The Effects of Red Yeast Rice Supplementation on Cholesterol Levels in Adults

A state-of-the-science review of recent evidence.

ABSTRACT

Purpose: Red yeast rice (RYR) supplementation has become a popular alternative to statin therapy in treating hypercholesterolemia. This state-of-the-science review seeks to explore the most recent evidence on the effectiveness and safety of RYR supplementation in treating dyslipidemic adults.

Methods: This review extends the time frame of a meta-analysis performed by Li and colleagues in 2014; specifically, we looked at the literature published between September 2013 and April 2016. We conducted a search of four electronic databases—PsycINFO, CINAHL, PubMed, and Scopus—using the terms *red yeast rice* and *cholesterol*. We excluded studies that included berberine or lovastatin.

Results: Fifteen articles met the inclusion criteria. Eleven articles reported on randomized controlled trials, one reported on an open-label pilot study, and one reported on an open-label clinical trial. Two articles were meta-analyses. The 13 studies involved a total of 1,246 participants, with an additional 7,467 participants reported in the two meta-analyses. Significant reductions in low-density lipoprotein cholesterol and total cholesterol levels with RYR supplementation were observed in all trials. There were no significant changes in liver and kidney function, and 10 studies noted no significant changes in creatine kinase levels.

Conclusions: Although RYR appears to be a safe and effective lipid-lowering agent, there is insufficient evidence to support the recommendation of RYR supplementation to patients. Further research is needed, including long-term studies, studies that include participants with comorbidities and complex medical histories, and studies that take into account the variability of formulation and dosage of RYR in the marketplace.

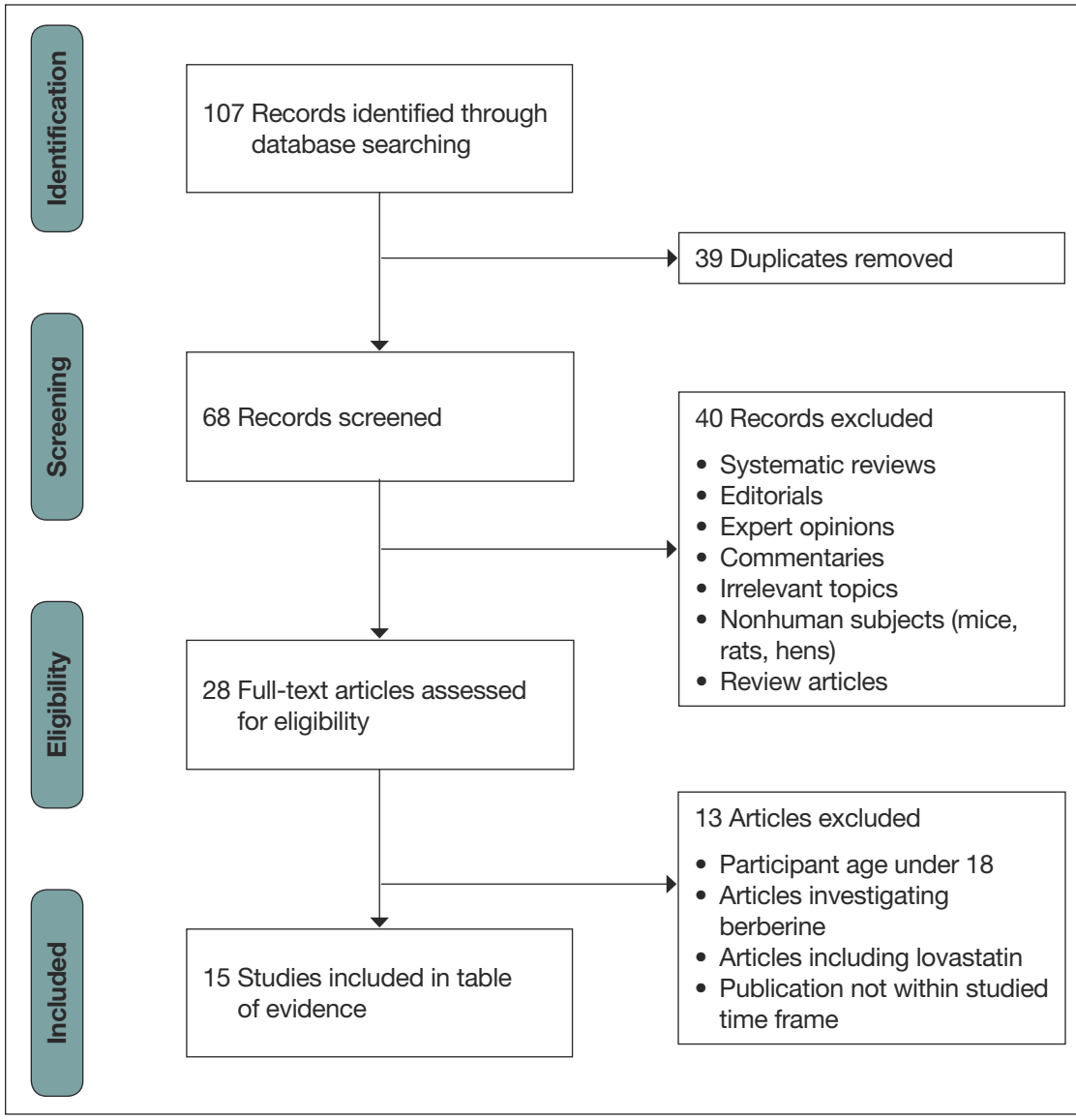
Keywords: cholesterol, hypercholesterolemia, hyperlipidemia, monacolin K, nutraceutical, red yeast rice

Hypercholesterolemia is widespread in the United States. According to the Centers for Disease Control and Prevention (CDC), an estimated 73.5 million U.S. adults (31.7%) have elevated serum levels of low-density lipoprotein (LDL) cholesterol (defined as 130 mg/dL or greater).[1,2] Fewer than half seek treatment, and only one out of three have this condition under control.[2] An elevated LDL cholesterol level is associated with increased risk of cardiovascular disease, such as heart attacks, stroke, and other vascular diseases.[3]

Statins are the most common treatment for hypercholesterolemia. The CDC has reported that between 2011 and 2012, among all adults who used a cholesterol-lowering medication, 83% used a statin, 10% used a statin–nonstatin combination, and 7% used a nonstatin.[4] But statins are also associated with various adverse effects; the most frequently reported are myalgias[5-7] and liver abnormalities.[8] One small, retrospective study examining 45 cases of statin-associated myopathy found that, of the 37 patients who were subsequently given an alternate statin, 21 (57%) reported recurrent muscle pain.[9]

Red yeast rice (RYR) supplementation has become an increasingly common alternative to statin therapy in treating elevated cholesterol levels.[10] RYR

Figure 1. PRISMA Flow Diagram of Studies



is made by fermenting white rice with the yeast *Monascus purpureus*, producing rice that is red in color.[11] Historically, RYR has been used both in Chinese cooking, as a food colorant and preservative, and in traditional Chinese medicine, as an aid to lowering cholesterol and improving circulation and digestion.[12] RYR contains elements known as monacolins. One of these, monacolin K, is chemically identical to the substance that has been synthetically isolated from *Aspergillus terreus* and approved as lovastatin by the U.S. Food and Drug Administration (FDA).[10, 13]

Like statins, monacolins are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme involved in cholesterol synthesis.[13, 14] At this writing, 13 different types of monacolins that may play a part in lowering cholesterol levels have been isolated from RYR, as well as two variants that may or may not affect such levels.[15] It seems possible that RYR might serve

as an alternative treatment for hypercholesterolemia in people who are statin intolerant.[10,16] Indeed, studies have found that, in addition to monacolins, RYR contains sterols (stigmasterol, sapogenin, campesterol, β-sitosterol), monounsaturated fatty acids, and isoflavones,[17] all of which have been shown to help reduce cholesterol levels.

RYR is considered a dietary supplement, and is available in various formulations in capsule or tablet form. Food-based supplementation is also possible. RYR is not currently regulated by the FDA, and there is no standardization of RYR products in the United States.[11] Thus the amount of monacolin K in RYR products can vary and is often unknown. One study evaluated 117 products listing RYR as a primary ingredient and found that 81% provided no specific information about the "lovastatin (monacolin K)" content.[18] Furthermore, as Childress and colleagues have noted, RYR products may contain unwanted byproducts if improperly prepared.[10] The FDA has issued consumer warnings advising that certain RYR products be avoided, stating that products that contain more than trace amounts of lovastatin constitute unauthorized new drugs.[19,20]

Studies suggest that RYR may be a safe alternative to statins in treating hyperlipidemia.

This is of clinical concern, since RYR supplementation has been found not only to effectively lower LDL cholesterol levels, but to do so without the common adverse effects associated with statin use, such as myalgias.[21] RYR supplementation may be an appealing "natural" alternative to mainstream treatments of hypercholesterolemia, which can include statins, bile acid sequestrants, fibrates, niacin, and cholesterol absorption inhibitors.[22]

This state-of-the-science review extends the time frame of the 2014 meta-analysis performed by Li and colleagues, which examined randomized controlled trials of RYR supplementation conducted between 1999 and 2013.[23] We sought to explore what newer studies of RYR supplementation, conducted between 2013 and 2016, add to the evidence for the effectiveness and safety of RYR in treating dyslipidemic adults.

METHODS

Search strategy. We conducted a search of four databases—PsycINFO, CINAHL, PubMed, and Scopus—using the search terms *red yeast rice* and *cholesterol* and limiting results to articles published in English. In PsycINFO, CINAHL, and PubMed, we limited results to articles published between September 1, 2013, and April 30, 2016. In Scopus, because of limitations to its search engine, we limited results to articles published after 2012 and before 2017, then manually eliminated those published before September 1, 2013, or after April 30, 2016. This initial search yielded 107 articles.

Inclusion and exclusion criteria. Of these 107 articles, 68 remained after the removal of 39 duplicates. Forty articles were then excluded using criteria that included low-quality-of-evidence articles and animal studies. The remaining 28 articles were then reviewed for eligibility. Thirteen articles were subsequently excluded, among them those that investigated berberine or lovastatin. Research has shown that berberine has cholesterol-lowering effects.[24] And although lovastatin is chemically identical to monacolin K, lovastatin is commercially available and regulated by the FDA, whereas RYR is considered a supplement and RYR products typically contain only small amounts of monacolin K. Because of these confounding properties, and to avoid confusion, we excluded studies of RYR products that specifically included berberine or lovastatin. After filtering the results, 15 articles remained.

Quality assessment method. The articles were filtered in accordance with the process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[25] This process is detailed in Figure 1.

RESULTS

The 15 articles were thoroughly read and reviewed for study design, sample size, study duration, and weaknesses. The level of evidence was reviewed and scored using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.[26] Findings are shown in Table 1.[23,27-40]

Study characteristics and interventions. Eleven of the articles reported on randomized controlled trials, one reported on an open-label pilot study, and one reported on an open-label clinical trial with a parallel control group. Two articles were meta-analyses. The 13 studies involved a total of 1,246 participants, with an additional 7,467 participants reported in the two

Table 1. Results of Selected Red Yeast Rice and Cholesterol Studies

Study	Design	Sample and Setting	Duration	Weaknesses	Cholesterol Findings	GRADE Score[a]
Barrat E, et al.[27] 2013	Randomized, double-blind, placebo-controlled trial	45 subjects; Nantes, France	4 weeks	Small sample size. Short duration of therapy. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Subjects were without major comorbidities.	Reductions in LDL-C and TC with RYR supplement.	Moderate
Barrat E, et al.[28] 2013	Randomized, double-blind, placebo-controlled trial	100 subjects; Nantes, France	16 weeks	Small sample size. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement (although lower dosages were given than in previous study). Unable to generalize to people with cardiometabolic abnormalities (metabolic syndrome and diabetes).	Reduction in LDL-C with RYR supplement. Effects seen starting at 4 weeks. No muscle aches reported. One patient reported abdominal symptoms and bitter taste in mouth.	High
Cicero AF, et al.[29] 2013	Randomized, double-blind, placebo-controlled trial	25 subjects; Bologna, Italy	4 weeks	Small sample size. Short study duration. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Noncomplicated patients (nonsmoking, no cardiovascular risks).	Favorable changes in LDL-C and TC with monacolins and coenzyme Q10 supplementation.	Moderate
Cicero AF, et al.[30] 2015	Open-label clinical trial with parallel control group	137 subjects; Italy	8 weeks	Small sample size. Short study duration. Risk of bias. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement.	Greater reductions in LDL-C, TC, and non-HDL-C in RYR group compared with phytosterol group. No observed safety issues.	Low
Cicero AF, et al.[31] 2016	Randomized, double-blind, crossover, placebo-controlled trial	25 subjects; Bologna, Italy	4 weeks	Small sample size. Short study duration. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Noncomplicated patients (nonsmoking, no cardiovascular risks).	Favorable changes in TC and LDL-C with monacolins and antioxidant supplementation.	Moderate
Cicero AF, et al.[32] 2016	Randomized, double-blind, placebo-controlled trial	40 subjects; Bologna, Italy	4 weeks	Small sample size. Short study duration. Noncomplicated patients (nonsmoking, no cardiovascular risks).	Favorable changes in TC and LDL-C with monacolins and coenzyme Q10 supplementation.	Moderate
Derosa G, et al.[33] 2014	Randomized, double-blind, placebo-controlled trial	134 subjects; Pavia, Italy	3 months	Small sample size. Short study duration. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Noncomplicated patients (no diabetes or hypertension). Only included white subjects.	Reductions in LDL-C, TC, and triglycerides with RYR supplement.	Moderate
Gerards MC, et al.[34] 2015	Meta-analysis of 20 studies	6,663 subjects; North America, Europe, and China	4 weeks to 6 months	Lack of representation of elderly population. Noncomplicated patients. In studies that involved multi-ingredient RYR supplements, unable to exclude individual and synergistic effects of other ingredients.	Reductions in LDL-C with RYR supplementation. Fewer adverse effects than with statin treatment.	High

Table 1. Continued.

Study	Design	Sample and Setting	Duration	Weaknesses	Cholesterol Findings	GRADE Score[a]
Hobbs T, et al.[35] 2014	Open-label pilot study, pre–post pragmatic design	19 subjects; California, Missouri	Minimum of 30 days, average of 118 days	Lack of standardization of collection of baseline and follow-up blood test results. Small sample size. Short study duration. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Risk of bias. No control group.	Reductions of LDL-C and TC from baseline with RYR supplement. Similar results with both the RYR and omega-3 supplement.	Low
Kasliwal RR, et al.[36] 2016	Randomized, double-blind, placebo-controlled trial	191 subjects; India	12 weeks	Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Small sample size. Short study duration. Unable to determine long-term safety of supplement.	Reduction of LDL-C and non-HDL-C at 12 weeks compared with baseline. No safety issues observed (no renal and liver function effects; no adverse effects).	High
Li Y, et al.[23] 2014	Meta-analysis of 13 randomized controlled trials comparing RYR and placebo	804 subjects; North America, Europe, China, and Japan	4 weeks or longer	Differences in diet, lifestyle, and medications taken by participants. Short study duration and small sample sizes. In studies that involved multi-ingredient RYR supplements, unable to exclude individual and synergistic effects of other ingredients.	LDL-C and TC were lower in RYR supplementation groups.	Moderate
Moriarty P, et al.[37] 2014	Randomized, double-blind, parallel group, placebo-controlled trial	116 subjects (74 in the United States, 42 in China)	12 weeks	Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. May not have generalizability to people with comorbidities and complex medical histories. Short study duration. Overrepresentation of female participants.	Significantly reduced LDL-C and non-HDL-C with daily controlled doses of Xuezhikang.	Moderate
Muscariello E, et al.[38] 2014	Randomized, positive-control study	191 subjects; Naples, Italy	6 months	Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement. Subjects lacked major comorbidities. Minimal subject oversight. Lack of control over confounding variables.	Improved LDL-C levels in group receiving RYR supplement. Minimal changes in HDL-C levels.	Moderate
Sartore G, et al.[39] 2013	Randomized, parallel-group controlled trial	171 subjects; Padova, Italy	24 weeks	Small sample size. Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement.	Significant decreases in LDL-C with Mediterranean diet combined with RYR supplement. No observed changes in liver or renal function.	Moderate
Verhoeven V, et al.[40] 2013	Randomized, double-blind, placebo-controlled trial	52 subjects; Flanders, Belgium	8 weeks	Small sample size. Amount of monacolin K in the RYR product was much higher than in "most commercially available products." Unable to exclude individual and synergistic effects of other ingredients in the RYR supplement.	Decreased LDL-C in intervention groups receiving RYR supplement as compared with diet-only intervention. Minimal adverse effects reported.	Moderate

GRADE = Grading of Recommendations Assessment, Development and Evaluation; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; RYR = red yeast rice; TC = total cholesterol.

[a] The GRADE method provides a framework for appraising evidence and determining the quality of a body of evidence. By using GRADE, the quality of evidence is scored through a review of study factors including risk of bias, precision, extent of effect studies, and presence of confounding variables.

meta-analyses.[23, 34] In the 13 studies, the number of participants per study varied from 19 to 191 individuals. All included only participants over the age of 18 years, with Hobbs and colleagues using the widest age range of 18 to 80 years.[35] Inclusion criteria for all 13 studies included elevated LDL cholesterol levels and no pharmaceutical interventions. Sartore and colleagues specifically included participants with type 2 diabetes to determine the effects of RYR treatment on both diabetic and nondiabetic individuals.[39] Exclusion criteria included history of cardiovascular events (such as myocardial infarction and stroke) and current tobacco use, among others. Studies were from numerous countries, with 10 trials conducted in Europe, one in the United States, one in the United States and China, and one in India. The studies in the two meta-analyses took place in Europe, North America, China, and Japan.

The 13 studies were conducted over a range of about four to 24 weeks, with various RYR-containing products administered and compared with placebo or other supplements. Nine studies used a two-group approach involving one placebo group and one intervention group. Barrat and colleagues divided participants into three groups: a placebo group, an intervention group receiving the "recommended" dose of three RYR tablets containing 0.67 mg monacolin K, and a third group receiving double the "recommended" dose (six tablets).[27] Moriarty and colleagues used a similar approach, administering a placebo to one group while observing the effects of two different doses of Xuezhikang (1,200 mg and 2,400 mg) in the other two groups.[37] (Moriarty and colleagues defined Xuezhikang as "a partially purified RYR" produced under pharmaceutical manufacturing conditions.[37] It is often marketed as a multi-ingredient supplement that includes RYR.[41]) Cicero and colleagues used a two-group approach: the intervention group received both Dif1Stat, a multi-ingredient RYR-containing product, and polyunsaturated fatty acids; a parallel control group received phytosterols.[30] Hobbs and colleagues used a two-group approach with an intervention group receiving Lipitall, a multi-ingredient RYR-containing product, and a control group receiving Vitality Ultra-Pure Omega-3, an omega-3 fatty acid supplement.[35]

Table 2[23, 27-40] lists the intervention supplements and ingredients in each study. Their composition ranged from single-ingredient supplements to various multi-ingredient formulations that included antioxidants, vitamins, and other elements. Three studies used an RYR supplement that contained artichoke leaf extract,[27, 28, 39] and six contained various levels of coenzyme Q10.[29, 31, 32, 35, 39, 40] The most common RYR element used in trials was monacolin K; various dosages ranging from 2 to 10,050 mg/day were reported.

Research outcomes. The overall response to treatment with RYR supplementation was positive, with reductions in both LDL and total cholesterol levels observed in all trials. Barrat and colleagues found that reductions in LDL cholesterol were significant regardless of whether the RYR supplement (a multi-ingredient product containing 0.67 mg of monacolin K) was given at the recommended dosage or was doubled, indicating the efficacy of RYR supplementation at lower dosages.[27] All 13 studies measured total cholesterol, LDL cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. The meta-analysis by Li and colleagues focused on these outcomes as well.[23] The meta-analysis by Gerards and colleagues focused primarily on LDL cholesterol reduction.[34]

Although RYR supplementation appears promising, there is insufficient regulation of RYR-containing supplements.

LDL cholesterol outcomes. All 13 studies and both meta-analyses reported that significant decreases in LDL cholesterol levels were seen with RYR supplementation when compared with placebo, other nutraceuticals, or diet and physical activity alone. (Nutraceuticals are fortified foods or dietary supplements that are held to have health benefits in addition to their nutritional value.) Such decreases were demonstrated in as little as four weeks of RYR administration, and when controlling for other lifestyle variables such as diet and physical activity.[27] The greatest decreases in LDL cholesterol levels were seen in a study by Kasliwal and colleagues, who found 22% and 29% declines after four and 12 weeks of RYR treatment, respectively.[36] The researchers described these findings as similar to those observed with moderate-intensity statin use.

HDL cholesterol outcomes. All of the studies concluded that no significant changes in HDL cholesterol occurred with RYR supplementation. No changes were noted with longer study durations.

Total cholesterol outcomes were generally positive. All of the studies reported greater decreases in total cholesterol levels with RYR supplementation than with

Table 2. Study Supplements and Their Ingredients

Study	Intervention Supplement and Ingredients
Barrat E, et al.[27] 2013	Limicol supplement (monacolin K, sugar cane extract, dry artichoke leaf extract, dry garlic extract, pine bark extract, vitamin E, riboflavin, vitamin B_3, dicalcium phosphate, microcrystalline cellulose, calcium citrate, tricalcium phosphate, magnesium stearate)
Barrat E, et al.[28] 2013	Limicol supplement (monacolin K, sugar cane extract, dry artichoke leaf extract, dry garlic extract, pine bark extract, vitamin E, riboflavin, vitamin B_3, dicalcium phosphate, microcrystalline cellulose, calcium citrate, tricalcium phosphate, magnesium stearate)
Cicero AF, et al.[29] 2013	Monacolins and coenzyme Q10
Cicero AF, et al.[30] 2015	Dif1Stat supplement (*Monascus purpureus*, linear aliphatic alcohols, and niacin) and polyunsaturated fatty acids
Cicero AF, et al.[31] 2016	Monacolins and antioxidants (green tea dry extract, coenzyme Q10, astaxanthin, resveratrol, quercetin)
Cicero AF, et al.[32] 2016	Monacolins and coenzyme Q10
Derosa G, et al.[33] 2014	Zeta Colest supplement (RYR, *Silybum marianum*, octasonol)
Gerards MC, et al.[34] 2015	Meta-analysis of 20 studies; all tested RYR with known content of monacolin K in dosages ranging from 1,200 to 4,800 mg/day; some used multi-ingredient supplements
Hobbs T, et al.[35] 2014	Lipitall supplement (RYR, bioflavonoids, polycosanol, omega-3 fatty acids, resveratrol, coenzyme Q10, folic acid, niacin, vitamin B_6, vitamin B_{12})
Kasliwal RR, et al.[36] 2016	PreLipid supplement (RYR powder, grapeseed powder, niacin, folic acid, black pepper seed powder)
Li Y, et al.[23] 2014	Meta-analysis of 13 studies; all tested RYR in dosages ranging from 200 to 3,600 mg/day; some used multi-ingredient supplements
Moriarty P, et al.[37] 2014	Xuezhikang supplement: described as containing "a family of naturally occurring statins (monacolins)—most prominently monacolin K"; other ingredients not specified; given at dosages of either 1,200 or 2,400 mg/day
Muscariello E, et al.[38] 2014	Erko supplement (RYR, guggulsterols, flavonoids, and *Sylimarin*)
Sartore G, et al.[39] 2013	Redulip supplement (RYR extract, artichoke extract, resveratrol, chromium, folic acid, coenzyme Q10)
Verhoeven V, et al.[40] 2013	Lipeq-10 supplement (monacolin K, coenzyme Q10, procyanidins, lecithin)

RYR = red yeast rice.

diet and exercise, placebo, or supplements other than RYR. Sartore and colleagues found that dyslipidemic participants who had diabetes demonstrated greater decreases in total cholesterol levels when treated with RYR than those without diabetes.[39] The researchers also noted that for all participants, those treated with both the Mediterranean diet and RYR showed greater improvements in lipid profiles than those treated with the Mediterranean diet alone. Two studies found that, after four weeks of RYR supplementation, participants had 10.7% to 21.1% decreases in total cholesterol levels.[27, 32] No significant differences were seen over longer durations of treatment.

Triglyceride outcomes. Nine studies reported no statistically significant decreases in triglyceride levels with RYR supplementation. Moriarty and colleagues found that triglyceride levels declined in participants given Xuezhikang, but not in those given a placebo.[37] Kasliwal and colleagues also reported significant decreases in triglyceride levels in patients given another multi-ingredient RYR supplement.[36] And a study by Muscariello and colleagues found that, compared

with controls, participants given an RYR supplement had significantly reduced triglyceride levels after three months of treatment; however, these levels appeared to plateau, as further reductions weren't seen at six months.[38]

Adverse events and safety. None of the studies reported changes in liver or kidney function in either intervention or control group participants. Ten studies specifically noted no significant alterations in creatine kinase levels. Participants in five of the studies reported no distressing symptoms associated with RYR supplementation. In the meta-analysis of 20 studies by Gerards and colleagues, although no participants were diagnosed with myopathy or discontinued RYR treatment, a range of 0% to 23.8% of patients reported muscle symptoms in the intervention groups, compared with 0% to 36% in the control groups.[34] Hobbs and colleagues reported that one participant experienced heartburn with RYR treatment, which resolved when the supplement was taken before meals instead of afterward.[35] Barrat and colleagues reported that one participant discontinued treatment, citing abdominal pain and an unpleasant taste in the mouth.[28] Participants taking Xuezhikang at either dosage appeared to experience the most bothersome effects, including nausea, epigastric pain, rash, and insomnia; such effects caused three participants to withdraw from the study.[37]

DISCUSSION

Future research. While it's apparent from our review that RYR offers significant benefits to patients and causes minimal adverse effects, further research is needed. The current research indicates that supplement formulations vary greatly, with numerous combinations of ingredients available at various dosages. Because RYR is unregulated, the formulation and production of RYR supplements lack standardization. That said, it's worth noting that some supplement manufacturers voluntarily follow the FDA's regulatory *Current Good Manufacturing Practices for Dietary Supplements* (see www.fda.gov/Food/GuidanceRegulation/CGMP/ucm079496.htm). The 13 studies and two meta-analyses we reviewed involved products that contained a wide variety of herbs, extracts, and antioxidants; such ingredients might themselves prove beneficial or pose drug interaction risks. To determine the safest, most effective formulation of RYR supplementation, more randomized controlled trials that may reveal adverse reactions and drug interactions are needed.

In the 13 studies we examined, the maximum study duration was six months; the average duration was four to six weeks. While the studies found favorable effects associated with RYR supplementation, these durations are too short to reveal the potentially delayed onset of adverse effects such as myopathies or altered liver or kidney function. Future research should examine longer-term RYR supplementation, in order to determine its efficacy and safety compared with statin treatment.

A major weakness in the current evidence is that most studies did not involve or control for participants with comorbidities or complex medical histories; thus the results can't be generalized. To date, most research has excluded people who have had a previous myocardial infarction, those with a history of cardiovascular disease, and those who are heavy smokers—probably because of the potentially confounding effects of these comorbidities. But these populations are known to be at increased risk for cardiovascular incidents and, as such, are likely to require cholesterol-lowering therapy to prevent such events and further complications. More research is warranted to examine the impact that RYR supplementation might have on these individuals.

CONCLUSIONS

This review indicates that RYR supplementation is effective in reducing LDL cholesterol to desirable levels. Studies suggest that RYR may be a safe alternative to statins in treating hypercholesterolemia or hyperlipidemia and may be especially useful in statin-intolerant patients. The European Food Safety Authority has approved RYR for maintenance of normal cholesterol levels, and recommends the consumption of monacolin K 10 mg per day for adults in the general population.[42] Lower dosages are being studied. RYR use may account in part for findings of minimal adverse effects, especially myalgias. But the long-term safety and possible adverse effects have yet to be determined.

Although RYR supplementation appears promising, there is insufficient regulation of RYR-containing supplements in the United States. Until there is standardization of product formulation and manufacturing, and until the amount of monacolin K in a given RYR supplement is clearly stated, the effectiveness and safety of these products will remain in question. Because of these limitations, practitioners cannot yet safely recommend RYR supplementation to their patients with hypercholesterolemia or hyperlipidemia or to those at high risk for cardiovascular events. That said, it should be recognized that some patients may be self-administering RYR supplements. Because RYR contains monacolin K, which is chemically identical to lovastatin, providers whose patients report taking RYR supplements might consider clinical and laboratory monitoring for adverse effects such as myalgias and impaired liver or kidney function. ▼

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