

Specification

Monascus Strain and Use Thereof

Cross-reference to related applications

The present application claims the priority of Chinese Patent Application No. 202311841573.2, filed on December 28, 2023, entitled “*Monascus* Strain and Use Thereof”, the entire content of which is incorporated herein by reference.

Technical field

The present application relates to the field of microbial fermentation, in particular to a *Monascus* strain, a red yeast rice, a red yeast rice decoction piece, a preparation method of red yeast rice, a red yeast rice extract and a drug.

Background art

Red yeast rice is a traditional fermented product in China. Owing to its diverse main components, red yeast rice is used in various fields including pharmaceuticals, food, and dyeing. The discovery of monacolin compounds in red yeast rice has made it a preferred natural drug for inhibiting cholesterol synthesis and lowering blood lipids, attracting worldwide attention.

There are many types of monacolin compounds, specifically including Monacolin K (MK), acid form of Monacolin K (MKA), Monacolin J (MJ), acid form of Monacolin J (MJA), Monacolin L (ML), acid form of Monacolin L (MLA), Monacolin M (MM), acid form of Monacolin M (MMA), and dehydromonacolin K (DMK). In some content determination methods, Monacolin K refers to the total content of monacolin K and acid form of monacolin K, serving as a detection indicator for red yeast rice. However, the studies have confirmed that other monacolin compounds also exhibit potent activities in inhibiting cholesterol synthesis and lowering blood lipids. Therefore, increasing the content of total monacolin compounds, together with elevating the levels of monacolin K and acid form of monacolin K, can enhance the pharmaceutical activity of red yeast rice.

At present, the red yeast rice is usually used in the form of red yeast rice decoction piece as a natural lipid-lowering drug. The state and some provinces and municipalities have put forward recommended standards for the contents of extractives and monacolin compounds in red yeast rice decoction pieces, so as to ensure the lipid-lowering effect of red yeast rice decoction pieces. Extractives refer to the soluble substances in medicinal materials and decoction pieces extracted with water or alcohol solvents, and the content of crude drug extractives is used as a criterion for quality control, which is generally adopted in the circumstances that the active ingredients in crude drug are present in very low contents, the indicator components are unclear, or no accurate quantitative method is available. Medicinal red yeast rice contains a variety of active ingredients with multiple pharmacological effects, such as sterols, γ -aminobutyric acid, pigments, organic acids and the like, which exert lipid regulation, hypoglycemic, cholesterol-lowering, immunity-enhancing, anti-tumor and other effects. Therefore, employing the content of extractives for quality control can objectively evaluate the comprehensive pharmacological effects of red yeast rice products. Accordingly, the contents of extractives and monacolin compounds are key indicators for evaluating the quality of red yeast rice.

The studies have shown that the contents of extractives, monacolin K, acid form of monacolin K, citrinin, and aflatoxin in commercially available products vary significantly, as recorded in Table 1.

Table 1

No.	Manufacturer	Lot No.	Standard $\geq 7.0\%$ (Beijing) extractives (%)	Acid form of monacolin K (mg/g)	Monacolin K (mg/g)	Citrinin ($\mu\text{g/kg}$)	Aflatoxin B1 ($\mu\text{g/kg}$)
1	A Traditional Chinese Medicine Decoction Pieces Co., Ltd. in Beijing	181114008	10.5	None	None	24.5	2.1731

2	A Traditional Chinese Medicine Decoction Pieces Co., Ltd. in Guangdong	180857 1131	13.2	2.3	None	62.3	3.3776
3	A company in Beijing	201503 14	8.9	None	None	37.965	0.4395
4	A company in Zhejiang	201806 03	5.2	1.31	1.95	12.1	0.4012

Some commercially available decoction piece products have a qualified extractive content, but do not contain the active ingredients such as monacolin K and acid form of monacolin K. Moreover, as the extractive content increases, the contents of toxic and harmful components including citrinin and aflatoxin also increase. Some products contain monacolin but do not have a qualified extractive content.

In addition, the content of toxic components also affects the safety of red yeast rice and limits its application.

Contents of the invention

The present application provides a *Monascus* strain, a red yeast rice, a red yeast rice decoction piece, a preparation method of red yeast rice, a red yeast rice extract, and a drug, so as to increase the contents of monacolin compounds and extractives in red yeast rice, red yeast rice decoction piece, or products thereof.

A first aspect of the present application is to provide a *Monascus* strain, the Latin name of which is *Monascus purpureus*, with a deposit number of CGMCC No. 40777.

A second aspect of the present application is to provide red yeast rice, which is obtained by fermentation using the *Monascus* strain provided in the first aspect.

In any embodiment of the second aspect, based on the dry matter of red yeast rice, a content of monacolin compounds in the red yeast rice is 4 mg/g to 40 mg/g, preferably 6 mg/g to 30 mg/g, more preferably 7.0 mg/g to 22 mg/g.

In any embodiment of the second aspect, it is preferred that the monacolin compounds include Monacolin K and acid form of Monacolin K. Based on the dry matter of red yeast rice, A content of Monacolin K in the red yeast rice is preferably 3.07 mg/g to 13.5 mg/g, more preferably 7.25 mg/g to 13.5 mg/g, further preferably 8.5 mg/g to 13.5 mg/g; based on the dry matter of red yeast rice, the content of acid form of Monacolin K in the red yeast rice is preferably 2.0 mg/g to 5.0 mg/g, more preferably 2.3 mg/g to 4.25 mg/g, further preferably 3.5 mg/g to 4.23 mg/g.

In any embodiment of the second aspect, it is further preferred that the monacolin compounds further include Monacolin L, acid form of Monacolin M, and dehydromonacolin K. Based on the dry matter of red yeast rice, a content of Monacolin L in the red yeast rice is preferably 0.3 mg/g to 1.33 mg/g, preferably 1.12 mg/g to 1.33 mg/g; a content of acid form of Monacolin M in the red yeast rice is preferably 0.27 mg/g to 0.81 mg/g, preferably 0.72 mg/g to 0.81 mg/g; a content of dehydromonacolin K in the red yeast rice is preferably 0.2 mg/g to 0.78 mg/g, preferably 0.65 mg/g to 0.78 mg/g.

In any embodiment of the second aspect, it is further preferred that the monacolin compounds further include acid form of Monacolin L, Monacolin J, and acid form of Monacolin J. Based on the dry matter of red yeast rice, a content of acid form of Monacolin L in the red yeast rice is preferably 0.29 mg/g to 0.46 mg/g, preferably 0.41 mg/g to 0.46 mg/g; a content of Monacolin J in the red yeast rice is preferably 0.11 mg/g to 0.43 mg/g, preferably 0.41 mg/g to 0.43 mg/g; a content of acid form of Monacolin J in the red yeast rice is preferably 0.16 mg/g to 0.28 mg/g, preferably 0.27 mg/g to 0.28 mg/g.

In any embodiment of the second aspect, based on the dry matter of red yeast rice, the content of extractives in the red yeast rice is preferably greater than 7%, preferably 7.5% to 30%; preferably 8% to 30%; preferably 10% to 29%; preferably 15% to 25%; preferably 17.4% to 23.6%.

A third aspect of the present application is to provide a red yeast rice decoction piece, which is prepared from the red yeast rice provided in any embodiment of the second aspect.

A fourth aspect of the present application is to provide a

preparation method of a red yeast rice, comprising performing fermentation using the *Monascus* strain provided in the first aspect as a strain to prepare red yeast rice.

In any embodiment of the fourth aspect, the preparation method comprises: performing expanded cultivation of the *Monascus* strain using a liquid medium to obtain a liquid strain; inoculating the liquid strain into a solid medium for fermentation to obtain a fermentation product containing red yeast rice.

In any embodiment of the fourth aspect, the liquid medium comprises glucose, peptone, a phosphorus source, and trace elements.

In any embodiment of the fourth aspect, preferably, a content of glucose in the liquid medium is 30 g/L to 150 g/L; preferably, a content of peptone in the liquid medium is 2 g/L to 30 g/L; preferably, a content of the phosphorus source in the liquid medium is 0.5 g/L to 7 g/L, and preferably, the phosphorus source includes $\text{NH}_4\text{H}_2\text{PO}_4$ and $(\text{NH}_4)_2\text{HPO}_4$.

In any embodiment of the fourth aspect, preferably, the trace elements include magnesium element and calcium element. More preferably, magnesium element is provided by $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, and the content of $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ in the liquid medium is 0.01 g/L to 1.2 g/L; further preferably, calcium element is provided by CaCl_2 , and the content of CaCl_2 in the liquid medium is 0.01 g/L to 0.8 g/L.

In any embodiment of the fourth aspect, preferably, the liquid of the liquid medium comprises an aqueous starch solution.

In any embodiment of the fourth aspect, the solid medium comprises rice, bran, peptone, glucose, and water.

In any embodiment of the fourth aspect, preferably, in parts by weight, the solid medium comprises 100 parts of rice, 6 to 9 parts of bran, 2 to 8 parts of peptone, and 1.4 to 3.0 parts of glucose. Preferably, the solid medium further comprises ethanol, and more preferably, the mass content of ethanol relative to the dry matter of the solid medium is 0.2% to 1%, further preferably 0.35% to 0.7%.

In any embodiment of the fourth aspect, preferably, the solid medium further comprises bean powder, more preferably 2 to 8 parts by weight of bean powder, and further preferably, the bean powder is

selected from one or more of the group consist of green pea powder, mung bean powder, black bean powder, red bean powder, and soybean powder.

In any embodiment of the fourth aspect, preferably the rice is subjected to steaming, boiling, or hot soaking, more preferably steaming or hot soaking.

In any embodiment of the fourth aspect, preferably a steaming temperature is 90°C to 120°C, and a steaming time is 25 min to 50 min, preferably 35 min to 45 min.

In any embodiment of the fourth aspect, preferably a mass ratio of water added to rice during steaming is 30% to 70%, more preferably 40% to 55%.

In any embodiment of the fourth aspect, preferably during hot soaking, a hot soaking temperature is 90°C to 100°C, and a hot soaking time is 6 h to 18 h, more preferably 10 h to 14 h.

In any embodiment of the fourth aspect, the process of inoculating the liquid strain into the solid medium for fermentation includes: sterilizing the solid medium and then inoculating the liquid strain into the solid medium, preferably a sterilization temperature is 120°C to 125°C and a time is 30 min to 90 min; performing primary cultivation of the inoculated solid medium at 30°C to 36°C with a relative humidity of 40% to 80% for 48 h to 120 h to obtain a primary culture; performing secondary cultivation of the primary culture at 18°C to 25°C with a relative humidity of 40% to 80% for 7 days to 30 days, preferably 7 days to 20 days, to obtain a fermented system.

In any embodiment of the fourth aspect, when the primary cultivation lasts for 48 h to 120 h, water is added to the solid medium and stirred, wherein the mass content of water added is 5% to 15%, preferably 6% to 10%, relative to the dry matter of the solid medium.

A fifth aspect of the present application is to provide a red yeast rice extract, which is prepared by extracting the red yeast rice provided in any embodiment of the second aspect with water or ethanol.

A sixth aspect of the present application is to provide a drug comprising red yeast rice or a red yeast rice extract, wherein the red

yeast rice comprises the red yeast rice provided in any embodiment of the second aspect or the red yeast rice decoction piece provided in any embodiment of the third aspect, and the red yeast rice extract comprises the red yeast rice extract provided in any embodiment of the fifth aspect. The drug is selected from lipid-lowering drugs, antihypertensive drugs, hypoglycemic drugs, and/or anticancer drugs.

In the red yeast rice products prepared by fermentation using the *Monascus* strain provided by the present application, the contents of monacolin compounds and extractives are both high, and the products contain polyhydroxysterols and flavonoids and exhibit favorable safety, thereby improving the pharmaceutical activity and quality of the red yeast rice products.

Biomaterial deposit information

The *Monascus* strain provided by the present disclosure was deposited on August 4, 2023, in the China General Microbiological Culture Collection Center (CGMCC), located at No. 3, Yard 1, Beichen West Road, Chaoyang District, Beijing, P. R. China, with postal code 100101. The deposit number is CGMCC No. 40777, the culture name is *Monascus purpureus*, and its Latin name is *Monascus purpureus*.

Description of figures

For a clearer description of the technical solutions in the examples of the present application, the accompanying figures required in the examples of the present application are briefly introduced below. Obviously, the figures described below are only some examples of the present application. For those of ordinary skill in the art, other figures can also be obtained based on these figures without creative effort.

Figure 1 shows the lethality rate at different chemical mutagenesis durations during the screening of the *Monascus* strain of the present application.

Figure 2 shows the lethality rate at different ultraviolet

mutagenesis durations during the screening of the *Monascus* strain of the present application.

Figure 3 shows the colony morphology and microscopic characteristics of the *Monascus* strain of the present application.

Figure 4 shows the fingerprint spectra of the red yeast rice decoction piece obtained on day 15 and day 26 in Example 5 of the present application.

Figure 5 shows the liquid chromatogram of aflatoxin in the red yeast rice decoction piece obtained on day 26 in Example 5 of the present application.

Figure 6 shows the liquid chromatogram of citrinin in the red yeast rice decoction piece obtained on day 26 in Example 5 of the present application.

Detailed description of specific embodiments

The embodiments of the present application are described in further detail below with reference to the accompanying figures and examples. The detailed description of the following examples is intended to illustrate the principles of the present application in an exemplary manner, but shall not be used to limit the scope of the present application, i.e., the present application is not limited to the described examples.

As analyzed in the background art of the present application, the contents of monacolin compounds and extractives in the red yeast rice products of the prior art cannot be increased simultaneously. To solve this problem, the present application provides a *Monascus* strain, a red yeast rice, a red yeast rice decoction piece, and a preparation method of red yeast rice.

In a first embodiment of the present application, a *Monascus* strain is provided, the Latin name of which is *Monascus purpureus*, with a deposit number of CGMCC No. 40777.

The red yeast rice products prepared by fermentation using the *Monascus* strain provided in the present application have high contents of both monacolin compounds and extractives, contain

polyhydroxysterols and flavonoids, and exhibit favorable safety, thereby improving the pharmaceutical activity and quality of the red yeast rice products.

In some embodiments, the 18S rRNA sequence of the *Monascus* strain is shown as SEQ ID No. 1, including the 18S rRNA fragment, the complete sequences of ITS I, 5.8S rRNA, ITS2, and the 28S rRNA region sequence fragment:

5'-TCATTACCGAGTGCGGGTCCCCTTCGTGGGACCCAA
CCTCCCACCCGTGATTATTGTACCTCCTGTTG TTCGGCGCG
GCCCCCGGGGCCCCGCCGGAGACATCTTCTCGAACGCTGT
CTTTGAAAAGGATTGCTGTCTGAGTAAACATACCAAATCGG
TTAAAACTTTCAACAACGGATCTCTTGGTTCCGGCATCGAT
GAAGAACGCAGCGAAATGCGATAAGTAATGTGAATTGCAG
AATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCC
CCTGGTATTCCGGGGGGGCATGCCTGTCCGAGCGTCATTACT
GCCCCCTCAAGCGCGGCTTGTGTGTTGGGCCGCCGTCCCCT
GCGCCTCCGGGCAAGGGGGACGGGCCCCGAAAGGCAGTGG
CGGCGCCGCGTCCGGTCCTCGAGCGTATGGGGCTTTGTCAC
CCGCTCAGTAGGTCGGGCCGGGGCCTTTGCCCTCTCCAAC
CTTTTTTTCCTTAGGTTGACCTCGGATCAGGTAGGGATACCC
GCTGAACTTAAGCATATCAA-3'.

In a second embodiment of the present application, red yeast rice is provided, which is obtained by fermentation using the *Monascus* strain provided in the above-mentioned first embodiment. The red yeast rice has relatively high contents of both monacolin compounds and extractives. Moreover, the studies of the present invention find that no toxic or harmful components are detected, such as citrinin and aflatoxin, even when the extractive content is increased.

In addition, the red yeast rice can be used as a raw material for functional red yeast rice or pharmaceutical red yeast rice. It can be used as a red yeast rice medicinal material, decoction pieces, or various raw materials, and when it used as raw materials, it can be used directly or after processing.

In some embodiments, based on the dry matter of red yeast rice, the content of monacolin compounds in the red yeast rice is 4 mg/g to 40 mg/g, preferably 6 mg/g to 30 mg/g, more preferably 7.0 mg/g to

22 mg/g.

In some embodiments, the monacolin compounds preferably include Monacolin K and acid form of Monacolin K. Based on the dry matter of red yeast rice, the content of Monacolin K in the red yeast rice is preferably 3.07 mg/g to 13.5 mg/g, more preferably 7.25 mg/g to 13.5 mg/g, further preferably 8.5 mg/g to 13.5 mg/g; the content of acid form of Monacolin K in the red yeast rice is preferably 2.0 mg/g to 5.0 mg/g, more preferably 2.3 mg/g to 4.25 mg/g, further preferably 3.5 mg/g to 4.23 mg/g.

In some embodiments, the monacolin compounds more preferably further include Monacolin L, acid form of Monacolin M, and dehydromonacolin K. Based on the dry matter of red yeast rice, the content of Monacolin L in the red yeast rice is preferably 0.3 mg/g to 1.33 mg/g, more preferably 1.12 mg/g to 1.33 mg/g; the content of acid form of Monacolin M in the red yeast rice is preferably 0.27 mg/g to 0.81 mg/g, more preferably 0.72 mg/g to 0.81 mg/g; the content of dehydromonacolin K in the red yeast rice is preferably 0.2 mg/g to 0.78 mg/g, more preferably 0.65 mg/g to 0.78 mg/g. More preferably, the monacolin compounds further include acid form of Monacolin L, Monacolin J, and acid form of Monacolin J. The content of acid form of Monacolin L in the red yeast rice is preferably 0.29 mg/g to 0.46 mg/g, preferably 0.41 mg/g to 0.46 mg/g; the content of Monacolin J in the red yeast rice is preferably 0.11 mg/g to 0.43 mg/g, preferably 0.41 mg/g to 0.43 mg/g; the content of acid form of Monacolin J in the red yeast rice is preferably 0.16 mg/g to 0.28 mg/g, preferably 0.27 mg/g to 0.28 mg/g.

Many red yeast rice products contain no or only trace amounts of acid form of Monacolin J that are undetectable, whereas the red yeast rice of the present disclosure contains a certain amount of this component.

In some embodiments, based on the dry matter of red yeast rice, the content of extractives in the red yeast rice is preferably greater than 7%, preferably 7.5% to 30%; preferably 8% to 30%; preferably 10% to 29%; preferably 15% to 25%; preferably 17.4% to 23.6%.

In a third embodiment of the present application, a red yeast rice decoction piece is provided, which is prepared using any red yeast rice

provided in the above-mentioned second embodiment.

In a fourth embodiment of the present application, a preparation method of red yeast rice is provided, which comprises performing fermentation using the *Monascus* strain provided in the first embodiment as a strain to prepare red yeast rice.

The red yeast rice products prepared by fermentation using the *Monascus* strain provided in the present application have relatively high contents of both monacolin compounds and extractives, thereby improving the pharmaceutical activity of the red yeast rice products.

In some embodiments of the present application, the preparation method comprises: performing expanded cultivation of the *Monascus* strain using a liquid medium to obtain a liquid strain; inoculating the liquid strain into a solid medium for fermentation to obtain a fermentation product containing red yeast rice.

The *Monascus* strain is first subjected to expanded cultivation and then to fermentation cultivation, which improves the efficiency of fermentation cultivation.

For the expanded cultivation of the *Monascus* strain, the composition of the liquid medium used may refer to that of conventional liquid medium for expanded cultivation of *Monascus* strains. In some embodiments, the liquid medium comprises glucose, peptone, a phosphorus source, and trace elements, so as to improve the efficiency of expanded cultivation. In some embodiments, the content of glucose in the liquid medium is preferably 30 g/L to 150 g/L; the content of peptone in the liquid medium is preferably 2 g/L to 30 g/L; the content of the phosphorus source in the liquid medium is preferably 0.5 g/L to 7 g/L, and the phosphorus source preferably includes $\text{NH}_4\text{H}_2\text{PO}_4$ and $(\text{NH}_4)_2\text{HPO}_4$. The trace elements preferably include magnesium element and calcium element; more preferably, magnesium element is provided by $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, and the content of $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ in the liquid medium is 0.01 g/L to 1.2 g/L; further preferably, calcium element is provided by CaCl_2 , and the content of CaCl_2 in the liquid medium is 0.01 g/L to 0.8 g/L, so as to improve the utilization rate of the liquid medium. Preferably, the liquid of the liquid medium comprises an aqueous starch solution, such as potato boiled juice or an aqueous solution of potato starch.

For the fermentation cultivation of the liquid strain, the composition of the solid medium may also refer to that of conventional solid medium for fermentation cultivation of *Monascus*. In some embodiments, the solid medium comprises rice, bran, peptone, glucose, and water. To optimize the nutritional composition of the solid medium and further increase the yield of monacolin compounds and the extractive content, in some embodiments, the solid medium preferably comprises, in parts by weight, 100 parts of rice, 6 to 9 parts of bran, 2 to 8 parts of peptone, and 1.4 to 3.0 parts of glucose.

In some embodiments, the solid medium further comprises ethanol, and more preferably the mass content of ethanol relative to the dry matter of the solid medium is 0.2% to 1%, preferably 0.35% to 0.7%. Herein, ethanol functions to inhibit contaminating bacteria and additionally acts as a trace alcoholic metabolic regulatory factor.

In some embodiments of the present application, the solid medium further comprises bean powder, preferably 2 to 8 parts by weight of bean powder, and more preferably the bean powder is selected from one or more of a group consist of green pea powder, mung bean powder, black bean powder, red bean powder and soybean powder, so as to further increase the contents of monacolin compounds and extractives.

The rice may be rice flour or rice grains. In some embodiments, to improve the fermentation efficiency of rice, the rice is preferably subjected to steaming, boiling, hot soaking or cold soaking, and more preferably steaming or hot soaking. Rice in the above-mentioned forms is more easily utilized by *Monascus* after maturation, thus helping to improve fermentation efficiency.

For example, rice and water are mixed at a mass ratio of water to rice of (30-120):100 (the mass content of rice in the solid medium is calculated on the dry weight of rice), followed by steaming, boiling, hot soaking or cold soaking. After boiling, hot soaking or cold soaking, the rice is drained before use.

In some embodiments, when the rice is subjected to steaming, boiling or hot soaking, the weight ratio of water to rice is (30-70):100. For instance, during steaming, the mass ratio of water added to rice is

30% to 70%.

In some embodiments, the steaming temperature is 90°C to 120°C (e.g., 90°C, 100°C, 110°C, 120°C), the mass ratio of water added to rice is 30% to 70%, more preferably 40% to 55% (e.g., 40%, 45%, 50% or 55%), and the steaming time is 25 min to 50 min (e.g., 25 min, 30 min, 35 min, 40 min, 45 min or 50 min), preferably 35 min to 45 min.

In some embodiments, the hot soaking temperature is preferably 50°C to 100°C (e.g., 60°C, 70°C, 80°C, 85°C, 90°C, 95°C), more preferably 90°C to 100°C, and the hot soaking time is 6 h to 18 h, preferably 10 h to 14 h.

In some embodiments, the process of inoculating the liquid strain into the solid medium for fermentation comprises: sterilizing the solid medium and then inoculating the liquid strain into the solid medium, preferably at a sterilization temperature of 120°C to 125°C for 30 min to 90 min; performing primary cultivation on the inoculated solid medium at 30°C to 36°C with a relative humidity of 40% to 80% for 48 h to 120 h to obtain a primary culture; performing secondary cultivation on the primary culture at 18°C to 25°C with a relative humidity of 40% to 80% for 7 days to 30 days, preferably 7 days to 20 days, more preferably 10 days to 20 days, to obtain a fermented system. Cultivation through the fermentation process can sufficiently increase the contents of monacolin compounds and extractives, reduce the production of citrinin and aflatoxin B1, and improve the overall quality of red yeast rice.

Experiments show that, in some embodiments, when the primary cultivation lasts for 72 h to 120 h, water is added to the solid medium to replenish moisture during fermentation, wherein the mass content of water added is 5% to 15% relative to the dry matter of the solid medium. Adding water during or at the end of high-temperature cultivation further increases the contents of monacolin compounds and extractives in red yeast rice.

In some embodiments, after fermentation, the preparation method further comprises, a step of drying the fermentation product. This step is not only a process of removing moisture but also involves an equilibrium process in which partial acidic components, such as acid form of monacolin, are converted into lactone-type monacolin. If

the conditions are harsh, i.e., the drying temperature is too high, the acidic and lactone-type monacolins may irreversibly degrade or convert into dehydrated monacolin, affecting the content. Other paired statin components exhibit similar variation patterns. Therefore, in some embodiments, the drying temperature is 50°C to 100°C, preferably 60°C to 70°C, and the drying time is 6 h to 15 h.

In some embodiments, the red yeast rice decoction piece is prepared by the preparation method provided in the second embodiment.

In a fifth embodiment of the present application, a red yeast rice extract is provided, which is prepared by extracting any red yeast rice provided in the second embodiment with water or ethanol.

In a sixth embodiment of the present application, a drug comprising red yeast rice or a red yeast rice extract is provided, wherein the red yeast rice comprises the red yeast rice provided in the second embodiment or the red yeast rice decoction piece provided in the third embodiment, and the red yeast rice extract comprises the red yeast rice extract provided in the fifth embodiment. The drug is selected from lipid-lowering drugs, antihypertensive drugs, hypoglycemic drugs and/or anticancer drugs.

Since the red yeast rice of the present application has high contents of both extractives and monacolin, it exhibits superior lipid-lowering, hypoglycemic and/or antihypertensive effects.

The beneficial effects of the present application are further illustrated below with reference to examples, but the scope of the present invention is not limited to these examples.

Experimental instruments and equipment: ZHWY-2102 Constant Temperature Incubator Shaker: Shanghai Zhicheng Analytical Instrument Manufacturing Co., Ltd.; LRH-250-HSE Constant Temperature and Humidity Incubator: Guangdong Taihongjun Scientific Instrument Co., Ltd.; BXM-110VE Vertical Pressure Steam Sterilizer: Shanghai Boxun Medical Biological Instrument Corp.; WGL-230B Electric Heating Air Blast Drying Oven: Tianjin Taisite Instrument Co., Ltd.; FW80 High-Speed Universal Grinder: Tianjin Taisite Instrument Co., Ltd.;

Liquid Chromatograph: Model LC20AT, Shimadzu Corporation, Japan, with UV detector. Chromatographic Column: Octadecylsilane-bonded silica gel as filler (Waters Symmetry C18, 3.9×150 mm, 5 μm). Electronic Balance: XS205DU, METTLER; Ultrapure Water System: PALL Cascada IX; Ultrasonic Cleaner: KH-500DB, Kunshan Hechuang Ultrasonic Instruments Co., Ltd.; Rapid Moisture Analyzer: Model MA50, Sartorius (Shanghai) Trading Co., Ltd;

Experimental materials and reagents: Acetonitrile: chromatographic grade, Fisher (Lot No.: 211921); Trifluoroacetic acid: chromatographic grade, Fisher (Lot No.: 145624); 95% Ethanol: analytical grade, Sinopharm Chemical Reagent Co., Ltd.; Purified Water: self-made; Methanol: chromatographic grade, Fisher (Lot No.: 157751). Reference Standard: Monacolin K (National Institutes for Food and Drug Control, purity >99%, Lot No.: 100600). 1-Methyl-3-nitro-1-nitrosoguanidine (MNNG): Sigma-Aldrich Co. LLC, USA.

Screening Process of *Monascus* Strain

Preparation method of spore suspension: The original strain (No. WP03) was inoculated on PDA medium and cultured at 29°C for 7 days. Then mycelia and spores were scraped off with an inoculation loop and transferred to an Erlenmeyer flask containing 20 mL of sterile water, with the bottom of the flask covered with glass beads. The flask was shaken at 180 r/min for 20 min, followed by filtration to prepare a spore suspension, which was diluted to a concentration of 10⁶ spores/mL.

Chemical mutagenesis: Preparation of MNNG solution: 50 mg of MNNG was weighed into a volumetric flask, and acetone was added till 5 mL to prepare a 1% stock solution. 0.9 mL and 0.8 mL of the spore suspension at a concentration of 10⁶ spores/mL were taken, and 0.1 mL and 0.2 mL of the 1% MNNG stock solution were added (resulting in final MNNG concentrations of 0.1% and 0.2%) respectively. After treatment for 10, 30, 60 and 90 min respectively, the suspensions were diluted in a gradient manner. 0.1 mL of each spore suspension was spread on plates and cultured at 29°C for 3 to 5 days for spore counting. The lethality rate was calculated using the untreated group as control (see Figure 1 for lethality rate). The strain treated with 0.2% MNNG for 90 min, which represented the optimal lethal conditions, was selected for subsequent ultraviolet mutagenesis.

Lethality rate/% = (number of colonies on control plate - number of colonies on mutagenesis plate)/number of colonies on control plate.

Ultraviolet mutagenesis: A spore suspension of 10^6 spores/mL was prepared from the MNNG-mutagenized strain according to the method described above. 5 mL of the spore suspension was placed 20 cm away from a 20 W UV lamp and irradiated for 0 s, 30 s, 60 s, 90 s, 120 s and 180 s respectively. The spore suspension was spread on plates according to the same method as described above, and the lethality rate was calculated using the untreated group as control (see Figure 2 for lethality rate). The optimal UV irradiation time was determined as 120 s.

Results: Through the above-mentioned repeated chemical and ultraviolet mutagenesis, the *Monascus* mutant strain of the present disclosure was finally obtained. The *Monascus* mutant strain was deposited in the China General Microbiological Culture Collection Center (CGMCC) with the deposit number CGMCC No. 40777.

The 18S rRNA sequence of the *Monascus* strain is shown as SEQ ID No. 1, including the 18S rRNA fragment, the complete sequences of ITS I, 5.8S rRNA, ITS2, and the 28S rRNA region sequence fragment:

5'-TCATTACCGAGTGCGGGTCCCCTTCGTGGGACCCAA
CCTCCCACCCGTGATTATTGTACCTCCTGTTG TTCGGCGCG
GCCCCCGGGGCCCCGCCGGAGACATCTTCTCGAACGCTGT
CTTTGAAAAGGATTGCTGTCTGAGTAAACATACCAAATCGG
TTAAAACTTTCAACAACGGATCTCTTGGTTCCGGGCATCGAT
GAAGAACGCAGCGAAATGCGATAAGTAATGTGAATTGCAG
AATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCC
CCTGGTATTCCGGGGGGGCATGCCTGTCCGAGCGTCATTACT
GCCCCCTCAAGCGCGGCTTGTGTGTTGGGCCGCCGTCCCCT
GCGCCTCCGGGCAAGGGGGACGGGCCCCGAAAGGCAGTGG
CGGCGCCGCGTCCGGTCCTCGAGCGTATGGGGCTTTGTCAC
CCGCTCAGTAGGTCGGGCCGGGGCCTTTGCCCTCTCCAAC
CTTTTTTTCCTTAGGTTGACCTCGGATCAGGTAGGGATACCC
GCTGAACTTAAGCATATCAA-3'.

The colony morphology and microscopic characteristics of the *Monascus* strain are shown in Figure 3.

The tested strain grows rapidly on wort agar medium. After incubation at 25°C in darkness for 10 days, the colony diameter reaches 40 to 45 mm. The aerial hyphae are luxuriant with a pale color at the initial stage (as shown in the upper-left panel of Figure 3), and turn orange-red at the later stage. The reverse side of the colony is dark orange, and the pigment is soluble in the medium.

A large number of conidia are produced. The conidiophores show insignificant specialization, being straight or slightly curved. The conidia are spherical, hyaline, with slightly rough walls and truncate bases, borne in chains, 5.5–10.1 μm (upper-right, lower-left and lower-right panels of Figure 3).

Strain stability study

After 20 subcultures of the strain, the contents of Monacolin K (MK) and acid form of Monacolin K (MKA) in the prepared red yeast rice decoction piece remained essentially unchanged, as detailed in Table 2, indicating good stability of the inventive strain (fermentation conditions of Example 5 were adopted, with a culture period of 23 days).

Table 2

Sample type	MK (mg/g)	MKA (mg/g)
Generation 1 of the new strain	7.98	1.83
After 20 subcultures	7.92	1.85

Example 1

The *Monascus* strain (CGMCC No. 40777, hereinafter referred to as Monascus Strain 1) and the original strain (WP03) were respectively inoculated into the liquid fermentation medium at an inoculum size of 5% (volume of slant spore suspension/volume of liquid medium). The liquid fermentation medium consisted of glucose 85 g/L, peptone 15 g/L, $\text{NH}_4\text{H}_2\text{PO}_4$ 1.5 g/L, $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ 0.8 g/L, and CaCl_2 0.2 g/L, which was prepared with distilled water. The fermentation temperature was 30°C, and the fermentation time was 40 to 48 h. Shake cultivation was performed at 30°C for 2 days, and a

liquid seed was obtained.

The liquid seed was pipetted into the solid medium and mixed uniformly. The solid medium was prepared as follows: rice was soaked at room temperature (20°C to 25°C) for 14 h at a water-to-rice mass ratio of 120:100, then drained. Nutritional components (comprising, per 100 parts of rice before water addition, 8 parts of bran, 2 parts of peptone, 2 parts of glucose) were added proportionally and mixed thoroughly. Primary cultivation was performed at 30°C to 36°C with a relative humidity of 40% to 80% for 5 days. Starting from day 6, secondary cultivation was performed at 18°C to 25°C with a relative humidity of 40% to 80% until day 25 to obtain the fermentation product. The product was dried at 70°C to obtain red yeast rice. Monacolin content was determined according to the method described in the *Chinese Pharmacopoeia* 2020 Edition.

The extractive content was determined according to the hot extraction method under the alcohol-soluble extractive determination method (General Principle 2201, *Chinese Pharmacopoeia* 2020 Edition), using 70% ethanol as the solvent.

Citrinin detection (limit of detection: 5 ppb): The content of citrinin was determined in accordance with Method 1 (immunoaffinity column purification-high performance liquid chromatography) specified in the national standard GB 5009.222-2016 «Determination of Citrinin in Foods».

For aflatoxin detection method, please refer to the aflatoxin assay method specified in the *Chinese Pharmacopoeia* (2020 Edition, Volume IV, General Principle 2351 – Liquid Chromatography/Photochemical Derivatization Method).

High performance liquid chromatography (HPLC) was used to determine the contents of various monacolins. The detection method was as follows: Liquid chromatographic conditions: Acetonitrile was used as mobile phase A, and 0.1% (v/v) trifluoroacetic acid (TFA) aqueous solution as mobile phase B with gradient elution. From 0 to 28 min, mobile phase A was maintained at 35% and mobile phase B at 65% (volume fraction, the same below); from 28 to 30 min, mobile phase A decreased linearly from 75% to 35%, while mobile phase B increased from 25% to 65%; from 30 to 35 min, the system returned to the initial conditions of 35% mobile phase A and 65% mobile phase

B. The flow rate was 1.0 mL/min, the column temperature was 30°C, and the injection volume was 20 µL. The PDA detection range was set at 200 to 350 nm, and the detection wavelength was 237 nm.

The test results are recorded in Table 3.

Table 3

	Monacolin K content (mg/g)	Acid form of monacolin K (mg/g)	Total monacolins (mg/g)	Citrinin (mg/g)	Aflatoxin (mg/g)
Original strain	0.7	0.45	1.23	0	0
<i>Monascus</i> Strain 1	1.5	0.81	3.2	0	0

The strain of the present disclosure has a monacolin content of approximately 2.14 times that of the original strain, and it contains no citrinin or aflatoxin.

In the following, *Monascus* Strain 1 was used for fermentation, to investigate the treatment method of rice used in the solid medium, the formula of the solid medium, and the cultivation process.

Example 2

The rice used in the solid medium was prepared as follows:

Hot soaked rice: Rice was mixed with high-temperature water (80°C) and soaked for 4 h, 12 h, and 18 h respectively, with the temperature maintained above 70°C, wherein the mass ratio of water to rice was 120:100.

Boiled rice: Rice was mixed with 100°C hot water and heated continuously at 90-100°C for 2 min, wherein the mass ratio of water to rice was 120:100.

Low-temperature soaking: Rice was soaked with water at 20-25°C for 14 h, wherein the mass ratio of water to rice was 120:100.

Fermentation was performed under the fermentation conditions described in Example 1 to compare the contents of extractives and monacolin K in the fermented red yeast rice. Details are shown in Table 4.

Table 4

	Boiled rice	Hot soaked rice 80°C			Low temperature soaking
Treatment method	2min	soaked for 4 h	soaked for 12 h	soaked for 18 h	14h
Alcohol extractives (%)	10.8	2.9	2.8	3.0	2.4
Monacolin K content (mg/g)	2.7	1.5	1.7	1.87	0.81

It can be seen that hot soaked rice and boiled rice yield favorable effects and can significantly increase the monacolin K content. In particular, under identical fermentation conditions, the monacolin K content in red yeast rice obtained using the solid medium with boiled rice is 3.33 times that of the group with rice soaked at low temperature, and the extractive content is increased by 4.5 times. However, it is found in the experiment that rice becomes rather viscous during boiling, and agglomerates during fermentation, leading to uneven fermentation. Therefore, boiling water soaking or steaming is mainly considered as the rice treatment method.

Example 3

Hot soaked rice soaked for 18 h as described above in Example 2 was used as the rice in the solid medium to investigate the effect of ethanol in the solid medium and the process of water supplementation during the 5-day primary cultivation stage. Table 5 shows the contents of peptone and ethanol, as well as the content of water replenishment (water replenishment% represents the mass content of water replenished relative to the dry matter of the solid medium).

Fermentation was carried out under the fermentation conditions of Example 1 to compare the contents of extractives and monacolin in the fermented red yeast rice. Details are shown in Table 5.

Table 5

	Formula composition					
Amount of peptone (parts)	2	2	2	2	2	2
Ethanol content (%)	0.7	0.7	0.7	0.7	0.3 5	0

Water replenishment (%)	10	8	5	None	No ne	None
Monacolin K content (mg/g)	4.4	5.1	3.9	3.5	3.2	1.87
Acid form of monacolin K (mg/g)	2.1	2.0	1.9	1.5	1.7	1.4
Extractive content (%)	7.8	8.3	7.1	4.5	3.9	3.0

The results show that the use of ethanol or water supplementation during the primary cultivation stage can increase the contents of monacolin K, acid form of monacolin K and extractives.

Example 4

The solid medium contained 0.7% ethanol (mass content relative to the dry matter). Experiments were carried out using soaked rice and steamed rice without water replenishment.

Herein, the soaking conditions for soaked rice were as follows: temperature 90°C, water addition 1.2 times of the rice mass, duration 18 h.

Steaming conditions for steamed rice were as follows:

Condition 1: temperature 110°C, water addition 45% of the rice mass, duration 40 min;

Condition 2: temperature 90°C, water addition 45% of the rice mass, duration 50 min;

Condition 3: temperature 120°C, water addition 45% of the rice mass, duration 25 min;

Condition 4: temperature 110°C, water addition 30% of the rice mass, duration 40 min;

Condition 5: temperature 110°C, water addition 70% of the rice mass, duration 40 min.

In addition, the original strain and Condition 1 were used for rice steaming.

Fermentation was performed under the fermentation conditions described in Example 1 to compare the contents of extractives and monacolin in the fermented red yeast rice. Details are shown in Table 6.

Table 6

Test groups	MK (mg/g)	MKA (mg/g)	MK+MKA (mg/g)	Total monacolins (mg/g)	Extractives (%)
Soaking	3.80	1.77	5.57	6.75	8.4
Condition 1	5.07	2.18	7.25	9.13	9.2
Condition 2	4.57	2.35	6.92	8.68	8.9
Condition 3	4.44	2.43	6.87	8.51	8.7
Condition 4	4.06	2.5	6.56	7.89	7.9
Condition 5	4.16	2.59	6.75	8.19	8.2

The results show that the rice steaming method is more stable than the soaking process, with a higher monacolin content.

In addition, determine the content of monacolin in red yeast rice fermented under Condition 4, Condition 5, and the original strain are recorded in Table 7 below.

Table 7

Corresponding condition s	MJ A (mg /g)	MJ (mg /g)	ML A (mg /g)	MK A (mg /g)	ML (mg /g)	MM A (mg /g)	MK (mg /g)	DM K (mg /g)	MK+ MKA (mg/g)	Total monac olins (mg/g)
4	0.16	0.11	0.29	2.5	0.3	0.27	4.06	0.2	6.56	7.89
5	0.18	0.13	0.29	2.59	0.32	0.31	4.16	0.21	6.75	8.19
Original strain	0.03	0.05	0.09	1.02	0.21	0.08	2.76	0.16	3.78	4.41

Example 5

The rice in the solid medium was treated according to Condition 1 of Example 4. On the basis of fermentation under the conditions described in Example 1, a process of 8% water replenishment during the primary cultivation stage was adopted, and the cultivation days were investigated. Starting from day 15, the appearance, content, extractives, citrinin, aflatoxin B1 and other indicators all met the strictest processing specifications of various provinces. The contents of extractives and monacolin in the fermented red yeast rice were compared. The results are recorded in Table 8.

Table 8

	MK (mg/g)	MKA (mg/g)	MK+MK A (mg/g)	Total monacolins (mg/g)
Day 15	3.07	2.18	5.25	6.63
Day 20	4.29	2.39	6.68	8.22
Day 26	7.25	3.31	9.56	12.57
Extractives %	7.9% (day 15)			
Citrinin (µg/kg, Limit of detection: 5ppb): 0				
Aflatoxin (B1, B2, G1, G2) (µg/kg): 0				

It can be seen that *Monascus* Strain 1 of the present application can significantly shorten the fermentation period to 15 days, with relatively high contents of monacolin and other components already being achieved. With regard to red yeast rice used for different purposes, the fermentation days can be even shorter.

In addition, the fingerprints of the red yeast rice decoction pieces obtained on day 15 and day 26 are recorded in Figure 4, which are determined using the red yeast rice fingerprint determination method specified in the *Chinese Pharmacopoeia* (2020 Edition). The studies find that the red yeast rice of the present invention contains abundant components, including not only monacolins but also flavonoid compounds, sterols, amides, pigments, and other constituents.

Furthermore, Figures 5 and 6 show the liquid chromatograms of aflatoxin and citrinin in the red yeast rice decoction pieces obtained on day 26. The test solution is prepared from the red yeast rice decoction pieces to be tested. No peaks appear at the retention times corresponding to aflatoxin and citrinin, the respective contents were considered to be zero.

Example 6

The rice in the solid medium was treated according to Condition 1 of Example 4. On the basis of fermentation under the conditions described in Example 1, a process of 8% water replenishment during the primary cultivation stage was adopted (adding sterilized water into the culture vessel and stirring), with a cultivation time of 30 days. The

addition amounts of peptone, green pea powder or mung bean powder in the solid medium were adjusted (see Table 9 for details).

The contents of extractives and monacolin in the fermented red yeast rice decoction pieces were compared. Details are shown in Table 9.

Table 9

Group No.	1	2	3	4	5	6
	Peptone 8 parts	Green pea powder 2 parts, peptone 8 parts	Green pea powder 5 parts, peptone 5 parts	Green pea powder 8 parts, peptone 2 parts	Green pea powder 8 parts	Mung bean powder 5 parts, peptone 5 parts
MKA mg/g	2.86	4.23	4.23	3.50	2.20	4.16
MK mg/g	3.31	2.33	12.08	8.43	9.12	13.1
MK+MKA(mg/g)	6.17	6.56	16.31	11.93	11.32	17.26
Total monacolins (mg/g)	7.17	7.77	19.9	15.17	14.93	21.35
Extractives %	7.9	8.5	24.5	7.8	17.4	23.6

The results show that in the case of using 5 parts of green pea powder and 5 parts of peptone in the solid medium formula, the content of monacolin K is 3.19 times that of using peptone alone, and the content of acid form of monacolin K is 1.53 times that of using peptone alone. In addition, black beans, red beans and soybeans can also be used in combination or as separate replacements.

In addition, the contents of nine kinds of monacolin compounds in the red yeast rice decoction pieces obtained from Group 3 and Group 6 in Table 9 are determined and recorded in Table 10.

Table 10

	MJA (mg/ g)	MJ (mg/ g)	ML A (mg/ g)	MK A (mg/ g)	ML (mg/ g)	MM A (mg/ g)	MK (mg/ g)	DM K (mg/ g)	MK+M KA (mg/g)	Total monacol ins (mg/g)
3	0.27	0.41	0.41	4.23	1.12	0.72	12.08	0.65	16.31	19.90
6	0.28	0.43	0.46	4.16	1.33	0.81	13.10	0.78	17.26	21.35

It should be noted that the present application is not limited to

the embodiments described above. The above embodiments are merely illustrative, and any embodiment that has a constitution substantially identical to the technical idea and exerts the same functions and effects within the scope of the technical solution of the present application shall be included in the technical scope of the present application. Furthermore, various modifications conceivable to those skilled in the art may be made to the embodiments without departing from the spirit of the present application, and other modes constructed by combining some components in the embodiments are also included within the scope of the present application.

Claims

1. A *Monascus* strain, the Latin name of which is *Monascus purpureus*, with a deposit number of CGMCC No. 40777.

2. Red yeast rice, which is obtained by fermentation using the *Monascus* strain as claimed in claim 1.

3. The red yeast rice as claimed in claim 2, wherein, based on the dry matter of red yeast rice, a content of monacolin compounds in the red yeast rice is 4 mg/g to 40 mg/g, preferably 6 mg/g to 30 mg/g, more preferably 7.0 mg/g to 22 mg/g;

the monacolin compounds preferably include Monacolin K and acid form of Monacolin K; based on the dry matter of red yeast rice, a content of Monacolin K in the red yeast rice is preferably 3.07 mg/g to 13.5 mg/g, more preferably 7.25 mg/g to 13.5 mg/g, further preferably 8.5 mg/g to 13.5 mg/g; based on the dry matter of red yeast rice, a content of acid form of Monacolin K in the red yeast rice is preferably 2.0 mg/g to 5.0 mg/g, more preferably 2.3 mg/g to 4.25 mg/g, further preferably 3.5 mg/g to 4.23 mg/g;

the monacolin compounds more preferably further include Monacolin L, acid form of Monacolin M, and dehydromonacolin K; based on the dry matter of red yeast rice, a content of Monacolin L in the red yeast rice is preferably 0.3 mg/g to 1.33 mg/g, preferably 1.12 mg/g to 1.33 mg/g; a content of acid form of Monacolin M in the red yeast rice is preferably 0.27 mg/g to 0.81 mg/g, preferably 0.72 mg/g to 0.81 mg/g; a content of dehydromonacolin K in the red yeast rice is preferably 0.2 mg/g to 0.78 mg/g, preferably 0.65 mg/g to 0.78 mg/g;

the monacolin compounds still more preferably further include acid form of Monacolin L, Monacolin J, and acid form of Monacolin J; based on the dry matter of red yeast rice, a content of acid form of Monacolin L in the red yeast rice is preferably 0.29 mg/g to 0.46 mg/g, preferably 0.41 mg/g to 0.46 mg/g; a content of Monacolin J in the red yeast rice is preferably 0.11 mg/g to 0.43 mg/g, preferably 0.41 mg/g to 0.43 mg/g; a content of acid form of Monacolin J in the red yeast rice is preferably 0.16 mg/g to 0.28 mg/g, preferably 0.27 mg/g to 0.28 mg/g.

4. The red yeast rice as claimed in claim 2 or 3, wherein, based

on the dry matter of red yeast rice, a content of extractives in the red yeast rice is preferably greater than 7%, preferably 7.5% to 30%; preferably 8% to 30%; preferably 10% to 29%; preferably 15% to 25%; preferably 17.4% to 23.6%.

5. A red yeast rice decoction piece, which is prepared from the red yeast rice as claimed in any one of claims 2 to 4.

6. A preparation method of red yeast rice, comprising performing fermentation using the *Monascus* strain as claimed in claim 1 as a strain to prepare red yeast rice.

7. The preparation method as claimed in claim 6, wherein, the preparation method comprises:

performing expanded cultivation of the *Monascus* strain using a liquid medium to obtain a liquid strain;

inoculating the liquid strain into a solid medium for fermentation to obtain a fermentation product containing red yeast rice.

8. The preparation method as claimed in claim 7, wherein, the liquid medium comprises glucose, peptone, a phosphorus source, and trace elements;

preferably, a content of glucose in the liquid medium is 30 g/L to 150 g/L; preferably, a content of peptone in the liquid medium is 2 g/L to 30 g/L; preferably, a content of the phosphorus source in the liquid medium is 0.5 g/L to 7 g/L, and preferably, the phosphorus source includes $\text{NH}_4\text{H}_2\text{PO}_4$ and $(\text{NH}_4)_2\text{HPO}_4$;

preferably, the trace elements include magnesium element and calcium element; more preferably, magnesium element is provided by $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, and a content of $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ in the liquid medium is 0.01 g/L to 1.2 g/L; further preferably, calcium element is provided by CaCl_2 , and a content of CaCl_2 in the liquid medium is 0.01 g/L to 0.8 g/L;

preferably, the liquid of the liquid medium comprises an aqueous starch solution.

9. The preparation method as claimed in claim 7 or 8, wherein, the solid medium comprises rice, bran, peptone, glucose, and water;

preferably, in parts by weight, the solid medium comprises 100 parts of rice, 6 to 9 parts of bran, 2 to 8 parts of peptone, and 1.4 to 3.0 parts of glucose; preferably, the solid medium further comprises ethanol, and more preferably, a mass content of ethanol relative to the dry matter of the solid medium is 0.2% to 1%, further preferably 0.35% to 0.7%;

preferably, the solid medium further comprises bean powder, more preferably 2 to 8 parts by weight of bean powder, and further preferably, the bean powder is selected from one or more of the group consist of green pea powder, mung bean powder, black bean powder, red bean powder, and soybean powder;

preferably the rice is subjected to steaming, boiling, or hot soaking, more preferably steaming or hot soaking;

preferably a steaming temperature is 90°C to 120°C, and the steaming time is 25 min to 50 min, preferably 35 min to 45 min;

preferably a mass ratio of water added to rice during steaming is 30% to 70%, more preferably 40% to 55%;

preferably during the hot soaking, a hot soaking temperature is 90°C to 100°C, and a hot soaking time is 6 h to 18 h, more preferably 10 h to 14 h.

10. The preparation method as claimed in any one of claims 7 to 9, wherein, the process of inoculating the liquid strain into the solid medium for fermentation includes:

sterilizing the solid medium and then inoculating the liquid strain into the solid medium, preferably a sterilization temperature is 120°C to 125°C and a time is 30 min to 90 min;

performing primary cultivation of the inoculated solid medium at 30°C to 36°C with a relative humidity of 40% to 80% for 48 h to 120 h to obtain a primary culture;

performing secondary cultivation of the primary culture at 18°C to 25°C with a relative humidity of 40% to 80% for 7 days to 30 days, preferably 7 days to 20 days, to obtain a fermented system.

11. The preparation method as claimed in claim 10, wherein, when the primary cultivation lasts for 48 h to 120 h, water is added to

the solid medium and stirred, wherein a mass content of water added is 5% to 15%, preferably 6% to 10%, relative to the dry matter of the solid medium.

12. A red yeast rice extract, which is prepared by extracting the red yeast rice as claimed in any one of claims 2 to 4 with water or ethanol.

13. A drug comprising red yeast rice or a red yeast rice extract, wherein the red yeast rice comprises the red yeast rice as claimed in any one of claims 2 to 4 or the red yeast rice decoction piece as claimed in claim 5, the red yeast rice extract comprises the red yeast rice extract as claimed in claim 12, and the drug is selected from lipid-lowering drugs, antihypertensive drugs, hypoglycemic drugs, and/or anticancer drugs.