous)], the Form A of the hydrogen fumarate of nicotinamide riboside from Example 4 [NR-hydrogen fumarate (Form A)], and the Form B of the hydrogen fumarate of nicotinamide riboside from Example 7 [NR-hydrogen fumarate (Form B)], each sample was weighed 30-50 mg and subjected to air isolation treatment using two layers of PE bags (the first layer tied tightly with a cable tie, the second layer vacuum-sealed) plus an aluminum foil bag (vacuum-sealed). The samples were placed in a constant temperature and humidity stability chamber at 25°C, 60% RH and 40°C, 75% RH, respectively. During testing, one package of sample was taken each time for HPLC sample purity testing.

[0119] Table 4 shows the purity changes of NR organic acid salts under the conditions of 25°C and 60% RH.

[0120] Table 4

Name	0 day	3 days	5 days	7 days
NR-dihydrogen citrate (amorphous)	92.13%	82.34%	77.39%	70.31%
NR-hydrogen fumarate (amorphous)	93.83%	59.83%	52.93%	42.53%
NR-acetate (amorphous)	89.55%	48.19%	55.86%	29.87%
NR-hydrogen fumarate (Form A)	99.49%	98.98%	98.68%	98.41%
NR-hydrogen fumarate (Form B)	99.31%	99.05%	98.93%	98.77%

[0121] Table 5 shows the purity changes of NR organic acid salts under the conditions of 40°C and 75% RH.

[0122] Table 5

Name	0 day	3 days	5 days	7 days
NR-dihydrogen citrate (amorphous)	92.13%	24.16%	15.58%	7.76%
NR-hydrogen fumarate (amorphous)	93.83%	11.91%	7.58%	4.26%
NR-acetate (amorphous)	89.55%	6.97%	4.20%	2.26%
NR-hydrogen fumarate (Form A)	99.49%	95.85%	94.58%	93.01%

NR-hydrogen fumarate (Form B)	99.31%	96.19%	94.33%	91.20%
-------------------------------	--------	--------	--------	--------

[0123] After storage at 25°C and 60% RH, the amorphous forms of NR-hydrogen fumarate, NR-dihydrogen citrate, and NR-acetate all exhibited decomposition. The purity of the two crystalline forms of NR-hydrogen fumarate remained essentially unchanged with no significant decomposition, indicating better stability of the crystalline forms. Under conditions of 40°C and 75% RH, decomposition of the amorphous forms became more pronounced, while the crystalline form samples decomposed at a relatively slower rate.

[0124] (II) Long-term stability data [NR-chloride Crystalline Form II, Form A of nicotinamide riboside hydrogen fumarate from Example 4 (NR-hydrogen fumarate Form A), Form B of nicotinamide riboside hydrogen fumarate from Example 7 (NR-hydrogen fumarate Form B), NR-succinate crystal]

[0125] Due to the small sample size (only 30-50 mg) in the aforementioned short-term stability experiments, the results were susceptible to moisture and oxygen in the air. Therefore, long-term stability experiments were conducted with 2.0 g per package. Among the test samples, NR-chloride Crystalline Form II was purchased from Hunan Xin'an Biotechnology Co., Ltd., batch number NB240101B, and crystallized at a substrate:water:ethanol volume ratio of 1:1:10. The NR-succinate crystal was self-prepared. The preparation method involved first preparing a succinate-type anion resin, then passing NR-chloride (purchased from Hunan Xin'an Biotechnology Co., Ltd., batch number NB240101B) through the anion resin. The column eluate was concentrated and crystallized at a substrate:water:ethanol volume ratio of 1:3:10.

[0126] Test method: Using NR-chloride Crystalline Form II, Form A of nicotinamide riboside hydrogen fumarate from Example 4 (NR-hydrogen fumarate Form A), Form B of nicotinamide riboside hydrogen fumarate from Example 7 (NR-hydrogen fumarate Form B), and NR-succinate crystal, 2.0 g of each sample was weighed, and air isolation treatment was performed using two layers of PE bags (the first layer tied tightly with a cable tie, the second layer vacuum-sealed) plus an aluminum foil bag (vacuum-sealed). The samples were placed in a constant temperature and humidity stability chamber at 25°C, 60% RH and 40°C, 75% RH, respectively. During testing, one package of sample was taken each time for appearance, pH, moisture, and HPLC sample purity and content (on a dry basis) testing.

[0127] Stability of NR-chloride Crystalline Form II

[0128] Table 6 shows the purity changes of NR-chloride Crystalline Form II under the conditions of temperature 25°C and humidity 60% RH.

[0129] Table 6

Storage Time	0 day	7 days	15 days	1 month	3 months	6 months
--------------	-------	--------	---------	---------	----------	----------

Appearance	White crystalline powder	White crystalline powder	White crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder
pH	4.5	4.4	4.2	4.1	3.9	3.7
Water content	0.12%	0.14%	0.57%	0.19%	0.33%	0.34%
Content	99.4%	100.4%	99.5%	99.5%	100.3%	100.7%
Purity	99.62%	99.68%	99.60%	99.59%	99.43%	99.08%

[0130] Table 7 shows the purity changes of NR-chloride Crystalline Form II under the conditions of temperature 40°C and humidity 75% RH.

[0131] Table 7

Storage Time	0 day	7 days	15 days	1 month
Appearance	White crystalline powder	White crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder
pH	4.5	4.1	3.7	3.6
Water content	0.12%	0.17%	0.56%	0.28%
Content	99.4%	99.9%	98.9%	98.2%
Purity	99.62%	99.51%	98.98%	98.65%

[0132] Note: Testing was stopped after purity fell below 99%.

[0133] Stability of NR-hydrogen fumarate Form B

[0134] Table 8 shows the purity changes of NR-hydrogen fumarate Form B under conditions of 25°C and 60% RH.

[0135] Table 8

Storage Time	0 day	15 days	1 month	2 months	3 months	6 months
Appearance	White crystalline powder	White crystalline powder	White crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder
pH	3.6	3.7	3.6	3.7	3.7	3.6
Water content	0.05%	0.23%	0.44%	0.29%	0.31%	0.46%
Content	99.2%	99.7%	100.3%	99.0%	99.6%	100.2%
Purity	99.76%	99.69%	99.61%	99.61%	99.51%	99.40%

[0136] Table 9 shows the purity changes of NR-hydrogen fumarate Form B under conditions of 40°C and 75% RH.

[0137] Table 9

Storage Time	0 day	3 days	5 days	7 days	15 days	1 month
Appearance	White crystalline powder	White crystalline powder	White crystalline powder	White crystalline powder	White crystalline powder	Almost-white crystalline powder
pH	3.6	3.6	3.6	3.6	3.7	3.6
Water content	0.05%	0.14%	0.24%	0.14%	0.23%	0.40%
Content	99.2%	99.4%	100.3%	100.0%	100.6%	100.0%
Purity	99.76%	99.62%	99.55%	99.55%	99.44%	98.97%

[0138] Stability of NR-succinate crystals

[0139] Table 10 shows the purity changes of NR-succinate crystals under conditions of 25°C and 60% RH.

[0140] Table 10

Storage Time	0 day	15 days	1 month	2 months	3 months	6 months
Appearance	Almost-white crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder	Light brown powder	Light brown powder	Brown powder
pH	4.7	4.8	4.8	4.8	4.8	4.8
Water content	0.37%	0.23%	0.33%	0.30%	0.36%	0.39%
Content	98.4%	97.7%	98.6%	97.5%	98.4%	96.8%
Purity	99.51%	99.34%	99.29%	99.06%	98.57%	97.89%

[0141] Table 11 shows the purity changes of NR-succinate crystals under conditions of 40°C and 75% RH.

[0142] Table 11

Storage Time	0 day	3 days	5 days	7 days	15 days	1 month
Appearance	Almost-white crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder	Brown powder	Yellowish-brown powder	Brown lumpy solid
pH	4.7	4.7	4.7	4.7	4.8	4.7
Water content	0.37%	0.22%	0.28%	0.50%	0.27%	0.95%

Content	98.4%	97.7%	97.8%	93.7%	96.9%	85.8%
Purity	99.51%	99.27%	98.64%	96.26%	96.88%	86.70%

[0143] Stability of NR-hydrogen fumarate Form A

[0144] Table 12 shows the purity changes of NR-hydrogen fumarate Form A under conditions of 25°C and 60% RH.

[0145] Table 12

Storage Time	0 day	15 days	1 month	2 months	3 months	6 months
Appearance	White crystalline powder	White crystalline powder	White crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder	Almost-white crystalline powder
pH	3.6	3.6	3.7	3.6	3.7	3.6
Water content	0.05%	0.15%	0.34%	0.33%	0.35%	0.45%
Content	99.2%	99.5%	99.7%	99.2%	99.3%	99.7%
Purity	99.76%	99.73%	99.68%	99.60%	99.58%	99.46%

[0146] Table 13 shows the purity changes of NR-hydrogen fumarate Form A under conditions of 40°C and 75% RH

[0147] Table 13

Storage time	0 day	3 days	5 days	7 days	15 days	1 month
Appearance	White crystalline powder	White crystalline powder	White crystalline powder	White crystalline powder	White crystalline powder	Almost-white crystalline powder
pH	3.6	3.7	3.6	3.6	3.6	3.6
Water content	0.05%	0.12%	0.19%	0.20%	0.28%	0.37%
Content	99.2%	99.3%	99.5%	99.7%	99.4%	99.3%
Purity	99.76%	99.60%	99.53%	99.47%	99.41%	98.95%

[0148] Based on Tables 6 to 13, NR chloride salt crystalline form II exhibits good stability under conditions of 25°C and 60% RH, with purity remaining above 99% after 6 months; under conditions of 40°C and 75% RH, its stability is slightly inferior, with purity dropping below 99% after 15 days.

[0149] NR-hydrogen fumarate Form B and Form A demonstrate good stability under conditions of 25°C and 60% RH, with purity remaining above 99% after 6 months. Under conditions of 40°C

and 75% RH, their stability is good, with purity remaining above 99% after 15 days.

[0150] NR succinate crystal exhibits slightly inferior stability under conditions of 25°C and 60% RH, with purity dropping below 99% after 3 months; under conditions of 40°C and 75% RH, its stability is the poorest, with purity dropping below 99% after 5 days.

[0151] In summary, long-term stability experiments indicate that NR-hydrogen fumarate Form B and NR-hydrogen fumarate Form A exhibit the best stability among the four.

[0152] In summary, the applicant conducted short-term and long-term stability experiments, with the main difference being the sample quantity. When the sample quantity is very small, it is more significantly affected by air and moisture, resulting in variations in purity data.

[0153] Example 13 Grinding Stability

[0154] An appropriate amount of NR-hydrogen fumarate Form B prepared in Example 7 and NR-hydrogen fumarate Form A prepared in Example 4 were separately placed in an agate mortar. Each sample was ground for 3 minutes with approximately the same force. XRPD tests were conducted before and after grinding. According to the test results, the XRPD patterns showed no significant changes before and after grinding, indicating that the crystalline forms of NR-organic acid salts possess strong grinding stability.

[0155] Example 14 Efficacy Results and Methods

[0156] Cell Proliferation Assay

[0157] HaCat cells were cultured in DMEM medium supplemented with 10% FBS and 1% PenStrep, with medium replacement every 2-3 days until 85% confluence was achieved. The cells were trypsinized with 0.25% trypsin solution, harvested, then resuspended in DMEM medium containing 0.1% serum and seeded into 96-well transparent plates at 1×10^4 cells/well, allowing cell adhesion and overnight growth. On the following day, serially diluted samples of NR-hydrogen fumarate Form B (prepared in Example 7), NR-hydrogen fumarate Form A (prepared in Example 4), NR-succinate crystals (self-prepared, procedure: first synthesizing an anion-exchange resin in succinate form, then passing NR chloride purchased from Hunan Xin'an Biotechnology Co., Ltd., batch No. NB240101B through the resin column, followed by concentration of the eluent and crystallization at a substrate:water:ethanol ratio of 1:3:10 [v/v/v]), NR chloride Form II (purchased from Hunan Xin'an Biotechnology Co., Ltd., batch No. NB240101B, crystallized at a substrate:water:ethanol ratio of 1:1:10 [v/v/v]), and NR-hydrogen malate crystals (purchased from Shandong Sihuan Pharmaceutical Co., Ltd., batch No. 2024061101) were added. Cell control wells and blank control wells were established, followed by thorough mixing via plate agitation and subsequent incubation for 24 h. After incubation for 24 h, the supernatant was removed, and the

96-well plate was gently washed with PBS using slow motions to prevent cell detachment. The prepared CCK-8 solution was added at 100 μ L/well, followed by incubation at 37°C for 30 min to 1 h. The results were read using a microplate reader with a 450 nm filter, and the relative cell viability of different samples was calculated. The relative cell viability for each sample was calculated according to the following formula: $(As-Ab)/(Ac-Ab)*100\%$, where As represents the absorbance of the sample well, Ab represents the absorbance of the blank well, and Ac represents the absorbance of the control well. As shown in FIG. 9, NR-hydrogen fumarate Form B, NR-hydrogen fumarate Form A, NR-hydrogen malate crystal, and NR succinate crystal all significantly promoted the proliferation of HaCat cells, while NR chloride crystalline form II showed a slightly weaker effect. Moreover, the NR-hydrogen fumarate Form B and Form A of the present application demonstrated more pronounced advantages at lower concentrations (0.078 mM and 0.0078 mM), significantly outperforming NR-hydrogen malate crystal, NR succinate crystal, and NR chloride crystalline form II.

[0158] Animal Experiment

[0159] This experiment was a 7-day repeated-dose study designed to evaluate the effects of NR-hydrogen fumarate Form A and Form B on blood NAD⁺ levels in male and female C57BL/6 mice. All test mice underwent a 14-day acclimation period prior to the start of the experiment. The test samples in this experiment included NR-hydrogen fumarate Form A prepared in Example 4, NR-hydrogen fumarate Form B prepared in Example 7, NR chloride solution, and nicotinamide mononucleotide (NMN). Each compound was administered to middle-aged and elderly mice (64 weeks old) at a dose of 1 mmol/kg/day or 0.33 mmol/kg/day for 7 consecutive days via oral gavage of an aqueous solution of the test sample. Blood samples were collected via cheek puncture on day 0 (baseline) and day 7 (post-administration). A positive control group consisting of young mice (10 weeks old) was established, and blood samples were collected via cheek puncture on day 0 (without administration). Blood samples were subjected to cell lysis treatment prior to testing. The internal standard compound used for analysis was procured from MedChemExpress (MCE). NAD⁺ concentration was quantitatively measured using high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS), as shown in FIG. 10.

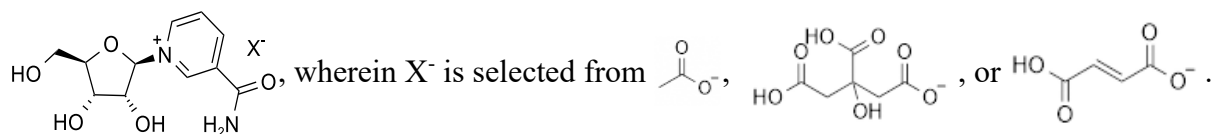
[0160] The above experiments demonstrated that both NR-hydrogen fumarate Form A solution and Form B solution had a greater effect on NAD⁺ levels in mouse blood than NR chloride solution and NMN solution. Moreover, the NR-hydrogen fumarate Form B and Form A of the present application exhibited more pronounced advantages at a lower dosage (0.33 mmol/kg/day), significantly outperforming NR chloride solution and nicotinamide mononucleotide (NMN).

[0161] The foregoing embodiments are merely illustrative of the principles and efficacy of the

present disclosure and are not intended to limit the disclosure. Any person skilled in the art may modify or alter the above embodiments without departing from the spirit and scope of the present disclosure. Therefore, all equivalent modifications or alterations made by those with ordinary knowledge in the technical field without departing from the spirit and technical concepts disclosed by the present disclosure shall still fall within the scope of the claims of the present disclosure.

What is claimed is:

1. An organic acid salt of nicotinamide riboside, wherein the organic acid is selected from acetic acid, citric acid, or fumaric acid; and the molar ratio of nicotinamide riboside to the organic acid is 1:1-1.5.
2. The organic acid salt of nicotinamide riboside according to claim 1, wherein the molar ratio of nicotinamide riboside to the organic acid is 1:1.
3. The organic acid salt of nicotinamide riboside according to claim 1 or 2, wherein the structural formula of the organic acid salt of nicotinamide riboside is:



4. A preparation method for the organic acid salt of nicotinamide riboside according to any one of claims 1 to 3, wherein the preparation method comprises the following steps:
 - 1) providing multiple resin columns connected in series, each filled with anion resin;
 - 2) washing the anion resin with an organic acid salt solution, followed by washing the anion resin with water until the pH of the effluent is 7-8;
 - 3) passing an aqueous solution of nicotinamide riboside chloride through the anion resin, then washing the anion resin with water, collecting and combining the eluate, and lyophilizing to obtain the organic acid salts of nicotinamide riboside.
5. The preparation method for the organic acid salt of nicotinamide riboside according to claim 4, wherein the preparation method further comprises one or more of the following features:
 - A1) in step 1), the anion resin is anion resin D301;
 - A2) in step 2), the organic acid salt solution is selected from an aqueous solution of sodium acetate, an aqueous solution of monosodium citrate, or an aqueous solution of monosodium fumarate;
 - A3) in step 2), the concentration of the organic acid salt solution is 3%-5%;
 - A4) in step 2), the amount of the organic acid salt solution is 380-420 mL;
 - A5) in step 2), the organic acid salt solution is used to wash the anion resin at a flow rate of 95-105 mL/h;
 - A6) in step 2), the water washing of the anion resin is performed at a flow rate of 95-105 mL/h;

- A7) in step 2), the amount of water is 380-420 mL;
- A8) in step 3), the mass of the aqueous solution of nicotinamide riboside chloride is 190-210 g;
- A9) in step 3), the mass concentration of the aqueous solution of nicotinamide riboside chloride is 1%-2%;
- A10) in step 3), the water washing of the anion resin is performed at a flow rate of 95-105 mL/h;
- A11) in step 3), the amount of water is 190-210 mL;
- A12) in steps 2) and 3), the water is deionized water.

6. The crystalline form of the organic acid salt of nicotinamide riboside according to any one of claims 1-3, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide riboside is Form A of nicotinamide riboside hydrogen fumarate; wherein the Form A exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $17.59^{\circ}\pm 0.2^{\circ}$, $21.52^{\circ}\pm 0.2^{\circ}$, $22.31^{\circ}\pm 0.2^{\circ}$, $25.46^{\circ}\pm 0.2^{\circ}$, or $29.17^{\circ}\pm 0.2^{\circ}$.

7. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 6, wherein the Form A exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $12.8^{\circ}\pm 0.2^{\circ}$, $17.46^{\circ}\pm 0.2^{\circ}$, $17.59^{\circ}\pm 0.2^{\circ}$, $21.52^{\circ}\pm 0.2^{\circ}$, $22.30^{\circ}\pm 0.2^{\circ}$, $23.36^{\circ}\pm 0.2^{\circ}$, $25.46^{\circ}\pm 0.2^{\circ}$, $26.04^{\circ}\pm 0.2^{\circ}$, $28.29^{\circ}\pm 0.2^{\circ}$, or $29.17^{\circ}\pm 0.2^{\circ}$.

8. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 6, wherein the Form A exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $11.25^{\circ}\pm 0.2^{\circ}$, $12.8^{\circ}\pm 0.2^{\circ}$, $12.19^{\circ}\pm 0.2^{\circ}$, $14.08^{\circ}\pm 0.2^{\circ}$, $16.47^{\circ}\pm 0.2^{\circ}$, $17.46^{\circ}\pm 0.2^{\circ}$, $17.59^{\circ}\pm 0.2^{\circ}$, $20.50^{\circ}\pm 0.2^{\circ}$, $21.32^{\circ}\pm 0.2^{\circ}$, $21.52^{\circ}\pm 0.2^{\circ}$, $21.50^{\circ}\pm 0.2^{\circ}$, $22.31^{\circ}\pm 0.2^{\circ}$, $22.56^{\circ}\pm 0.2^{\circ}$, $23.36^{\circ}\pm 0.2^{\circ}$, $24.50^{\circ}\pm 0.2^{\circ}$, $25.46^{\circ}\pm 0.2^{\circ}$, $25.7^{\circ}\pm 0.2^{\circ}$, $26.04^{\circ}\pm 0.2^{\circ}$, $26.19^{\circ}\pm 0.2^{\circ}$, $26.39^{\circ}\pm 0.2^{\circ}$, $27.30^{\circ}\pm 0.2^{\circ}$, $28.29^{\circ}\pm 0.2^{\circ}$, $29.17^{\circ}\pm 0.2^{\circ}$, $31.10^{\circ}\pm 0.2^{\circ}$, $35.54^{\circ}\pm 0.2^{\circ}$, or $37.89^{\circ}\pm 0.2^{\circ}$.

9. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 6, wherein the Form A exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $11.25^{\circ}\pm 0.2^{\circ}$, $12.19^{\circ}\pm 0.2^{\circ}$, $12.8^{\circ}\pm 0.2^{\circ}$, $13.80^{\circ}\pm 0.2^{\circ}$, $14.08^{\circ}\pm 0.2^{\circ}$, $15.66^{\circ}\pm 0.2^{\circ}$, $16.47^{\circ}\pm 0.2^{\circ}$, $17.46^{\circ}\pm 0.2^{\circ}$, $17.59^{\circ}\pm 0.2^{\circ}$, $18.51^{\circ}\pm 0.2^{\circ}$, $20.50^{\circ}\pm 0.2^{\circ}$, $21.32^{\circ}\pm 0.2^{\circ}$, $21.52^{\circ}\pm 0.2^{\circ}$, $21.95^{\circ}\pm 0.2^{\circ}$, $22.31^{\circ}\pm 0.2^{\circ}$, $22.56^{\circ}\pm 0.2^{\circ}$, $23.36^{\circ}\pm 0.2^{\circ}$, $24.50^{\circ}\pm 0.2^{\circ}$, $24.65^{\circ}\pm 0.2^{\circ}$, $25.11^{\circ}\pm 0.2^{\circ}$, $25.46^{\circ}\pm 0.2^{\circ}$, $25.7^{\circ}\pm 0.2^{\circ}$, $26.04^{\circ}\pm 0.2^{\circ}$, $26.19^{\circ}\pm 0.2^{\circ}$, $26.39^{\circ}\pm 0.2^{\circ}$, $27.09^{\circ}\pm 0.2^{\circ}$, $27.30^{\circ}\pm 0.2^{\circ}$, $27.54^{\circ}\pm 0.2^{\circ}$, $27.66^{\circ}\pm 0.2^{\circ}$, $28.01^{\circ}\pm 0.2^{\circ}$, $28.29^{\circ}\pm 0.2^{\circ}$, $28.50^{\circ}\pm 0.2^{\circ}$, $29.17^{\circ}\pm 0.2^{\circ}$, $29.65^{\circ}\pm 0.2^{\circ}$, $31.10^{\circ}\pm 0.2^{\circ}$, $32.82^{\circ}\pm 0.2^{\circ}$, $32.96^{\circ}\pm 0.2^{\circ}$, $35.47^{\circ}\pm 0.2^{\circ}$, $35.54^{\circ}\pm 0.2^{\circ}$,

35.80°±0.2°, 36.39°±0.2°, 37.71°±0.2°, 37.90°±0.2°, 38.15°±0.2°, 38.44°±0.2°, 38.56°±0.2°, 39.05°±0.2°, 39.32°±0.2°, 41.57°±0.2°, 42.18°±0.2°, 43.81°±0.2°, 45.06°±0.2°, 45.23°±0.2°, or 47.53°±0.2°.

10. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 6, wherein the Form A exhibits characteristic peaks at 2θ values of 17.59°±0.2°, 21.52°±0.2°, 22.31°±0.2°, 25.46°±0.2°, and 29.17°±0.2° as determined by X-ray powder diffraction; preferably, the Form A exhibits characteristic peaks at 2θ values of 12.8°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 21.52°±0.2°, 22.30°±0.2°, 23.36°±0.2°, 25.46°±0.2°, 26.04°±0.2°, 28.29°±0.2°, and 29.17°±0.2° as determined by X-ray powder diffraction; more preferably, the Form A exhibits characteristic peaks at 2θ values of 11.25°±0.2°, 12.8°±0.2°, 12.19°±0.2°, 14.08°±0.2°, 16.47°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 20.50°±0.2°, 21.32°±0.2°, 21.52°±0.2°, 22.31°±0.2°, 22.56°±0.2°, 23.36°±0.2°, 24.50°±0.2°, 25.46°±0.2°, 25.7°±0.2°, 26.04°±0.2°, 26.19°±0.2°, 26.39°±0.2°, 27.30°±0.2°, 28.29°±0.2°, 29.17°±0.2°, 31.10°±0.2°, 35.54°±0.2°, and 37.89°±0.2° as determined by X-ray powder diffraction; still more preferably, the Form A exhibits characteristic peaks at 2θ values of 11.25°±0.2°, 12.19°±0.2°, 12.8°±0.2°, 13.80°±0.2°, 14.08°±0.2°, 15.66°±0.2°, 16.47°±0.2°, 17.46°±0.2°, 17.59°±0.2°, 18.51°±0.2°, 20.50°±0.2°, 21.32°±0.2°, 21.52°±0.2°, 21.95°±0.2°, 22.31°±0.2°, 22.56°±0.2°, 23.36°±0.2°, 24.50°±0.2°, 24.65°±0.2°, 25.11°±0.2°, 25.46°±0.2°, 25.7°±0.2°, 26.04°±0.2°, 26.19°±0.2°, 26.39°±0.2°, 27.09°±0.2°, 27.30°±0.2°, 27.54°±0.2°, 27.66°±0.2°, 28.01°±0.2°, 28.29°±0.2°, 28.50°±0.2°, 29.17°±0.2°, 29.65°±0.2°, 31.10°±0.2°, 32.82°±0.2°, 32.96°±0.2°, 35.47°±0.2°, 35.54°±0.2°, 35.80°±0.2°, 36.39°±0.2°, 37.71°±0.2°, 37.90°±0.2°, 38.15°±0.2°, 38.44°±0.2°, 38.56°±0.2°, 39.05°±0.2°, 39.32°±0.2°, 41.57°±0.2°, 42.18°±0.2°, 43.81°±0.2°, 45.06°±0.2°, 45.23°±0.2°, and 47.53°±0.2° as determined by X-ray powder diffraction.

11. The crystalline form of the organic acid salt of nicotinamide riboside according to any one of claims 6-10, wherein: further comprising one or more of the following features:

- B1) the Form A is further determined by differential scanning calorimetry (DSC), and exhibits an endothermic peak at least at 113-118°C as measured by DSC;
- B2) the Form A exhibits decomposition at 165-200°C as measured by DSC.

12. The crystalline form of the organic acid salt of nicotinamide riboside according to any one of claims 1-3, wherein the organic acid is fumaric acid, and the crystalline form of the organic acid salt of nicotinamide riboside is Form B of nicotinamide riboside hydrogen fumarate; the Form B exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: 13.57°±0.2°, 21.40°±0.2°, 22.64°±0.2°, or 24.44°±0.2°.

13. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 12, wherein the Form B exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $13.42^{\circ}\pm 0.2^{\circ}$, $13.57^{\circ}\pm 0.2^{\circ}$, $19.15^{\circ}\pm 0.2^{\circ}$, $21.40^{\circ}\pm 0.2^{\circ}$, $22.64^{\circ}\pm 0.2^{\circ}$, $24.44^{\circ}\pm 0.2^{\circ}$, $25.85^{\circ}\pm 0.2^{\circ}$, or $29.47^{\circ}\pm 0.2^{\circ}$.

14. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 12, wherein the Form B exhibits characteristic peaks at least one of the following 2θ values as determined by X-ray powder diffraction: $10.52^{\circ}\pm 0.2^{\circ}$, $10.63^{\circ}\pm 0.2^{\circ}$, $12.81^{\circ}\pm 0.2^{\circ}$, $13.42^{\circ}\pm 0.2^{\circ}$, $13.57^{\circ}\pm 0.2^{\circ}$, $13.78^{\circ}\pm 0.2^{\circ}$, $15.19^{\circ}\pm 0.2^{\circ}$, $15.48^{\circ}\pm 0.2^{\circ}$, $17.64^{\circ}\pm 0.2^{\circ}$, $17.80^{\circ}\pm 0.2^{\circ}$, $17.97^{\circ}\pm 0.2^{\circ}$, $19.15^{\circ}\pm 0.2^{\circ}$, $19.86^{\circ}\pm 0.2^{\circ}$, $21.02^{\circ}\pm 0.2^{\circ}$, $21.40^{\circ}\pm 0.2^{\circ}$, $22.64^{\circ}\pm 0.2^{\circ}$, $23.05^{\circ}\pm 0.2^{\circ}$, $24.44^{\circ}\pm 0.2^{\circ}$, $24.85^{\circ}\pm 0.2^{\circ}$, $25.85^{\circ}\pm 0.2^{\circ}$, $26.17^{\circ}\pm 0.2^{\circ}$, $27.12^{\circ}\pm 0.2^{\circ}$, $27.56^{\circ}\pm 0.2^{\circ}$, $27.99^{\circ}\pm 0.2^{\circ}$, $29.47^{\circ}\pm 0.2^{\circ}$, $29.70^{\circ}\pm 0.2^{\circ}$, $30.85^{\circ}\pm 0.2^{\circ}$, $30.94^{\circ}\pm 0.2^{\circ}$, $31.42^{\circ}\pm 0.2^{\circ}$, $31.83^{\circ}\pm 0.2^{\circ}$, $32.17^{\circ}\pm 0.2^{\circ}$, $32.47^{\circ}\pm 0.2^{\circ}$, $34.61^{\circ}\pm 0.2^{\circ}$, $35.29^{\circ}\pm 0.2^{\circ}$, $35.89^{\circ}\pm 0.2^{\circ}$, $36.72^{\circ}\pm 0.2^{\circ}$, $37.48^{\circ}\pm 0.2^{\circ}$, $37.69^{\circ}\pm 0.2^{\circ}$, $38.96^{\circ}\pm 0.2^{\circ}$, $40.45^{\circ}\pm 0.2^{\circ}$, $45.73^{\circ}\pm 0.2^{\circ}$, $46.29^{\circ}\pm 0.2^{\circ}$, or $46.45^{\circ}\pm 0.2^{\circ}$.

15. The crystalline form of the organic acid salt of nicotinamide riboside according to claim 12, wherein the Form B exhibits characteristic peaks at 2θ values of $13.57^{\circ}\pm 0.2^{\circ}$, $21.40^{\circ}\pm 0.2^{\circ}$, $22.64^{\circ}\pm 0.2^{\circ}$, and $24.44^{\circ}\pm 0.2^{\circ}$ as determined by X-ray powder diffraction; preferably, the Form B exhibits characteristic peaks at 2θ values selected from $13.42^{\circ}\pm 0.2^{\circ}$, $13.57^{\circ}\pm 0.2^{\circ}$, $19.15^{\circ}\pm 0.2^{\circ}$, $21.40^{\circ}\pm 0.2^{\circ}$, $22.64^{\circ}\pm 0.2^{\circ}$, $24.44^{\circ}\pm 0.2^{\circ}$, $25.85^{\circ}\pm 0.2^{\circ}$, and $29.47^{\circ}\pm 0.2^{\circ}$ as determined by X-ray powder diffraction; more preferably, the Form B exhibits characteristic peaks at 2θ values of $10.52^{\circ}\pm 0.2^{\circ}$, $10.63^{\circ}\pm 0.2^{\circ}$, $12.81^{\circ}\pm 0.2^{\circ}$, $13.42^{\circ}\pm 0.2^{\circ}$, $13.57^{\circ}\pm 0.2^{\circ}$, $13.78^{\circ}\pm 0.2^{\circ}$, $15.19^{\circ}\pm 0.2^{\circ}$, $15.48^{\circ}\pm 0.2^{\circ}$, $17.64^{\circ}\pm 0.2^{\circ}$, $17.80^{\circ}\pm 0.2^{\circ}$, $17.97^{\circ}\pm 0.2^{\circ}$, $19.15^{\circ}\pm 0.2^{\circ}$, $19.86^{\circ}\pm 0.2^{\circ}$, $21.02^{\circ}\pm 0.2^{\circ}$, $21.40^{\circ}\pm 0.2^{\circ}$, $22.64^{\circ}\pm 0.2^{\circ}$, $23.05^{\circ}\pm 0.2^{\circ}$, $24.44^{\circ}\pm 0.2^{\circ}$, $24.85^{\circ}\pm 0.2^{\circ}$, $25.85^{\circ}\pm 0.2^{\circ}$, $26.17^{\circ}\pm 0.2^{\circ}$, $27.12^{\circ}\pm 0.2^{\circ}$, $27.56^{\circ}\pm 0.2^{\circ}$, $27.99^{\circ}\pm 0.2^{\circ}$, $29.47^{\circ}\pm 0.2^{\circ}$, $29.70^{\circ}\pm 0.2^{\circ}$, $30.85^{\circ}\pm 0.2^{\circ}$, $30.94^{\circ}\pm 0.2^{\circ}$, $31.42^{\circ}\pm 0.2^{\circ}$, $31.83^{\circ}\pm 0.2^{\circ}$, $32.17^{\circ}\pm 0.2^{\circ}$, $32.47^{\circ}\pm 0.2^{\circ}$, $34.61^{\circ}\pm 0.2^{\circ}$, $35.29^{\circ}\pm 0.2^{\circ}$, $35.89^{\circ}\pm 0.2^{\circ}$, $36.72^{\circ}\pm 0.2^{\circ}$, $37.48^{\circ}\pm 0.2^{\circ}$, $37.69^{\circ}\pm 0.2^{\circ}$, $38.96^{\circ}\pm 0.2^{\circ}$, $40.45^{\circ}\pm 0.2^{\circ}$, $45.73^{\circ}\pm 0.2^{\circ}$, $46.29^{\circ}\pm 0.2^{\circ}$, and $46.45^{\circ}\pm 0.2^{\circ}$ as determined by X-ray powder diffraction.

16. The crystalline form of the organic acid salt of nicotinamide riboside according to any one of claims 12-15, wherein: further comprising one or more of the following features:

- C1) the Form B is further determined by differential scanning calorimetry (DSC), and exhibits an endothermic peak at least at $110-117^{\circ}\text{C}$ as measured by DSC;
- C2) the Form B exhibits decomposition at $165-185^{\circ}\text{C}$ as measured by DSC.

17. A preparation method for the crystalline form of the organic acid salt of nicotinamide riboside according to any one of claims 6-16, wherein the preparation method comprises: dissolving the

organic acid salt of nicotinamide riboside in water to obtain a clear solution, adding an organic solvent at room temperature, stirring at low temperature to obtain a white suspension, centrifuging, performing solid-liquid separation, and drying to obtain the crystalline form of the organic acid salt of nicotinamide riboside, wherein the organic acid salt of nicotinamide riboside is nicotinamide riboside hydrogen fumarate.

18. The preparation method for the crystalline form of the organic acid salt of nicotinamide riboside according to claim 17, wherein, comprising one or more of the following conditions:

- D1) when the organic solvent is selected from alcoholic solvents, Form A of the organic acid salt of nicotinamide riboside is obtained;
- D2) when the organic solvent is selected from one or more of acetone, acetonitrile, and ethyl acetate, Form B of the organic acid salt of nicotinamide riboside is obtained;
- D3) the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to water is 1.0-1.2 g: 4.8-5.3 mL;
- D4) the mass-to-volume ratio of nicotinamide riboside hydrogen fumarate to the organic solvent is 1.0-1.2 g: 13.3-14.7 mL;
- D5) the low-temperature stirring temperature is 5-10°C;
- D6) the low-temperature stirring time is 10-12 h;
- D7) the drying temperature is 40-45°C.