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## Q / Is red-yeast rice a safe and effective alternative to statins?

### EVIDENCE-BASED ANSWER

**A** / YES, but perhaps not the red-yeast rice extracts available in the United States.

In patients with known coronary artery disease and dyslipidemia (secondary prevention), therapy with red-yeast rice extract containing naturally-occurring lovastatin is associated with a 30% reduction in coronary heart disease (CHD) mortality and a 60% reduction in myocardial infarction (MI), similar to the effect of statin medications (strength of recommendation [SOR]: **B**, randomized controlled trials [RCTs] in China).

In patients older than 65 years with

hypertension and a previous MI, the rate of adverse effects from lovastatin-containing red-yeast rice is 2.1% (SOR: **B**, RCT in China).

In patients with previous statin intolerance, the rates of myalgias and treatment discontinuation with lovastatin-containing red-yeast rice therapy are similar to either placebo or another statin (SOR: **C**, low-powered RCTs).

The US Food and Drug Administration (FDA) doesn't allow lovastatin-containing red-yeast rice products on the US market; physicians should be aware that products purchased by patients online contain variable amounts of lovastatin.

### Evidence summary

Red-yeast rice is a Chinese dietary and medicinal product of yeast (*Monascus purpureus*) grown on rice. It contains a wide range of biologically active compounds, including lovastatin (monacolin K). The FDA has banned the sale of red-yeast rice products with more than trace amounts of lovastatin.<sup>1</sup>

#### Red-yeast rice beats placebo, similar to statins

A systematic review of 22 RCTs (N=6520), primarily conducted in China using 600 to 2400 mg red-yeast rice extract daily (lovastatin content 5-20 mg), assessed outcomes in patients with known CHD and dyslipidemia.<sup>2</sup> In one trial of 4870 patients, users of red-yeast rice had significant reductions in CHD mortality (relative risk [RR]=0.69; 95% confidence interval [CI], 0.54-0.89), incidence of MI (RR=0.39; 95% CI, 0.28-0.55), and revascu-

larization (RR=0.67; 95% CI, 0.50-0.89) compared with placebo users.

However, when compared with statin therapy, red-yeast rice didn't yield statistically significant differences in CHD mortality (2 trials, N=220; RR=0.26; 95% CI, 0.06-1.21), incidence of MI (1 trial, N=84; RR=0.95; 95% CI, 0.30-3.05) or revascularization (1 trial, N=84; RR=1.14; 95% CI, 0.38-3.46).

#### Red-yeast rice outperforms placebo in CHD and MI—but not stroke

A secondary analysis of an RCT evaluated the impact of red-yeast rice extract (600 mg twice a day) for 4.5 years on cardiovascular events and mortality in 1530 Chinese patients 60 years of age and older with hypertension and a previous MI.<sup>3</sup> The lovastatin content of the red-yeast rice was 5 to 6.4 mg/d.

Compared with placebo, red-yeast rice was associated with a lower incidence of

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CHD events (RR=0.63; 95% CI, 0.36-0.83), nonfatal MI (RR=0.48; 95% CI, 0.37-0.71), and all-cause mortality (RR=0.65; 95% CI, 0.49-0.83) but not with a statistically significant difference in stroke (RR=0.63; 95% CI, 0.47-1.09) or cardiac revascularization (RR=0.68; 95% CI, 0.52-1.19).

Total adverse events in this study were similar for red-yeast rice and placebo (2.1% vs 1.2%, respectively;  $P>.05$ ). They included gastrointestinal discomfort, allergic reactions, myalgias, edema, erectile dysfunction, and neuropsychological symptoms.

### Red-yeast rice is similar to placebo or another statin in statin-induced myalgia

In a small community-based trial of 62 adults with dyslipidemia and a history of statin-induced myalgia, investigators randomized patients to receive either red-yeast rice extract at 1800 mg (with 3.1 mg lovastatin) or placebo twice daily for 24 weeks.<sup>4</sup> Patients' weekly self-reports of pain (on a 10-point scale) were skewed at baseline (1.4 in the red-yeast rice group vs 2.6 in the placebo group;  $P=.026$ ) but similar at 12 weeks (1.4 with red-yeast rice vs 1.9 with placebo;  $P=.30$ ) and 24 weeks (1.2 with red-yeast rice vs 2.0 with placebo;  $P=.120$ ).

An RCT of 43 adults with dyslipidemia

and history of statin intolerance compared red-yeast rice extract (2400 mg, with 10 mg lovastatin) with pravastatin (20 mg) dosed twice a day.<sup>5</sup> At the end of 12 weeks, mean self-reported pain scores (on a 10-point scale) were similar (1.4 with red-yeast rice vs 1.1 with pravastatin;  $P=.82$ ), as were discontinuation rates because of myalgia (5% with red-yeast rice vs 9% with pravastatin;  $P=.99$ ).

### Recommendations

A narrative review of alternative therapies for heart failure and hypercholesterolemia states that red yeast rice may be a cost-saving option for hypercholesterolemia in patients who can't afford other medications (purchased mostly online, cost \$8-\$20/month for a dosage equivalent to lovastatin 20 mg/d).<sup>6</sup>

A ConsumerLab review of red yeast rice products available since the FDA ban in 2011 tested products marketed in the United States and found variable amounts of lovastatin.<sup>1,7</sup> The group determined that labeling was a poor guide to lovastatin content, which ranged from 0 to 20 mg per daily dose, and that the products may not have been standardized. The group concluded that therapeutic effects weren't predictable. **JFP**



In patients with known coronary artery disease and dyslipidemia, therapy with red-yeast rice extract is linked to reductions in CHD mortality and myocardial infarction similar to statins.

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