

Red Fermented Rice (Hongqu) – On the Topicality of a Traditional Chinese Medicinal Product

Abstract

Red fermented rice (*hongqu* 紅麴, 紅麴, simplified characters 红曲) is cooked white rice that has been cultivated with the mould *Monascus purpureus*, thereby acquiring a red colour. It is obtained through an ingenious and complicated fermentation process and in China it has been used for centuries as a flavouring and colouring agent for foods. The first part of this article sheds light on the historical background and the methods of production as described in two Chinese encyclopaedias (from the 13th and 17th centuries respectively), and discusses the effects of red fermented rice as they are presented in dietetic and pharmacological works. The second part of the article presents red fermented rice as a traditional Chinese medicinal that can be classified under 'substances that relieve food stagnation' (*xiaoshiyao* 消食藥), which regulate digestion and the metabolic processes and invigorate blood. On these grounds, red fermented rice can be considered for application in differential diagnostic treatments with the modern biomedical diagnosis of hyperlipidemia. In addition to pharmacological research on both red fermented rice and synthetic statins - which are comparable in their clinical effect on increased cholesterol levels - the side effects and safety of red fermented rice are discussed, as well as its dosage. The article concludes with an illustrative case study.

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Red fermented rice (*hongqu* 紅麴, 紅麴, simplified characters 红曲) is cooked white rice that has been cultivated with the mould *Monascus purpureus* thereby acquiring a red colour. In the West, it is also misleadingly known as 'red rice', 'red yeast', 'red mould rice' or 'red yeast rice'. Red fermented rice has been used in China from relatively early times as a flavouring and colouring agent for foods, as well as a food preservative and for making so-called 'red wine' (*hongjiu* 紅酒).

The umbrella term *qu* (麴, 麴, simplified character 曲, *koji* in Japanese) refers to a substance that has its origin in a mould that grows on cooked grains or soy beans, and has been used since very early times for highly complex fermentations (Kupfer, 2010, p.17; Huang, 2010, p.42). The radical *mai* 麥 (麦) 'wheat', contained in the traditional forms of the Chinese character *qu* (麴, 麴), indicates that this is a fermentation in which the substrate or nutrient is the grain.

The prominent role played by *qu* in the processing of foodstuffs in China is unique among the food cultures of the world (Huang, 2000, pp.8, 167) (see Illustration 1). Since the Han period (206 BCE – 220 CE), *qu* ferments have been used for making wine. In this process, water is added to the cooked grain, which is then incubated with a *qu*-fermented microbial culture containing fungal enzymes, spores, mycelia and yeast cells. According to H.T. Huang, there is no precise equivalent in western languages for the term *qu*. Until now it has been inadequately translated as yeast, leavening, or starter culture. None of these translations,

however, is truly accurate as *qu* contains both enzymes and living microorganisms (Huang, 2000, p.154). Therefore we find it more accurate to translate the Chinese term *hongqu* as 'red fermented rice'.



Illustration 1: Production and description of the effects of the *qu* ferment (麴, 麴, 曲) in *Dietetic Pharmacology, Shiwu bencao* 食物本草 from the Ming Dynasty

The historical background of red fermented rice

Even though there are a few references to foods cooked with red fermented rice or wine made with red fermented rice in poems from the late Han and Tang dynasties (618 – 907 CE), they are all rather vague. It is only in the year 960 that we find a recipe - for stewed lamb - with red fermented rice. This is in the collection of anecdotes *Records of Pure Marvels* (*Qingyi lu* 清異錄) by Tao Gu 陶穀 (903–970). When ‘the meat is stewed with red fermented rice, it should be weighed down with stones so that it is completely covered with the wine [mash]’ (*Qingyi lu* 清異錄, pp.31–32, translation by Ute Engelhardt; the same applies to all quotes from Chinese within this article, unless otherwise specified). H.T. Huang comments on this text excerpt to the effect that not only is red fermented rice used as an agent for wine production, but that the red mash left over from the winemaking process is also used in cooking (Huang, 2000, p.193).

The famous poet, statesman and philosopher Su Dongpo 蘇東坡 (also known as Su Shi 蘇軾, 1037–1101) mentions red fermented rice in two poems. In one he reports how, when he was sojourning in southern China, he sent an old friend some red fermented rice from the region. In another poem, while gazing at the moon and remembering an old friend, he writes, ‘Last year we shared a plate of alfalfa, tonight I pour myself a glass of wine from Min 閩 that is as red as cinnabar.’ (Huang, 2000, p.193). Min is a synonym for the Fujian (Fukien) province, which shows that red fermented rice and red wine were then specialties from southern China, as it is still the case today.

In the Yuan Dynasty (1271–1368), red fermented rice and red wine enjoyed wider distribution and were therefore mentioned more often in literature on food culture (Huang, 2000, pp.191, 194). Since that time, detailed instructions exist on its production process, which is elaborate and requires great patience.

Its intrinsic significance is that of obtaining wonderful forces from something stinking and rotting.

Production of red fermented rice

In the household encyclopaedia *Useful Hints for the Family* (*Jujia biyong* 居家必用, dated mid-thirteenth century), the production of red fermented rice is described as follows:

In order to make red fermented rice, you must take 15 *dou* 斗¹ of white (round grain) rice (*gengmi* 粳米), wash

it thoroughly and leave to soak overnight. The next day, steam the rice until it is 80 per cent cooked and then divide it into 15 portions. To each of these portions add two *jin* 斤² of the above-mentioned [mother] ferment. Mix each portion with your hands until the ferment is completely incorporated, then combine all 15 portions together – in winter cover the pile with a piece of cloth. Lay a thick mat on top of the pile and cover the ground with straw. It is important to take care that the pile does not get too hot or too cold. If it gets too hot, it will spoil. If it feels too warm, remove the covering and divide the large pile into smaller ones. If the pile is only mildly warm, heap everything together again and cover it as before. Once the necessary heat has been reached, the pile should no longer be moved. Do not sleep during this night but only pay attention [to the pile].

At noon of the next day, make three piles, one hour later five piles, after a further one to two hours later make one more pile and continue until 15 piles have been made within a further one to two hours. If, after dividing up the large pile, you sense that it is not warm enough, make one large pile again. If the heat appears to be sufficient after one to two hours, then divide the large pile into several piles again. Repeat this process several times.

On the third day, the thriving ferments are distributed among five-six bamboo baskets and rinsed with plenty of fresh spring water. Then everything is put back in a large pile. If it gets too hot, then it is separated as before until you have numerous portions. After one to three hours, you can make one pile again and this can be repeated as often as necessary.

On the fourth day, divide the fermented rice into five-seven portions, put them in bamboo baskets and rinse once again with fresh spring water. If not all the fermented rice swims to the top, but half sinks to the bottom and only half to the top, then one should repeat the [same] process as before and continue making piles throughout a whole day.

On the fifth day, everything is rinsed again with fresh water until all the fermented rice rises to the surface. At noon, the rice grains are dried in the sun and then used for winemaking. (*Jujia biyong shilei quanji* 居家必用事类全集, Beijing 1986, pp.38–39; see also Huang, 2000, p.195)

In the production process described here, the main emphasis is on the correct temperature that promotes fermentation. The fermented rice grains are its result. This process required patience and a great deal of experience as at that time it was not possible to measure temperature with precision.

¹ One *dou* 斗 corresponds to 10 litres.

² One *jin* 斤 corresponds to 500 grams.

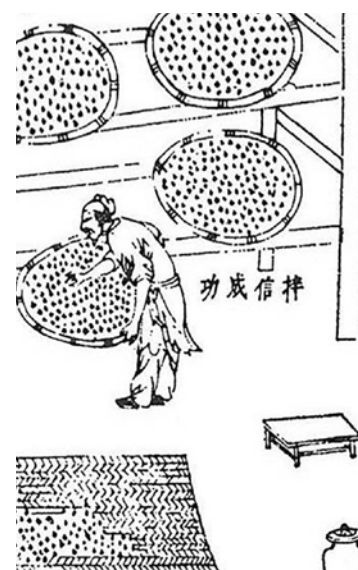
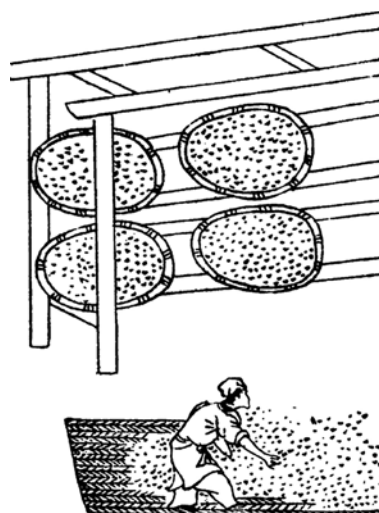
We can recognise a marked development in this method in *Exploitation into the Works of Nature* (*Tiangong kaiwu* 天工開物), written in 1637 by Song Yingxing 宋應星. The description is introduced as follows:

The method of producing red fermented rice (*danqu* 丹麴) is a recent innovation. Its intrinsic significance is that of obtaining wonderful forces from something stinking and rotting. Its practical significance can be seen in that the *qi* [of the grain] is refined and transformed. Fish and meat are generally seen as particularly perishable but when this ferment is spread thinly upon them, they can keep their original characteristics even in the hottest summer. Flies will not approach them for ten days, and colour and smell will remain as fresh as on the first day. This is truly an extraordinary medicine!’ (*Tiangong kaiwu* 天工開物, chapter 17, Song, 1966, pp.292–3)

Here is a brief overview of the procedure:

1. Instead of round grain rice, long grain rice (*xianmi* 粳米) is used that has been soaked in water for seven days. When the smell becomes unbearable, the rice is washed at the river with clear mountain water (Illustration 2).
2. The rice, which still smells unpleasant, is now steamed and a pleasant aroma develops. As soon as the rice is half-done, the steaming process is interrupted and the rice plunged once again into cool water. Once it has cooled, it is steamed again until it is completely done.
3. The rice is then shaped into piles and while it is still hot two *jin* of the mother ferment are added to one *dan* 石³ of rice. Through many hands taking part in the mixing of the rice, the rice now cools. Now the pile must be carefully watched at all times. When the fermentation begins, the pile will become somewhat warmer.
4. The mixture of rice and ferment is now distributed among large baskets and rinsed once with alum water (*fanshui* 礬水). Subsequently it is spread on large bamboo trays, which are stored on shelves in a room in order to be aired thoroughly (Illustrations 3 and 4).

‘From now on, it is the power of the wind (i.e. the air) that is important while water and fire are of little significance.’ (*Tiangong kaiwu* 天工開物, chapter 17, Song 1966, pp.292–3)



Illustrations 2-4: Depictions from *Exploitations of the Works of Nature*, *Tiangong kaiwu* 天工開物 by Song Yingxing, written in 1637. From top to bottom: Washing the in the river, mixing in the mother ferment, and spreading the rice out on bamboo trays.

³ One *dan* 石 corresponds to 100 litres.

5. Each of the bamboo trays holds roughly five sheng 升⁴ of steamed rice. The room should be large and have a high ceiling in order to hold off the heat of the tiled roof; it should also face south in order to avoid the evening sun from the west. Every hour the rice is to be turned three times. The workers entrusted with the fermentation must maintain guard over the shelves for seven days. They must not fall into deep sleep and must get up several times in the night.
6. To begin with, the rice is snow-white, but after one or two days it turns into a deep black. Then it becomes brown, then ochre-coloured and finally red. When the red colour has reached its apex, it changes to yellow. Thanks to correct ventilation, the rice will undergo all these visible stages. The product made in this way is twice as effective and valuable as normal ferments. Between the black and brown phases as well as between the brown and red phases, the rice is washed with water. Once it has turned red, it is no longer rinsed.
7. In this production process, it is necessary that the workers' hands as well as the trays and mats that are used are kept very clean. Even the slightest impurity can spoil the rice.

An essential difference between this and earlier methods is that here the rice is no longer shaped into piles but spread out on trays and kept well ventilated, which allows for better temperature regulation. In addition to temperature, particular attention is paid to the smell and the colour of the substance. The measurement of quantities and hygiene regulations are also more precise.

Red fermented rice in materiae medicae and dietetic works

At approximately the same time as the first procedure described above was written, red fermented rice was also mentioned for the first time in a text on dietetics, namely *Important Principles of Food and Drink* (*Yinshan zhengyao* 飲膳正要), written in 1330 by Hu Sihui 忽思慧. In this work, written mainly for the health and benefit of the Mongol emperor, red fermented rice is itemised in chapter one in a list of seasonings and flavourings (*liao wu* 料物) (*Yinshan zhengyao*, chapter 1, p.9; Buell, 2000, p.259). In chapter three, red fermented rice is once again listed under the seasonings, this time with a brief description of its properties:

Red fermented rice, sweet flavour (*wei* 味), neutral, not poisonous. Strengthens the Spleen (*pi* 脾), increases qi and warms the centre. It is to be applied to the inside surfaces of meat and fish. (*Yinshan zhengyao*, chapter 3, p.176; Buell, 2000, p.595)

The most comprehensive description of red fermented rice comes from Li Shizhen 李時珍 (1518–1593) in chapter 25 of his elaborate work *Systematic Materia Medica* (*Bencao gangmu* 本草綱目, published in 1596), in which he also lists other *qu* ferments. He adds his own brief introduction to the description of the effects of red fermented rice:

Red fermented rice has not been mentioned previously in materia medica works; the production process has only been discovered recently and constitutes an extraordinary skill. (*Bencao gangmu*, chapter 25, p.1547)

This is followed by a description of the production process that is very close to the instructions mentioned above, translated from the *Useful Hints for the Family*. Li Shizhen closes this commentary with the words, 'If it [the red colour] has not penetrated to the centre of the grain, then it [the red fermented rice] is not regarded as truly good. It would be advisable to store it [the red fermented rice] for a long time if one desires to use it as medicine.' This in turn is followed by a description of the effects:

Red fermented rice, sweet, warm, not poisonous. Relieves food stagnation, invigorates the blood, strengthens the Spleen, dries the Stomach (*wei* 胃). In the treatment of red and white dysentery, it keeps the food moving down [properly]. If wine is made from it, then its medicinal effect lies in that it breaks blood and promotes the action of medicinals; it lifts the 'miasma qi of the mountains' (*shanggang zhangqi* 山崗瘴氣) and is also suitable for treating wounds. For the treatment of female pain due to qi [stagnation] and blood [stasis] as well as persisting lochia (*exue bujin* 惡血不盡), the recommendation is to grind the red fermented rice, mix it with wine and drink it.

This is followed by another comment by Li Shizhen himself:

When the food arrives in the Stomach, it is broken down and steamed by means of the moisture and heat of the middle burner (*zhongjiao* 中焦). Then it flows as essential qi (*jingqi* 精氣) through the body and turns into a red colour. It is distributed among the bowels and viscera (*zangfu* 臟腑) and channels (*jingluo* 經絡), creating construction qi (*yingqi* 營氣) and blood. What a wonderful natural transformation!

During the production of red fermented rice, the white rice is transformed by the effects of moisture and heat, as well as by being steamed, and becomes red, which is actually its true colour and which remains for a long time. This is thanks to human skill. This is why red fermented rice is capable of regulating the Spleen and Stomach, as well as the construction qi and

⁴ One sheng 升 corresponds to one litre.

the blood, which is in harmony with the principle that similar qi support each other. (*Bencao gangmu*, chapter 25, pp.1547–8)

In contrast to the effects of red fermented rice as described in the *Important Principles of Food and Drink*, Li Shizhen ascribes more importance to its blood-invigorating properties and, in order to increase this effect, recommends taking it together with wine. Of interest is also the comment in which he draws an analogy between the digestion of food in the human body and the production of red fermented rice.

Several later *materiae medicae* also mention that red fermented rice is contraindicated in the case of Spleen yin deficiency (*piyin xu* 脾陰虛) (*Zhongyao da cidian* 1997, p.991). Today, the properties of red fermented rice are usually described as follows:

Red fermented rice, sweet, warm, [enters the] Liver, Spleen and Large Intestine (*gan pi dachang* 肝脾大腸). Actions and indications: invigorates the blood; transforms stasis; strengthens the Spleen; disperses food stagnation. For post-partum lochia; stasis with abdominal pain; food accumulation with feelings of distension and fullness; vaginal discharge (leucorrhoea), red and white diarrhoea (赤白下痢); wounds and sprains of the limbs (*Zhongyao da cidian*, 1997, p.991).

Red fermented rice as medicine

Li Shizhen's remark quoted above - 'Red fermented rice has not been mentioned previously in *materiae medicae*' - astonishingly applies to our times, too. In the established Western pharmacopoeias of Chinese medicine, there is no monograph on red fermented rice (Porkert, 1978; Bensky, 2004; Hempen, 2007, 2009). However, for some years now, there has been a flourishing market for products made of red fermented rice that are marketed under misleading names such as 'red rice flour', 'red rice' and 'red yeast rice'. These products have increasingly become the object of official regulations, while their health benefits and side-effects are controversial.

We would like to emphasise that red fermented rice is made from cooked white rice that has been cultivated with the mould *Monascus purpureus* as described above in detail, thereby acquiring a red colour. This is not to be confused with red rice or red-husked types of rice. The descriptions in the *materia medicae* and dietetic works indicate that red fermented rice has, in particular, a digestive effect. Through its flavour and its temperature characteristic (*xing* 性) it has an explicit affinity to the organs of the 'centre', whereby its effect is not supplementing (*bu* 補) but mainly digestive, dispersing food stagnation and even blood-invigorating. Therefore, it can be appropriately classified in the category of herbs that disperse food stagnation (Chen, 2004). Within this category, its ability to

invigorate blood is reminiscent of hawthorn berry, *Shanzha* (*Crataegi fructus*). In particular, in the preparation with wine as explained by Li Shizhen, the blood-stimulating properties of red fermented rice come into play affecting the construction qi and the Heart (*xin* 心). Complaints of the upper abdomen as well as thoracic unease and pain can be mentioned here as clinical indications, as in the case of *Shanzha* (*Crataegi fructus*). Red fermented rice now comes closer to blood-invigorating medicinals (*huoxueyao* 活血藥) and can be deployed in disorders caused by blood-stasis in orthopaedics (injuries) and gynaecology (pain, post-partum problems). Therefore, from a clinical standpoint, *Shanzha* can be combined advantageously with red fermented rice. Comparing the two remedies, red fermented rice (at least in the form prepared with wine) has a strong invigorating effect on the blood and is better at transforming stagnation in the middle burner. This explains its contraindication, mentioned frequently in the *materia medicae*, in the case of Spleen yin deficiency, because this requires a remedy that does not disperse but, on the contrary has a cooling and moistening effect (Wang, 2013).

Pharmacological research and importance

At the beginning of the 1970s, the Japanese biochemist Akira Endō (1933-) systematically tested extracts from various fungi and, in 1976, identified the cholesterol-lowering effect of compactin, which he had isolated from *Penicillium citrinum*. This was followed in 1979 by the isolation of monacolin K from *Monascus ruber* or *purpureus*. Since 1987, monacolin K bears the non-proprietary name lovastatin; under the brand name Mevacor it appeared on the US market in the same year as the first available statin drug. Its therapeutic dose is 10 to 80 milligrams daily and is available only on prescription. Together with a number of other monacolins, monacolin K occurs naturally in red fermented rice. Monacolins block endogenous production of cholesterol in the liver. The lipid-lowering characteristics depend, as is the case with all statins, on the dose-dependent inhibition of the HMG-CoA reductase. Statins are among the most important – and profitable – medications for treating hypercholesterolaemia and coronary heart disease (CHD).

The pharmacological effect of the monacolin K contained in red fermented rice led to discussions as to whether or not it should be regarded as a medication.

Subsequent to these discoveries and developments, red fermented rice became increasingly fashionable in the 1990s as a dietary supplement thought to lower cholesterol levels and protect against CHD. The pharmacological

effect of the monacolin K contained in red fermented rice led to discussions as to whether or not it should be regarded as a medication. Products made of red fermented rice repeatedly became the subject of warnings and restrictions by health authorities in the USA and Europe.

As is the case with all statins, monacolin K (alias lovastatin) has a large number of possible adverse side-effects.

This problem still exists. The European Food Safety Authority (EFSA) approved a health claim for red fermented rice as a dietary supplement. The following declaration is therefore permitted in the EU: 'Monacolin K made from red mould rice contributes to the maintenance of normal cholesterol levels in the blood.' The condition for its use is as follows, 'This declaration may only be applied to foods which guarantee a daily intake of 10 mg monacolin K' (*Official Journal of the European Union*, May 25, 2012). On the other hand, the German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM) warned in February 2016 against dietary supplements made from red fermented rice, as '... products supplying a daily dose of 5 milligrams of monacolin K are to be classified as medication' (BfArM press release 3/16, February 24, 2016).

The decision to classify a product as dietary supplement or medication is made independently of whether a 'health claim' has been approved or not. The classification is significant against the background of medication and foodstuffs being subject to different laws and regulations. In some countries, the health authorities have classified red fermented rice products as drugs, thereby prohibiting trading. This is the case in Switzerland, for instance, where 'red mould rice products' are therefore not marketable (Swissmedic, 2014). In the US, the FDA (Food and Drug Administration) determined in 1998 that a red yeast rice product that contains monacolin K was an unapproved new drug, rather than a dietary supplement. Since then, the FDA has taken action several times against companies selling red yeast rice products that contain more than trace amounts of monacolin K.

In addition to the hypolipidemic properties of red fermented rice, safety issues also play a large role in official regulations. This is because, as is the case with all statins, monacolin K (alias lovastatin) has a large number of possible adverse side-effects. On this long list, which ranges from autoimmune phenomena to liver damage and a higher risk of developing diabetes mellitus, clinically the greatest role is played by damage to the striated muscles, which is not uncommon. The pain associated with it results in patients discontinuing treatment. In rare cases the damage can lead to rhabdomyolysis, with fatal

consequences (it is this danger that led to the recall of the statin preparation cerivastatin in 2001). A change of medication might be the answer, however this side effect is a characteristic of all statins.

It is important to be aware of the side effects of statins when using red fermented rice as they could theoretically also occur with this natural product, which should therefore be used with careful consideration. However, we are here dealing with a similar comparison as 'oranges versus vitamin C'. Red fermented rice has a different composition and therefore a different effect than isolated or synthesised monacolin K. In addition to further compounds from the secondary metabolism of *Monascus purpureus* (e.g. monascin, phytosterols and isoflavones), fourteen different monacolins alone have been found in red fermented rice (Li, 2004). This research also showed that only two out of the ten manufactured products that were analysed had a chromatographic profile similar to that of natural red fermented rice, the others being significantly different.

Monacolins in red fermented rice derive from a natural process of fermentation, and in China have been subject to a very long period of clinical application and observation. There are reasons to hope that red fermented rice administered for the biomedical goal of lowering cholesterol to protect against CHD would have only minor undesirable side-effects.

Clinical effectiveness

A meta-analysis of clinical studies on the cholesterol-lowering effect of red fermented rice was published in 2006 (Liu, 2006). Ninety-three controlled and randomised clinical studies were included, of which 91 were published in China. Even though the methodological quality of most of these studies was classified as low, this analysis, which involved three different manufactured products made of red fermented rice, showed a significant lowering of overall cholesterol (35 milligrams per decilitre) as well as of LDL cholesterol (28 milligrams per decilitre) and triglycerides (35 milligrams per decilitre) – with a slight increase of 'good' HDL cholesterol of 6 milligrams per decilitre. These effects are comparable to those of standard synthetic statin preparations.

A series of articles, which appeared following this meta-analysis, reported on a very large-scale Chinese study, the China Coronary Secondary Prevention Study (CCSPS). Following a heart attack, for a period of 4.5 years on average, almost 5,000 patients were given either a placebo or a manufactured product of red fermented rice known as *Xuezhikang* (血脂康). *Xuezhikang* is an ethanol extract of red fermented rice obtained through a patented procedure with an overall monacolin content of roughly 0.8 per cent. The results were impressive, showing a significant lowering of the risk of further heart attacks and general mortality that was greater than the effects obtained with

conventional statins (Lu 2008).

Another interesting prospective study from the Mayo Clinic compared simvastatin, a frequently used statin, with changes in lifestyle habits that included intake of red fermented rice and fish oil. Comparable results with regard to a lowering of LDL cholesterol – which is highlighted as a trigger of CHD – were achieved in both groups (Becker, 2008).

Side effects and safety

There are several case studies on the side effects experienced when using red fermented rice or the manufactured products made from it. These, in line with the side-effects of statins, are mainly liver damage and myopathies (Mueller, 2006; Lapi, 2008). Here one must critically note the differing compositions of the over-the-counter manufactured products (that are also available via the internet). In some products, in addition to very different concentrations of monacolin K, raised levels of the mycotoxin Citrinin have been found (Gordon, 2010). However, in the above-mentioned meta-analysis by Liu et al., only 'non-serious adverse effects such as dizziness and gastrointestinal discomfort' were reported; also in the very large-scale study by Lu et al., *Xuezhikang* red fermented rice was found to be 'safe and well-tolerated'.

There are also studies that have investigated whether red fermented rice or products derived from it are suitable for patients who do not tolerate synthetic statin preparations. In a randomised study, this possibility was tested on 62 patients with statin-associated myalgia. The verum group, who achieved a significant lowering of their cholesterol levels with 3,600 milligrams per day of red fermented rice, did not report increased pain nor were there significantly raised levels of the enzyme CK indicating damage to the muscles (Becker, 2009). Similar results were obtained in a study where 2,400 milligrams of red fermented rice were administered daily (Halbert, 2010).

During pregnancy the use of red fermented rice is not recommended as, in addition to the above-mentioned possible side effects, from the viewpoint of Chinese medicine its blood-invigorating properties are contraindicated.

Dosage

Most studies use red fermented rice or corresponding manufactured products with a daily dose of 1,200 to 2,400 milligrams (taken in two equal portions). This corresponds to an approximate daily dose of 10 milligrams of monacolin, of which roughly half is monacolin K. This amount lies noticeably below the dose of lovastatin deemed necessary of 10-80 milligrams. However, if one looks at the equivalent lipid-lowering effects mentioned above, the question arises of what role is played by other monacolins and other constituents found in red fermented rice and what their synergisms are.

If one uses manufactured products, then one should not only consider the information on the safety and reliability of the production methods but also the standardised content of monacolin K. This is usually in the region of two to three per cent. As a daily dose, manufacturers often recommend amounts below five milligrams of monacolin K, probably in order to avoid the official regulations, as mentioned above. For effective lowering of cholesterol levels, however, a daily dose of more than five milligrams (and up to 10) of monacolin K is considered necessary.

In Chinese medicine, red fermented rice can be prescribed in the traditional way, that is within the framework of a personalised prescription containing several medicinals, but also as a single medication. For decoctions, the daily dosage of the ground powder is 6-12 grams or 10-20 grams, depending on the reference text (Chen, 2004, p.528; *Zhongyao da cidian*, 1997, p.991). However, as this powder is not readily water-soluble, it is not suitable to be taken as a decoction. From a practical point of view we recommend instead that it is stirred directly into liquid or solid food. As a customary commodity, it is standardised to a monacolin K content of 0.8 or 3 per cent. In the case of the 3 per cent product, this would require a daily intake of about 150-300 milligrams of the ground powder, corresponding to a daily dose of monacolin K of 5-10 milligrams. Also to be noted, with this delivery method the costs are markedly lower than with manufactured products.

With a daily dose of six milligrams of monacolin K, the desired LDL value was achieved and adverse side-effects such as pain or increased muscle enzymes did not arise.

Concluding remarks

Red fermented rice has been known in China for centuries as a flavouring and colouring agent used in the production of foodstuffs. It is obtained by an ingenious and complicated fermentation process. Its medicinal effect and characteristics were discovered in very early times. It can be classified as a medicinal that relieves food stagnation; it regulates digestion and metabolism and invigorates the blood. As food stagnation and blood stasis can be observed quite often in patients with hyperlipidemia, its application can be considered within a Chinese medicine treatment for elevated blood lipid levels. Interestingly, its hypolipidic effects have been confirmed by modern scientific research. The first statin for lowering lipids was isolated from red fermented rice.

Red fermented rice is considered whenever lipid-lowering medication, statins in particular, is indicated, but the patient rejects them either because of their personal preference or out of necessity due to their adverse side effects. Ideally, from the point of view of Chinese medicine,

it should be used to treat cases where food stagnation and blood stasis are also present. However, studies undertaken without Chinese medicine differential diagnosis have nonetheless shown the practical effectiveness and tolerability of red fermented rice.

A concluding case study will illustrate how worthwhile the application of red fermented rice can be, effectively combining Chinese medicine with modern requirements.

Case study

In 2015, a 62-year-old senior company executive suddenly felt acute thoracic unease on his left side. The patient, who until then had been symptom-free, had undergone a PTCA (percutaneous transluminal coronary angioplasty) fifteen years previously for angina pectoris and CHD. A quick cardiological examination showed an atypical heart attack involving two coronary vessels. After carrying out a lysis, a bypass operation followed two weeks later without any post-operative complications. Risk factors to be mentioned are the death of the patient's father at the age of 46 following a heart attack; smoking one packet of cigarettes a day until six years previously; and considerable and long-term stress at work. In the case history, a tendency to heartburn was also mentioned. The patient's weight had reduced from 104 kilograms (with a height of 186 centimetres) before the heart attack to 83 kilograms at the time of consultation. He had been suffering from sleeping problems for many years and was often awake from three or four am onwards. The patient engaged regularly in sporting activities, but overall felt exhausted and had a tendency to depressive moods. Tongue and pulse reports were, by and large, unremarkable. Blood pressure, previously not high, had recently increased to 160/100 mmHG and was particularly high at night. Overall cholesterol levels were (without medication) at maximum 170 milligrams per decilitre (standard value is up to 200); LDL was around 110 milligrams per decilitre (health range: below 160); HDL at 45 milligrams per decilitre (recommended value is above 40).

Medication consisted of ASA (acetylsalicylic acid) 100 milligrams once daily, bisoprolol 5 milligrams twice daily, ramipril 2.5 milligrams twice daily, esomeprazol 40 milligrams once daily and atorvastatin 20 milligrams once daily.

The patient was referred by a cardiologist. Due to the treatment with statins (most recently atorvastatin), diffuse muscle pains were reported (an orthopaedic examination was unremarkable) with increasing CK levels (593 [standard value <190] most recently) as a manifestation of muscle damage. The question arose whether it was possible within the framework of Chinese medicine to lower the LDL cholesterol to under 100 milligrams per decilitre (2.5 mmol/l) as recommended by cardiological guidelines for cases like this, presenting as it did high cardiovascular risk.

In addition to phytotherapy - initially carried out for the improvement of his general well-being by addressing qi, and blood and phlegm (*tan* 痰) stasis, the patient was given a manufactured product of red fermented rice. With a daily dose of six milligrams of monacolin K, the desired LDL value was achieved and adverse side-effects such as pain or increased muscle enzymes did not arise. Phytotherapy was discontinued after approximately two months; the patient has been taking the red ferment preparation regularly for more than two years now and continues to have low LDL cholesterol.

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References

- Anonymous (1986). *Jujia biyong* 居家必用 (Useful Hints for the Family), mid-thirteenth century, Chinese Commercial Press: Beijing
- Becker, D.J., Gordon, R.Y., Morris, P.B., Yorko, J., Gordon Y.J., Li, M. & Iqbal, N. (2008). Simvastatin vs therapeutic lifestyle changes and supplements: randomized primary prevention trial, *Mayo Clin Proc.*, 83(7), pp.758–64
- Becker, D.J., Gordon, R.Y., Halbert, S.C., French, B., Morris, B. & Rader, D.J. (2009). Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial, *Ann Intern Med.*, 150(12), pp.830–9, W147–9
- Bensky, D., Clavey, S. & Stöger E. (2004). *Chinese Herbal Medicine: Materia Medica*. Third edition. Eastland Press: Seattle
- BfArM Press release 3/16 of February 24, 2016: www.bfarm.de/SharedDocs/Pressemitteilungen/DE/2016/pm3-2016.html [last accessed 30.04.2018]
- Buell, P. & Anderson, E. (2000). *A Soup for the Qan - Introduction, Translation, Commentary and Chinese Text*. Kegan Paul: London, New York
- Chen, J.K. & Chen, T.T. (2004). *Chinese Medical Herbology and Pharmacology*. Art of Medicine Press: City of Industry
- Endo, A. (1979). Monacolin K, a new hypocholesterolemic agent produced by a *Monascus* species, *J Antibiot*, 32 (8), pp.852–854
- Endo, A. (2004). The origin of the statins. 2004. *Atheroscler Suppl.*, 5 (3), pp.125–30
- Engelhardt, U. & Hempen, C.-H. (2006). *Chinesische Diätetik*. Third edition. Elsevier: Munich
- Engelhardt, U., Nögel, R. & Nosse, B. (2008). *Rezepte der chinesischen Diätetik*. Elsevier: Munich
- Fang Chunyang (2011). Die diätetische Anwendung von Pilzen in der Chinesischen Medizin, *Chinesische Medizin*, 4, pp.237–245
- Gordon, R.Y., Cooperman, T., Obermeyer, W. & Becker, D.J. (2010). Marked Variability of Monacolin Levels in Commercial Red Yeast Rice Products: Buyer Beware!, *Archives of Internal Medicine*, 170(19), pp.1722–1727
- Halbert, S.C., French, B., Gordon, R.Y., Farrar, J.T., Schmitz, K., Morris, P.B., Thompson, P.D., Rader, D.J. & Becker D.J. (2010). Tolerability of red yeast rice (2,400mg twice daily) versus pravastatin (20mg twice daily) in patients with previous statin intolerance, *Am J Cardiol.*, 105 (2), pp.198–204
- Hempen, C.-H. & Fischer, T. (2007). *Leitfaden Chinesische Phytotherapie*. Second edition. Elsevier: Munich
- Hempen, C.-H. (2009) *A Materia Medica for Chinese Medicine*. Churchill Livingstone: London
- Hempen, C.-H., Fischer, S., Hummelsberger, J., Koch, A., Leonhardy, H., Nögel, R., Thede, C. & Wullinger, M. (2006). *Leitfaden Chinesische Rezepturen*. Elsevier: Munich
- Hu Sihui 胡思思 (1993). *Yinshan zhengyao* 飲膳正要 (Important Principles of Food and Drink) written in 1330, Taiwan Commercial Press: Taipei
- Huang, H.T. (2000). *Fermentation and Food Science*. In *Science and Civilization in China*. Volume 6, Part 5. Cambridge University Press: Cambridge
- Huang, H.T. (2010). The origin of alcoholic fermentations in ancient China. In: Kupfer, P. (ed). *Wine in Chinese Culture*, pp.41–56
- Kupfer, P. (2010). *Wine in Chinese Culture – Historical, Literary, Social and Global Perspectives*. LIT Verlag: Berlin
- Lapi, F., Gallo, E., Bernasconi, S., Vietri, M., Menniti-Ippolito, F., Raschetti, R., Gori, L., Firenzuoli, F., Mugelli, A. & Vannacci A. (2008). Myopathies associated with red yeast rice and liquorice: spontaneous reports from the Italian Surveillance System of Natural Health Products, *Br J Clin Pharmacol.*, 66 (4), pp.572–4
- Li Shizhen (1982). *Bencao gangmu* 本草綱目 (Systematic Materia Medica) written in 1596. *Renmin weisheng chubanshe* 人民卫生出版社 (People's Medical Publishing House): Beijing
- Li, Y.G., Zhang, F., Wang, Z.T. & Hu, Z.B. (2004). Identification and chemical profiling of monacolins in red yeast rice using high-performance liquid chromatography with photodiode array detector and mass spectrometry, *J Pharm Biomed Anal.*, 35 (5), pp.1101–12
- Liu, J., Zhang, J., Shi, Y., Grimsgaard, S., Alraek, T. & Fønnebo, V. (2006). Chinese red yeast rice (*Monascus purpureus*) for primary hyperlipidemia: a meta-analysis of randomized controlled trials, *Chin Med.*, 23, pp.1:4
- Lu Di (2014). Ancient Chinese People's Knowledge of Macrofungi during the Period from 220 to 589, *EASTM*, 37, pp.36–68
- Lu, Z., Kou, W., Du, B., Wu, Y., Zhao, S., Brusco, O.A., Morgan, J.M., Capuzzi, Chinese Coronary Secondary Prevention Study Group & Li, S.D.M. (2008). Effect of xuezhi kang, an extract from red yeast Chinese rice, on coronary events in a Chinese population with previous myocardial infarction, *Am. J. Cardiol.*, 101 (12), pp.1689–93
- Mueller, P.S. (2006). Symptomatic myopathy due to red yeast rice, *Ann. Intern. Med.*, 145 (6), pp.474–5
- Official Journal of the European Union of May 25, 2012: REGULATION (EU) No. 432/2012 THE COMMISSION of May 16, 2012, https://www.fsai.ie/uploadedFiles/Reg432_2012.pdf. [accessed 13.05.2018]
- Porkert, M. (1978). *Klinische Chinesische Pharmakologie*. Verlag für Medizin Fischer: Heidelberg
- Powell, M. (2010). *Medicinal Mushrooms: A Clinical Guide*. Mycology Press: Eastbourne
- Schäfer, D. (2011). *The Crafting of the 10,000 Things: Knowledge and Technology in Seventeenth-Century China*. University of Chicago Press: Chicago
- Song Yingxing (1966). *T'ien-kung k'ai-wu: Chinese Technology in the 17th Century*. Translated and annotated by Sun, E-tu Zen & Sun, Shiou-chuan. Pennsylvania State University Press: Pennsylvania
- Swissmedic: https://www.swissmedic.ch/dam/swissmedic/de/dokumente/marktueberwachung/abrenzung_sfragen/vermarktung_von_praeparatenmitmonascuspurpureusrotschimmelreiso.pdf. download.pdf [last accessed 15.05.2018]
- Tao Gu 陶穀 (1985). *Qingyi lu* 清異錄 (Records of Pure Marvels), Chinese Commercial Press: Beijing
- Wang Shaohua (2013). Zum Krankheitsbild *depletiō yin liēnāle* (energetische Schwäche des Yin des Fk „Milz“, *piyin xu*), *Chinesische Medizin*, 1, pp.19–30
- Zhongyao da cidian* 中药大辞典 (Great Dictionary of Chinese Medicine), Shanghai Publishing House for Science and Technology (Shanghai kexue jishu chubanshe): Shanghai, 1977/1997