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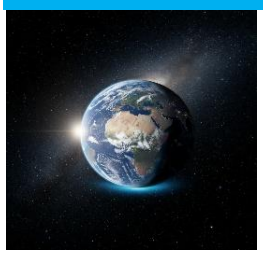

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Red Yeast Rice as a natural source of Monacolin K – the efficacy among patients with dyslipidemia. A literature review

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ABSTRACT

Background: Dyslipidemia is a common disease worldwide associated with increased cardiovascular risk. It is associated with many possible health consequences. An important issue in the treatment of dyslipidemia is lifestyle modification. Moreover, the use of nutraceuticals and pharmacological treatment is equally important. Red yeast rice contains monacolin K, which can reduce plasma levels of low-density lipoprotein cholesterol and total cholesterol. Moreover, contains gamma-aminobutyric acid, which has antihyperlipidemic effects.

Aim: This article aims to review current evidence on the effectiveness of the treating of dyslipidemia with Monacolin K, which is contained in Red Yeast Rice.

Material and Methods: A literature review was conducted from the PubMed and Google Scholar databases. Key phrases as “red yeast rice”, “monacolin K” and “LDL-cholesterol” were used.

Results and conclusion: Supplementation with a low daily dose of red yeast rice, which contains Monacolin K can reduce the risk of cardiovascular diseases among patients with dyslipidemia by lowering plasma levels of low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC).

Keywords: Red yeast rice, Monacolin K, LDL-cholesterol

INTRODUCTION

Dyslipidemia is an important risk factor for cardiovascular diseases (CVD). As a matter of fact, cardiovascular diseases are the major cause of mortality worldwide. Epidemiological research has shown a correlation between the risk of myocardial infarction and atherosclerosis as well as low-density lipoprotein cholesterol (LDL-C). An effective strategy for preventing CVD is reducing LDL-C and total cholesterol (TC) plasma levels[1]. The first step in the treatment of patients with dyslipidemia is using hydroxymethylglutaryl-CoA (HMG-CoA) reductase (statins), but some patients don’t decide to undergo this kind of therapy because of nocebo effects. Moreover, these patients prefer to modify their diet, introduce nutraceuticals and increase their physical activity[2].

The definition of nutraceuticals was created in 1989 by dr Stephen Defelice, combining the words "nutrition" and "pharmaceutical". Nutraceuticals are naturally occurring oral dietary ingredients that have beneficial health effects[32]. These substances fall somewhere between food and pharmaceuticals. Currently, there is no single internationally recognized definition of this term, so its use varies from country to country. Most nutraceuticals are taken as dietary supplements and are widely used. Numerous studies have demonstrated the effectiveness and safety of nutraceuticals, although possible interactions with other products should be considered[33][34]. Among the most commonly used nutraceuticals are compounds derived

from vegetables and fruits. They are believed to have anti-inflammatory and antioxidant properties, which may contribute to the fight against many systemic diseases[35]. Among the currently known nutraceuticals, there is a noteworthy red fermented rice, the component of which is monacolin K, which is very similar to lovastatin, thanks to which it is used to support the treatment of lipid disorders that are associated with numerous cardiovascular diseases, which are a risk factor for death[5].

In East Asian countries, red yeast rice is a traditional food commonly used as a digestive aid. It is produced by fermenting white rice with the fungus Monascus purpureus, which imparts a unique flavor to the rice[2]. Red yeast rice contains organic acids, pigments, monacolins and gamma-aminobutyric acid (GABA), a neurotransmitter with antihyperlipidemic effects. Among the various components found in fermented Red Yeast Rice, the pigment responsible for its vivid red colour warrants particular attention[16]. There are several types of monacolin, among which monacolin K stands out, as it has a chemically identical molecule to lovastatin[21]. Therefore, the intake of this type of supplementation with the diet can reduce LDL plasma levels[3][4][5]. As a result, red fermented rice has been used in Asia for many years as a medicinal food. Currently, it is used as an ingredient in dietary supplements that lower lipids. In Europe, products containing monacolin K are available over-the-counter as dietary supplements, whereas in the United States, they are regulated as medications[16].

STRUCTURE OF MONACOLIN K

The chemical structure of monacolin K is identical to lovastatin. Monacolin K at low pH forms two distinct structures: the lactone form (inactive) and the acidic form (active). The acid form is responsible for inhibiting HMG-Co reductase, the enzyme that catalyzes certain steps in cholesterol synthesis. The structure of the lactone form is identical to that of lovastatin. Lovastatin is hydrolyzed to the acid form, which is the only form that can bind to part of the amino acids and inhibit HMG-Co reductase[6][15].

MECHANISM OF LIPID REDUCTION BY MONACOLIN K

The mechanism of action in lipid reduction by Monacolin K is complex. The substance can lower lipid levels by decreasing the digestion of lipids in the digestive tract, thereby lowering internal lipid production[8]. Monacolin K acts as a reversible inhibitor of the enzyme HMG-CoA reductase, which is crucial in the endogenous synthesis of cholesterol in the liver[9][10]. As a result of the action of the Monacolin K, the conversion of the HMG-CoA to mevalonate is reduced – it is the first step of the cholesterol synthesis pathway.

Through the inhibition of HMG-CoA reductase, hepatic cholesterol synthesis is limited, resulting in a decrease in cholesterol levels within hepatocytes[9][11]. Reducing cholesterol levels within the liver causes a compensatory increase in the number of LDL receptors on the surface of hepatocytes. The result is a decrease in the escape of LDL-cholesterol from the blood and the levels of LDL-cholesterol are significantly reduced[9]. As a result of the above mechanism, the following changes are observed: a reduction in TC, a significant decrease in LDL-C, a reduction in TG and an increase in HDL-C[9][12].

THE EFFICACY OF THE MONACOLIN K

According to available research, there are indications that supplementation of preparations containing Monacoline K can lead to decreased cholesterol levels.

Numerous studies demonstrated that monacolin K can be effective among patients with low-intermediate cardiovascular risk and intermediate levels of LDL[10]. The authors of one of the studies from China presented the results of a survey involving 1445 patients who received 2,5-3,2 mg per day of extract RYR. There was a 12,1% reduction in TG levels and a 17,7% reduction in LDL-C levels. Moreover, taking monacolin caused a decrease in coronary incidents, reducing the number of deaths due to cardiovascular causes. [36] Another study from Europe showed that supplementation with 10mg monacolin K and coenzyme Q10 in patients with metabolic syndrome can reduce TC and TG levels within 2 months[37]. Furthermore, a different study showed that a supplement containing 10mg of Monacolin K, L-arginine, coenzyme Q10 and ascorbic acid reduced LDL-C levels by 23-25% during 8 weeks[38]. The authors noticed that people who don’t tolerate statins also can’t tolerate Monacolin K because of its similarity to lovastatin[10].

In a systematic review, Hadjimbei et al. (2024) included 12 Randomized Controlled Trials RCTs (769 participants) associated with the dose of monacolin K in the scope 2-10 mg per day and a 12-week duration of the study. All of the research showed a significantly decreased level of LDL-C and TC, independently of dose and duration. Emphasize that even a low dose of monacolin K (3mg/d) can have beneficial effects in reducing cholesterol levels. However, the duration of the study was short, so this limits the possibility of determining long-term effects and safety.[13].

Another study showed that among patients with LDL-C levels ≥ 4,14 ≤ 5,69 mmol/l after supplementation with a dose of 3mg monacolin K per day and 200 µg of folic acid, after 12 weeks, the levels of LDL-C decreased by 14,8% and the levels of TC decreased by 11,2%[14]. In addition to the lipid-lowering effect, a decrease in blood pressure was also observed in this

study after monacolin supplementation. It can be concluded that even a low dose of monacolin K supplementation for 8 weeks may have beneficial effects in patients with mild dyslipidemia, potentially reducing their cardiovascular risk[2][14].

In the narrative review by English (2025), the author states that supplementation containing up to 10mg per day of monacolin K can reduce LDL-C levels by 15-34% over a period of 6-8 weeks compared to a placebo. The study suggests that in the population of patients with mild-moderate dyslipidemia and low to moderate cardiovascular risk, supplementation of monacolin K can be a reasonable option as an intermediate option between lifestyle changes and statin therapy[15].

The LDL-lowering effect of monacolin K is significant; however, the results are typically smaller than those achieved with statins. Monacolin preparation may be considered for patients with mild to moderate dyslipidemia who are at low to moderate cardiovascular risk or who are ineligible for statins[10]. Clinical guidelines must also take into account that monacolin preparations are often treated as dietary supplements, which affects quality, doses and standardization[8][13].

Study (year)	**Project**	**Dose**	**Time**	**LDL-C results**	**Extra comment**	**Refs.**
Minamizuka 2021 (RCT, Japan)	RCT Only diet among patients with mild dyslipidemia	vs.2mg/day	8 weeks	Reducing 0,96 mmol/l; 24% from the initial level	–↓TC, ↓apoB, ↓BP.	[2]
Cicero 2023 (narrative review of data, observation)	RYR among patients with mild to moderate hypercholesterolemia	3mg/day	6-12 weeks	Reducing 15-34% vs placebo	Safety profile similar to low dose of “old” statins; useful among patients who don’t tolerate statins	[16]

Trogkanis 2024 (meta-analises)	12 studies of RYR in hypercholesterolemia	2-10mg/day	Up to 12 weeks	Significantly reduced LDL-C and TC vs placebo	Lack of growth of Adverse Drug Reactions	[17]
English 2025 (narrative review)	RYR-monacolin K	Up to 10mg/day	6-8 weeks	Reducing LDL-C levels 34%	Effects similar to 20mg bypravastatin vs placebo	[15]

Most patients with mild to moderate dyslipidemia achieved the expected 15-30% decrease in LDL-C levels within 6-12 weeks with a dose of 2-10 mg monacolin K per day[15][16][17]. Moreover, low doses work – even 2-3mg per day can significantly reduce LDL-C levels[2]. However, among patients with high cardiovascular risk, statins remain the standard of first choice. RYR/monacolin K is useful in patients with mild to moderate dyslipidemia or patients who don't tolerate statins[16].

SAFETY OF SUPPLEMENTATION MONACOLIN K

In the short and medium term of use of RYR preparations containing Monacolin K, LDL-C levels are reduced; this type of supplement is well tolerated and there is no risk of serious side effects compared to the control or placebo trial in studies among patients with mild to moderate dyslipidemia[17][12]. The Adverse Drug Reactions (ADR) profile is similar to low-dose statins due to the same mechanism of action of monacolin and lovastatin[7][12].

The most common side effects of mild to moderate intensity include: muscle symptoms, myopathies (cramps, weakness, myalgia), usually mild symptoms that rarely require discontinuation of therapy[7][12]. Occasionally, studies describe symptoms related to gastrointestinal complaints (abdominal pain, dyspepsia) and dizziness or headache[12]. Rare but significant ADR include rhabdomyolysis or myopathy, as well as liver damage (from increased ALT/AST to acute hepatitis)[7][12]. However, the LiverTox NIH study showed that in controlled trials, there was no association between the use of monacolin and hepatotoxicity but in reality, sporadic acute liver damage occurred among patients, especially in people with poor tolerance of lovastatin[21]. Robert's study reminds us that a significant part of the reported symptoms associated with statin intolerance may result from the nocebo effect[18].

Some factors may increase the risk of ADR. An important aspect in this regard is the drug interactions specific to lovastatin, which may interact with substances that inhibit CYP3A4, which includes azoles, grapefruit juice and some macrolides. Such interactions may result in increased hepatotoxicity and an increased risk of myopathy[13]. Moreover, there may be an accumulation of ADR when statins and RYR/monacolin K are used concomitantly, which also increases the risk of hepatotoxicity and myopathy[7].

RYR currently on the market has extremely variable monacolin content, which is associated with poor standardization[19]. EFSA 2025 confirms the high variability of monacolin in currently available supplements[20].

COOPERATION OF THE MONACOLIN K WITH OTHER NUTRACEUTICALS

Monacolin K and Omega-3 acids (EPA/DHA). Among adults with dyslipidemia, a double-blind RCT during an 8-week supplementation with Monacolin K and PUFAs showed a significant reduction of LDL-C and TC levels, as well as apo-B and CRP, compared to the placebo group. The preparation was well tolerated[22]. Monacolin and Omega-3 Acid may work together through overlapping mechanisms. Monacolin inhibits HMG-CoA reductase, resulting in a decrease in cholesterol and LDL-C synthesis. Omega-3 acids, on the other hand, reduce VLDL/TG by inhibiting hepatic export and TG synthesis. Combined, these two compounds have a broader profile of action[22].

Monacolin K and silymarin (Silybum marianum). In a randomized controlled trial involving RYR and silymarin in patients with low cardiovascular risk, the lipid profile, inflammation and endothelial parameters improved compared to the placebo group. The preparation was well tolerated[25]. In another study lasting 8 weeks, the combination of Monacolin and silymarin also produced beneficial cardiometabolic changes, which reduced 20-27% LDL-C levels, reduced 15-22% TC levels, reduced 10-15% TG levels and a slight reduction of HDL-C of about 2-5%. The lipid effect was comparable to low-dose statins and was maintained throughout the observation period[25]. Moreover, there was an effect on vascular and inflammatory parameters, with improvements in endothelial function, a decrease in CRP protein levels and a decrease in IL-6 levels. The above changes suggest an anti-inflammatory and vascular-protective effect resulting from the synergy of Monacolin K with the hepatoprotective and antioxidant effects of silymarin[25]. Furthermore, a study was conducted using a multi-ingredient product containing Monacolin at a dose of 10mg, policosanol at a dose of 30mg and silymarin at a dose of 150mg. The study lasted 3 months and demonstrated a decrease in LDL-C compared to the placebo group as well as a reduction in inflammatory parameters. Despite

the beneficial effects, the authors emphasize that the evidence is limited due to the short study period and small number of participants. They suggested the need for further research[23].

Monacolin K and berberine. The action of monacoline K involves the inhibition of the enzyme HMG-CoA reductase, resulting in reduced cholesterol synthesis in the liver and a decrease in LDL-C levels. On the other hand, berberine works slightly differently. It increases the expression of LDL-C receptors in hepatocytes, resulting in a reduction in PCSK9 levels and the activation of AMPK (AMP-activated protein kinase), which may lead to a decrease in TC and TG levels and an improvement in metabolism[24][26][27]. As a result of combining these two substances, a synergistic effect will occur: Monacolin K will reduce cholesterol production, while berberine will increase LDL-C retention and limit the degradation of LDL receptors[24][27]. In the study by Kłosiewicz-Latoszek et al., lasting 6-48 weeks, a preparation combining Monacolin K at a dose of 3mg with berberine at a dose of 500mg was used and it was shown that LDL-C was reduced by 15-30%[24].

Monacolin K and artichoke. Artichoke contains flavonoids and phenolic acids that can limit the absorption of cholesterol in the digestive tract, have antioxidant properties and can increase the excretion of bile acids. Monacolin reduces cholesterol synthesis, while artichoke may act as a support by reducing cholesterol absorption and improving liver function[7][28]. A study was conducted in which 60 patients with polygenic hypercholesterolemia were divided into three groups: the first group received a supplement containing monacolin K and standardized artichoke extract, the second group received a preparation with RYR and berberine and the third group served as a placebo group. After 8 weeks of RYR and artichoke supplementation, a decrease in TC, LDL-C and apo-B levels and an improvement in liver function tests were observed. No significant adverse events were reported[29].

Among patients with mild to moderate hypercholesterolemia and low cardiovascular risk, studies were conducted to assess the safety and efficacy of a low-dose monacolin in combination with additional supplements such as coenzyme Q10, grape seed extract and olive extract[30]. The aim of the study was to see whether even a small dose of monacolin could decrease LDL-C levels and whether it was well tolerated. The study lasted 8 weeks and during its duration the participants were divided into three groups. The first group used a diet combined with Monacolin K at a dose of 10mg per day additionally containing coenzyme Q10, grape seed extract and olive extract, the second group used a diet and a supplement with Monacolin K at a dose of 3mg per day with coenzyme Q10, grape seed extract and olive extract, while the third group was the control group and used only dietary treatment[30]. After 8 weeks, LDL-C levels in group one were reduced by 26% compared to baseline. In the second group, LDL-C levels

decreased by 16%. In the control group, LDL-C levels increased by 1,6%. Total cholesterol levels also decreased significantly – by 18% in the first group and by 5% in the second group. TG levels only decreased slightly in the first group[30].

SIDE EFFECTS OF MONACOLIN K

Among patients taking Monacolin K, the most common side effects are muscle symptoms, including myalgia, cramps and weakness. This occurs especially in people with hypersensitivity to statins and usually disappears after their discontinuation[15]. Moreover, during monacolin supplementation, there were isolated reports of headache and gastrointestinal complaints such as abdominal pain, nausea and dyspepsia[13]. A narrative review (2025) found that monacolin is generally well-tolerated and that some individuals may experience mild myalgia, a mechanism similar to that of statins[15]. EFSA indicates that the use of Monacolin K can lead to serious muscle side effects such as rhabdomyolysis, even at low doses. Furthermore, hepatotoxicity associated with elevated ALT/AST levels may occur[31].

According to the systematic review, all studies (2-10mg per day for < 12 weeks) confirmed lipid benefits, with adverse events reported in 3 of 13 studies. However, the authors emphasize that safety requires patient monitoring[13]. The risk of adverse side effects will increase if the patient consumes alcohol in excess while taking monacolin K or takes statins or CYP3A4 inhibitors at the same time[15].

CONCLUSION

Dyslipidemia remains one of the most significant modifiable risk factors for cardiovascular diseases (CVD), which are the leading cause of mortality worldwide. There are many studies that verify a relationship between the risk of myocardial infarction and atherosclerosis and elevated LDL-C levels. An important issue in the treatment and prevention of cardiovascular diseases is the reduction of LDL-C and TC levels. Standard therapy for dyslipidemia is based on the use of statins. However, due to intolerance or nocebo effects, some patients prefer alternative options such as nutraceutical supplementation, dietary changes and physical activity. Monacolin K supplementation effectively lowers LDL-C, TC and TG levels while increasing HDL-C. It works by blocking the endogenous cholesterol synthesis step, specifically by inhibiting the conversion of HMG-CoA to mevalonate.

Most reported side effects are mild and transient, including muscle pain, muscle cramps, fatigue and gastrointestinal symptoms. Monacolin K is therefore well tolerated. Less common but more

significant side effects include hepatotoxicity and rhabdomyolysis, but these mainly occur in patients concomitantly taking alcohol or CYP3A4 inhibitors.

The authors emphasized the need for standardization and quality control because the variability in monacolin content among commercial RYR products remains a significant issue.

Combination therapy with other nutraceuticals, such as omega-3 fatty acids, silymarin, berberine, artichoke extract, coenzyme Q10, or polyphenols, has shown synergistic lipid-lowering and anti-inflammatory effects, thereby improving overall metabolic and vascular outcomes.

In conclusion, monacolin K is a relatively safe and effective nutraceutical option for reducing cholesterol levels in patients with mild to moderate dyslipidemia and a low cardiovascular risk. Although it cannot replace statin therapy in patients with high cardiovascular risk, it is a valuable addition to pharmacotherapy.

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