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(54) **Titre :** SEL D'ACIDE ORGANIQUE DE NICOTINAMIDE RIBOSIDE, COMPOSITION ASSOCIEE ET PROCEDE DE PREPARATION CORRESPONDANT

(54) **Title:** ORGANIC ACID SALT OF NICOTINAMIDE RIBOSIDE, COMPOSITION INCLUDING ORGANIC ACID SALT, AND PREPARATION METHODS OF ORGANIC ACID SALT AND COMPOSITION

(57) **Abrégé/Abstract:**

An organic acid salt of nicotinamide riboside; the organic acid is selected from malic acid, citric acid, royal jelly acid, and so on, and the molar ratio of nicotinamide riboside to organic acid is 1:2 or 1:1. A compound composition of the organic acid salt of nicotinamide riboside and a carrier, and the carrier is selected from nicotinic acid, glutamic acid, royal jelly acid, cervic acid, microcrystalline cellulose, or apple cider vinegar powder. Organic acids that are more acidic are used, and said organic acids form a close ion pair with nicotinamide riboside and have a certain degree of hydrophobicity so as to improve the stability of nicotinamide riboside. The carrier can prevent the penetration of water and improve the stability of the organic acid salt in water.

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(54) Title: ORGANIC ACID SALT OF NICOTINAMIDE RIBOSIDE, COMPOSITION THEREOF AND PREPARATION METHOD THEREFOR

(54) 发明名称: 烟酰胺核糖的有机酸盐及其组合物与制备方法

(57) Abstract: An organic acid salt of nicotinamide riboside; the organic acid is selected from malic acid, citric acid, royal jelly acid, and so on, and the molar ratio of nicotinamide riboside to organic acid is 1:2 or 1:1. A compound composition of the organic acid salt of nicotinamide riboside and a carrier, and the carrier is selected from nicotinic acid, glutamic acid, royal jelly acid, cervic acid, microcrystalline cellulose, or apple cider vinegar powder. Organic acids that are more acidic are used, and said organic acids form a close ion pair with nicotinamide riboside and have a certain degree of hydrophobicity so as to improve the stability of nicotinamide riboside. The carrier can prevent the penetration of water and improve the stability of the organic acid salt in water.

(57) 摘要: 一种烟酰胺核糖的有机酸盐，所述有机酸选自苹果酸、柠檬酸、王浆酸等，烟酰胺核糖与有机酸的摩尔比为1：2或1：1。烟酰胺核糖的有机酸盐与载体复配的组合物，所述载体选自烟酸、谷氨酸、王浆酸、神经酸、微晶纤维素或苹果醋粉。采用了酸性更强的有机酸，这些有机酸与烟酰胺核糖形成紧密离子对，具有一定的疏水性，使得烟酰胺核糖的稳定性提升；载体可以防止水分渗入，提高有机酸盐对水的稳定性。

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ORGANIC ACID SALT OF NICOTINAMIDE RIBOSIDE, COMPOSITION INCLUDING ORGANIC ACID SALT, AND PREPARATION METHODS OF ORGANIC ACID SALT AND COMPOSITION

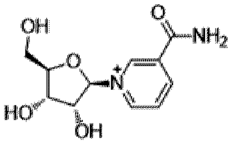
TECHNICAL FIELD

The present disclosure belongs to the technical field of medicine, and specifically relates to an organic acid salt of nicotinamide riboside (NR), a composition including the organic acid salt, and preparation methods of the organic acid salt and the composition.

BACKGROUND

NR is a derivative of vitamin B3 (also known as niacin). A large number of studies have shown that NR has the functions of enhancing the metabolism of an organism, preventing the aging of stem cells, maintaining the functions of stem cells, and the like. Liver cancer research results have shown that the dietary supplementation of NR can prevent the development of liver cancer in mice and induce tumor regression, which shows no side effects at a high dosage. In addition, β-nicotinamide mononucleotide (β-NMN) obtained through phosphorylation of β-nicotinamide ribose (β-NR) is a synthetic substrate of coenzyme I in organisms. Studies have shown that β-NMN has the activities of anti-aging, regulating insulin secretion, and affecting an mRNA expression level. Therefore, β-NR and β-NMN have become hot compounds in the fields of drug development, regenerative medicine, and skin care, which have promising market demand prospects.

NR can freely exist in the form of a cation (formula I), which is unstable and needs to form an ion pair (structure II) with an anion to be stable.



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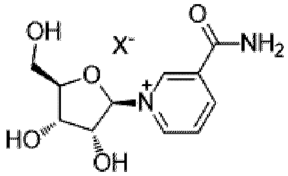

II

A chloride salt of NR has been reported in a literature, but is still not very stable, particularly sensitive to water, light, and temperature. Therefore, in order to facilitate the use of NR and expand a use scope of NR, it is necessary to study a more stable form of NR. In addition, NR is currently used in a relatively single mode and cannot play a complementary role with other compounds.

SUMMARY

A first objective of the present disclosure is to provide a novel organic acid salt of NR that can exist stably.

A second objective of the present disclosure is to provide a preparation method of the organic acid salt of NR.

A third objective of the present disclosure is to provide a composition including organic acid salt of NR.

A fourth objective of the present disclosure is to provide a preparation method of the composition.

In order to achieve the above objectives, the present disclosure adopts the following technical solutions.

The present disclosure provides an organic acid salt of NR, where an organic acid is selected from the group consisting of malic acid, tannic acid, eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), caffeic acid, trans-cinnamic acid, trans-4-hydroxy-cinnamic acid, monosodium citrate, disodium citrate, citric acid, chlorogenic acid, gluconic acid, ferulic acid, royal jelly acid, nervonic acid, chicoric acid, rosmarinic acid, carnosic acid, niacin, adipic acid, lauric acid, salicylic acid, monopotassium glycyrrhizinate (MPG), folic acid, chondroitin sulfate (CS), potassium hydrogen tartrate, glutamic acid, and aspartic acid.

The above organic acids each have at least one free carboxyl group and are in a solid state at room temperature.

Further, a molar ratio of the NR to the organic acid may be 1:2.

Further, a molar ratio of the NR to the organic acid may be 1:1.

Further, the organic acid may be citric acid, malic acid, or royal jelly acid.

The present disclosure also provides a preparation method of the organic acid salt of NR, including: under the protection of nitrogen, dissolving NR in methanol, adding an organic acid, and stirring a resulting mixture; adding methyl *tert*-butyl ether (MTBE) or ethyl acetate, and further stirring; and filtering, washing, and drying to obtain a product.

The present disclosure also provides a composition of an organic acid salt of NR, including organic acid salt of NR and a carrier, where the carrier is selected from the group consisting of malic acid, tannic acid, EPA, DHA, caffeic acid, trans-cinnamic acid, trans-4-hydroxy-cinnamic acid, lactic acid, monosodium citrate, disodium citrate, citric acid, chlorogenic acid, gluconic acid, ferulic acid, royal jelly acid, nervonic acid, chicoric acid, rosmarinic acid, carnosic acid, niacin, adipic acid, lauric acid, MPG, folic acid, CS, potassium hydrogen tartrate, salicylic acid, glycine, glutamic acid, alanine, arginine, leucine, isoleucine, valine, cystine, cysteine, methionine, threonine, serine, phenylalanine, tyrosine, tryptophan, proline, hydroxyproline, and aspartic acid; the organic acid salt is the organic acid salt described above; and a molar ratio of the NR to the organic acid is 1:2 or 1:1.

Further, the carrier may be selected from the group consisting of niacin, glutamic acid, royal jelly acid, and nervonic acid.

Further, the organic acid salt may be a malate of NR.

Further, a molar ratio of the organic acid salt of NR to the carrier may be 1:1.

The present disclosure also provides a composition of an organic acid salt of NR, including organic acid salt of NR and a carrier, where the carrier is selected from the group consisting of microcrystalline cellulose (MCC) and apple cider vinegar powder; the organic acid salt is the organic acid salt described above; and a molar ratio of the NR to the organic acid is 1:2 or 1:1.

Further, the organic acid salt may be selected from the group consisting of a malate and citrate of NR.

Further, a mass ratio of the organic acid salt of NR to the carrier may be 1:1.

The present disclosure also provides a preparation method of the composition of an organic acid salt of NR, including: under the protection of nitrogen, mixing and grinding an organic acid salt of NR and a carrier.

The present disclosure has the following beneficial effects.

1. The organic acid salt of NR of the present disclosure adopts an organic acid with strong acidity, and such an organic acid has a free carboxyl group, which can provide a lone paired electron to form an intimate ion pair with a nitrogen cation of NR and lead to some hydrophobicity. The hydrophobicity results in a very prominent stabilization effect on NR and improves the stability of the organic acid salt of NR.

2. When NR and an organic acid are present in a molar ratio of 1:2, one molecule of the NR and two molecules of the organic acid can exist stably. One molecule of the organic acid forms an ion pair with the NR, and then the other molecule of the organic acid forms a hydrogen bond with basic amide in the NR due to acid-base interaction, thereby achieving acid-base pairing, which further improves the stability of the organic acid salt of NR.

3. The organic acid salt of NR is compounded with MCC. The MCC has hydrophobicity and heat resistance, which can prevent moisture penetration and improve the water resistance of the organic acid salt.

4. NR can be converted into nicotinamide adenine dinucleotide (NAD^+, also known as coenzyme I) capable of transferring protons in the organism. NAD^+ participates in physiological reactions such as energy metabolism, ATP synthesis, DNA repair, cell apoptosis inhibition, and decomposition of proteins, carbohydrates, and fats in an organism. In the present disclosure, an organic acid and apple cider vinegar powder that can participate in the above-mentioned metabolism and other physiological activities are selected and compounded with NR to form a composite nutritional additive, and the components can be complementary and coordinated to produce a superimposed effect. Tests have confirmed that the addition of an organic acid and apple cider vinegar powder as a carrier does not significantly affect the stability of the organic acid salt of NR, and this composite nutritional additive has potential application value.

DETAILED DESCRIPTION OF THE EMBODIMENTS

The present disclosure is further described below with reference to specific examples. The parts below all refer to parts by weight.

Example 1

Preparation of a citrate of NR (1:1)

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0220 mol, 1 eq) was dissolved in 60 mL of methanol, then anhydrous citric acid (0.0264 mol, 1.2 eq) was added, and a resulting mixture was stirred for 2 h; and then 75 mL of anhydrous MTBE was added, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain a product (0.0123 mol). In the product (NRX), a molar ratio of NR to citric acid (X) was 1:1; and a yield was 55.91%.

Characterization data:

HNMR(400MHz,MeOD):δ9.72 (s,1H), 9.42-9.43 (d,1H), 9.01-9.03 (d,1H), 8.25-8.30 (m,1H), 6.18-6.19 (d,1H), 4.42-4.464 (m,2H), 4.30-4.32 (t,1H), 4.01-4.05 (dd,1H), 3.85-3.89 (dd,1H), 2.67-2.79 (q,4H);

MS(ESI+):254.96[M-1],MS(ESI-):191.12[M-1];

IR (KBr) ν_{max} 3412, 2940, 2375, 1692, 1612, 1516, 1395, 1232, 1098, 894, 677, 622 cm^{-1}.

Example 2

Preparation of a citrate of NR (1:2)

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0220 mol, 1 eq) was dissolved in 60 mL of methanol, then anhydrous citric acid (0.0495 mol, 2.25 eq) was added, and a resulting mixture was stirred for 2 h; and then 150 mL of anhydrous MTBE was added, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain a product (0.0125 mol). In the product (NRX_2), a molar ratio of NR to citric acid (X) was 1:2; and a yield was 56.82%.

Characterization data:

HNMR(400MHz,MeOD):δ9.73 (s,1H), 9.43-9.45 (d,1H), 9.04-9.06 (d,1H), 8.27-8.32 (m,1H), 6.20-6.21 (d,1H), 4.43-4.45 (m,2H), 4.30-4.33 (t,1H), 4.02-4.05 (d,1H), 3.85-3.89 (d,1H), 2.74-2.86 (q,8H);

MS(ESI+):254.97[M-1],MS(ESI-):191.16[M-1];

IR (KBr) ν_{max} 3425, 2929, 2370, 1697, 1624, 1516, 1394, 1219, 1097, 893, 678, 623 cm^{-1}.

When the NR and the anhydrous citric acid were fed in a molar ratio of 1:3.3, characterization data of an obtained product were the same, indicating that the product was a product (NRX_2) in which a molar ratio of NR to citric acid (X) was 1:2.

Example 3

Preparation of a malate of NR (1:1)

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0195 mol, 1 eq) was dissolved in 60 mL of methanol, then anhydrous malic acid (0.0234 mol, 1.2 eq) was added, and a resulting mixture was stirred for 2 h; and then 100 mL of anhydrous MTBE was added, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain a product (0.01334 mol). In the product (NRX), a molar ratio of NR to malic acid (X) was 1:1; and a yield was 57%.

Characterization data:

HNMR(400MHz,MeOD): δ9.72 (s,1H), 9.42-9.44 (d,1H), 9.02-9.04 (d,1H), 8.25-8.29 (t,1H), 6.18-6.19 (d,1H), 4.41-4.44 (m,2H), 4.26-4.30 (m,2H), 3.99-4.03 (dd,1H), 3.83-3.87 (dd,1H), 2.49-2.80 (dd,2H);

MS(ESI+):254.96[M-1],MS(ESI-):133.04[M-1];

IR (KBr) ν_{max}3379, 2937, 1691, 591, 1100, 677, 6cm^{-1}.

Example 4

Preparation of a malate of NR (1:2)

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0195 mol, 1 eq) was dissolved in 45 mL of methanol, then anhydrous malic acid (0.043875 mol, 2.25 eq) was added, and a resulting mixture was stirred for 2 h; and then 80 mL of anhydrous MTBE was added, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain a product (0.0118 mol). In the product (NRX_2), a molar ratio of NR to malic acid (X) was 1:2; and a yield was 60.51%.

Characterization data:

HNMR(400MHz,MeOD): δ9.73(s,1H), 9.43-9.45 (d,1H), 9.04-9.06 (d,1H), 8.27-8.31 (m,1H), 6.19-6.20 (d,1H), 4.43-4.45 (m,2H), 4.31-4.34 (m,3H), 4.01-4.05 (dd,1H), 3.85-3.89 (dd,1H), 2.53-2.83 (dd,4H);

MS(ESI+):254.94[M-1],MS(ESI-):133.03[M-1];

IR (KBr) ν_{max}3409, 2940, 1698, 1580, 1411, 1293, 1181, 1098, 1028, 658 cm^{-1}.

When the NR and the anhydrous malic acid were fed in a molar ratio of 1:3.3, characterization data of an obtained product were the same, indicating that the product was a product (NRX_2) in which a molar ratio of NR to malic acid (X) was 1:2.

Example 5

Preparation of a royal jelly acid salt of NR (1:2)

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0400 mol, 1 eq) was dissolved in 60 mL of methanol, then royal jelly acid (0.0860 mol, 2.15 eq) was added, and a resulting mixture was stirred for 2 h; and then 120 mL of anhydrous ethyl acetate was slowly added, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain 12.5 g of a product (0.02 mol). In the product (NRX_2), a molar ratio of NR to royal jelly acid (X) was 1:2; and a yield was 50%.

Characterization data:

HNMR(400MHz,MeOD): δ9.73 (s,1H), 9.44 (s,1H), 9.04-9.05 (d,1H), 8.30 (m,1H), 6.58-6.66 (m,2H), 6.18 (m,1H), 5.81-5.85 (d,2H), 4.92 (m,2H), 4.31-4.43 (t,1H),3.85-4.05 (dd,2H), 3.54-3.57 (t,4H), 2.13-2.18 (m,4H), 1.51-1.56 (m,4H), 1.45-1.49 (m,4H), 1.37 (m,12H);

MS(ESI+):254.96[M-],MS(ESI-):185.23[M-1];

IR (KBr) ν_{max}3384, 2924, 1705, 1654, 1555, 1421, 1389, 1187, 1098, 1053, 977, 869, 677 cm^{-1}.

Example 6

Preparation of a malate of NR with niacin as a carrier

Under the protection of nitrogen, 0.01 mol of the malate of NR in Example 4 was added to 0.01 mol of niacin, and a resulting mixture was ground at a low temperature (about 16°C, the same below) for about 10 min until the mixture had a particle size of about 200 mesh to obtain 6.4 g of a mixture of malate and nicotinate of NR.

IR (KBr) ν_{max}3409, 2927, 1695, 1584, 1398, 1319, 1101, 1028, 747, 677, 636cm^{-1}.

Example 7

Preparation of a malate of NR with glutamic acid as a carrier

Under the protection of nitrogen, 0.01 mol of the malate of NR in Example 4 was added to 0.01 mol of glutamic acid, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 6.65 g of a mixture of malate and glutamate of NR.

IR (KBr) ν_{max}3415, 2937, 1692, 1593, 1404, 1092, 1028, 670 cm^{-1}.

Example 8

Preparation of a malate of NR with royal jelly acid as a carrier

Under the protection of nitrogen, 0.01 mol of the malate of NR in Example 4 was added to 0.01 mol of royal jelly acid, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 7.05 g of a mixture of malate and royal jelly acid salt of NR.

IR (KBr) ν_{max}3437, 2934, 1698, 1651, 1401, 1095, 684 cm^{-1}.

Example 9

Preparation of a malate of NR with nervonic acid as a carrier

Under the protection of nitrogen, 0.01 mol of the malate of NR in Example 4 was added to 0.01 mol of nervonic acid, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 8.85 g of a mixture of malate and nervonic acid salt of NR.

IR (KBr) ν_{max}3415, 2924, 1695, 1465, 1418, 1290, 1098, 728, 674 cm^{-1}.

Example 10

Preparation of a malate of NR with MCC as a carrier

Under the protection of nitrogen, 1 g of the malate of NR in Example 4 was added to 1 g of MCC, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 2 g of a mixture of malate of NR and MCC.

IR (KBr) ν_{max}3425, 2930, 1688, 1644, 1513, 1395, 1095, 1018, 667 cm^{-1}.

Example 11

Preparation of a malate of NR with MCC as a carrier

Under the protection of nitrogen, 1 g of the malate of NR in Example 3 was added to 1 g of MCC, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 2 g of a mixture of malate of NR and MCC.

IR (KBr) ν_{max}3365, 2906, 1695, 1591, 1396, 1099, 675 cm^{-1}.

Example 12

Preparation of a citrate of NR with MCC as a carrier

Under the protection of nitrogen, 1 g of the citrate of NR in Example 2 was added to 1 g of MCC, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 2 g of a mixture of citrate of NR and MCC.

R (KBr) ν_{max} 3437, 2927, 2378, 1740, 1698, 1641, 1513, 1398, 1111, 897, 671 cm^{-1}.

Example 13

Preparation of a citrate of NR with MCC as a carrier

Under the protection of nitrogen, 1 g of the citrate of NR in Example 1 was added to 1 g of MCC, and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 2 g of a mixture of citrate of NR and MCC.

IR (KBr) ν_{max} 3415, 2921, 2368, 1698, 1625, 1513, 1401, 1098, 894, 670, 619 cm^{-1}.

Example 14

Preparation of a malate of NR with apple cider vinegar powder as a carrier

Under the protection of nitrogen, 1 g of the malate of NR in Example 4 was added to 1 g of apple cider vinegar powder (10%), and a resulting mixture was ground at a low temperature for about 10 min until the mixture had a particle size of about 200 mesh to obtain 2 g of a mixture of malate of NR and apple cider vinegar powder.

IR (KBr) ν_{max}3406, 2930, 1692, 1584, 1408, 1092, 1028, 674 cm^{-1}.

Comparative Example

Preparation of a chlorine salt of NR

Under the protection of nitrogen and at a temperature of -10°C to -5°C, NR (0.0220 mol, 1 eq) was dissolved in 50 mL of methanol, then 10 g of a 17% hydrogen chloride-methanol solution was added dropwise, and a resulting mixture was stirred for dissolution; then 1 g of activated carbon was added, and a resulting mixture was further stirred for 1 h and filtered; a resulting filtrate was added to 150 ml of anhydrous MTBE, and a resulting mixture was further stirred for 30 min, filtered under the protection of nitrogen, rinsed with anhydrous diethyl ether, and dried at a temperature below -5°C to obtain 8 g of a product.

The method in Example 10 was used to prepare a chlorine salt of NR with MCC as a carrier.

Characterization data:

HNMR(400MHz,MeOD): 9.72 (s,1H), 9.44-9.46 (d,1H), 9.05-9.07 (d,1H), 8.29-8.33 (t,1H), 6.22-6.23 (d,1H), 4.45-4.47 (t,1H), 4.41-4.43 (q,1H), 4.31-4.33 (t,1H), 3.99-4.03 (d,1H), 3.84-3.88 (d,1H).

IR (KBr) ν_{max}3336, 2935, 1687, 1616, 1400, 1100, 675 cm^{-1}.

Stability test

I. Preparation of samples

1. The products of Examples 1 to 4, Examples 10 to 13, and the comparative example were each dispensed into 13 bottles, each of 50 mg; and the bottles were filled with nitrogen and sealed. One of the bottles (initial sample) was first tested, and the remaining 12 bottles were divided into two groups (each with 6 bottles) and stored. The bottles in each group were numbered 1 to 6 according to a test sequence. The two groups of bottles were stored at 2°C to 8°C and -20°C, respectively; and one sample was tested every month.

2. The products of Examples 6 to 9 and Example 14 were each dispensed into 7 bottles, each of 50 mg; and the bottles were filled with nitrogen and sealed. One of the bottles (initial sample) was first tested, and the remaining 6 bottles were numbered 1 to 6 according to a test sequence and then stored at 2°C to 8°C. One sample was tested every month.

II. Preparation of test sample solutions

One bottle of sample was taken at a time and prepared into a 5 mL or 10 mL solution using a 5 mL or 10 mL volumetric flask, and then the solution was filtered through a membrane to be ready for purity test by HPLC.

III. HPLC test

Mobile phase: isocratic elution: 5% water (0.1% formic acid) + 95% methanol (0.1% formic acid)

Wavelength: 254 nm

Temperature and humidity: 23.0°C and 54% RH

Sample dissolution: dissolution by methanol

Chromatographic column: ODS-2, 4.6 * 250 mm, 5 μm, and constant pressure: 12 Mpa to 13 Mpa

Flow rate: 1.0 mL/min

Injection volume: 5 μL

Running time: ≥ 15 min

IV. Decomposition rate = (purity of initial sample - purity of sample 6)/purity of initial sample × 100%

Table 1 (-20°C)

Time (month)	Example 1	Example 2	Example 3	Example 4	Comparative Example
0	98.930	98.471	98.573	98.818	98.525
1	98.828	98.317	98.691	98.547	98.284
2	98.450	98.079	98.310	98.629	98.087
3	98.190	98.168	98.288	98.316	97.701
4	98.252	97.933	98.076	98.207	97.449
5	97.978	97.806	97.912	98.081	97.575
6	97.814	97.788	97.645	98.100	97.210
Decomposition rate	1.13%	0.69%	0.94%	0.73%	1.33%

Table 2 (2°C to 8°C)

Time (month)	Example 1	Example 2	Example 3	Example 4	Comparative Example
0	98.930	98.471	98.573	98.818	98.525
1	98.198	98.492	98.482	98.424	98.171
2	98.409	98.240	98.185	98.360	98.206
3	98.171	98.097	98.270	98.298	97.540
4	97.957	97.626	97.946	98.239	97.612
5	97.823	97.704	97.592	97.707	97.384
6	97.670	97.498	97.337	97.816	97.109
Decomposition rate	1.27%	0.99%	1.25%	1.01%	1.44%

It can be seen from Table 1 and Table 2 that the lower the temperature, the better the stability of the salt of NR; and the malate and citrate of NR (in a molar ratio of either 1:1 or 1:2) are both better than the chlorine salt of NR (comparative example), this is because malic acid or citric acid can form an intimate ion pair with NR, which leads to some hydrophobicity and thus improves the stability.

From the comparison of Example 1 with Example 2 and Example 3 with Example 4, it is found that the molar ratio (NR to organic acid) of 1:2 leads to higher stability than the molar ratio (NR to organic acid) of 1:1. In a molar ratio of 1:1, NR and an organic acid are preferably present in the form of an ion pair according to the electron effect. When NR and an organic acid are fed in a molar ratio of 1:2, according to HNMR, it is found that one molecule of the NR and two molecules of the organic acid can exist stably. One molecule of the organic acid forms an ion pair with the NR, and then the other molecule of the organic acid forms a hydrogen bond with basic amide in the NR due to acid-base interaction, thereby achieving acid-base pairing, which helps to improve the stability of the salt. In addition, the two molecules of acid can provide a strongly acidic environment, and the stronger the acidity, the higher the stability of NR. For example, the acidity of NMN is stronger than that of NR, and thus the stability of NMN is much higher than that of NR. Furthermore, when NR and an organic acid are present in a molar ratio of 1:2, an NR content decreases, the influence of free hydroxyl and amide functional groups among molecules is weakened, and the stability increases.

Table 3 (2°C to 8°C)

Time (month)	Example 6	Example 7	Example 8	Example 9	Example 14
0	58.585	97.487	91.719	97.812	97.086
1	58.918	96.170	90.593	96.397	95.776
2	58.755	96.818	92.279	97.108	96.931
3	59.925	96.836	91.762	96.870	96.510
4	57.507	96.504	90.745	96.607	96.208
5	58.363	96.701	90.329	95.914	96.350
6	57.150	95.257	90.140	95.128	95.601
Decomposition rate	2.45%	2.29%	1.72%	2.74%	1.53%

After an organic acid salt of NR is compounded with another organic acid or apple cider vinegar powder, the stability is reduced, but still acceptable. Therefore, the addition of an organic acid or apple cider vinegar powder as a carrier does not significantly affect the stability of the organic acid salt of NR. After an organic acid or apple cider vinegar powder is compounded with NR to form a composite nutritional additive, the components can be complementary and coordinated to produce a superimposed effect, which has potential application value.

Table 4 (-20°C)

Time (month)	Example 10	Example 11	Example 12	Example 13	Comparative Example
0	98.759	98.550	98.316	98.694	97.917
1	98.632	98.180	98.440	98.633	97.874
2	98.714	98.442	98.259	98.441	97.656
3	98.557	98.395	98.213	98.527	97.326
4	98.324	98.308	98.007	98.372	97.470
5	98.491	98.273	98.110	98.393	97.319
6	98.425	98.112	98.041	98.238	97.277
Decomposition rate	0.34%	0.45%	0.28%	0.46%	0.65%

Table 5 (2°C to 8°C)

Time (month)	Example 10	Example 11	Example 12	Example 13	Comparative Example
0	98.759	98.550	98.316	98.694	97.917
1	98.691	98.339	98.282	98.625	97.776
2	98.506	98.031	98.326	98.458	98.015
3	98.239	98.274	98.028	98.083	97.693
4	98.317	97.932	97.805	98.121	97.542
5	98.342	97.786	97.734	97.833	97.380
6	98.251	97.875	97.782	98.017	97.154
Decomposition rate	0.51%	0.68%	0.54%	0.69%	0.78%

After an organic acid salt of NR is compounded with MCC, the organic acid salt of NR with MCC as a carrier exhibits higher stability (comparison of Examples 10 to 13 with Examples 1 to 4). This is because MCC has hydrophobicity and heat resistance, which can prevent moisture penetration. When MCC is added, the molar ratio (NR to organic acid) of 1:2 (Examples 10 and 12) leads to higher stability than the molar ratio (NR to organic acid) of 1:1 (Examples 11 and 13). The malate or citrate of NR compounded with MCC exhibits higher stability than the corresponding chloride salt of NR compounded with MCC (comparative example), which further supports the previous conclusion.

The above described are merely specific implementations of the present disclosure, and the protection scope of the present disclosure is not limited thereto. Any modification or replacement easily conceived by those skilled in the art within the technical scope of the present disclosure should fall within the protection scope of the present disclosure. Therefore, the protection scope of the present disclosure should be subject to the protection scope of the claims.

What is claimed is:

1. An organic acid salt of nicotinamide riboside, wherein the organic acid is citric acid or malic acid; the molar ratio of the nicotinamide riboside to the organic acid is 1:2.

2. A method of preparing the organic acid salt of nicotinamide riboside of claim 1, comprising: under a protection of nitrogen, dissolving the nicotinamide riboside in methanol, adding the organic acid to obtain a first resulting mixture, and stirring the first resulting mixture; adding methyl *tert*-butyl ether (MTBE) or ethyl acetate to the first resulting mixture to obtain a second resulting mixture, and further stirring the second resulting mixture; and filtering, washing, and drying to obtain the organic acid salt of nicotinamide riboside of claim 1.

3. A composition comprising the organic acid salt of nicotinamide riboside of claim 1 and a carrier, wherein the carrier is selected from the group consisting of malic acid, tannic acid, eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), caffeic acid, trans-cinnamic acid, trans-4-hydroxy-cinnamic acid, lactic acid, monosodium citrate, disodium citrate, citric acid, chlorogenic acid, gluconic acid, ferulic acid, royal jelly acid, nervonic acid, chicoric acid, rosmarinic acid, carnosic acid, niacin, adipic acid, lauric acid, monopotassium glycyrrhizinate (MPG), folic acid, chondroitin sulfate (CS), potassium hydrogen tartrate, salicylic acid, glycine, glutamic acid, alanine, arginine, leucine, isoleucine, valine, cystine, cysteine, methionine, threonine, serine, phenylalanine, tyrosine, tryptophan, proline, hydroxyproline, and aspartic acid.

4. The composition of claim 3, wherein the carrier is selected from the group consisting of niacin, glutamic acid, royal jelly acid, and nervonic acid, and the organic acid salt of nicotinamide riboside is a malate of nicotinamide riboside.

5. A composition comprising the organic acid salt of nicotinamide riboside of claim 1 and a carrier, wherein the carrier is selected from the group consisting of microcrystalline cellulose (MCC) and apple cider vinegar powder.

6. A method of preparing the composition of any one of claims 3 to 5, comprising: under a protection of nitrogen, mixing and grinding the organic acid salt of nicotinamide riboside and the carrier.