



## Red Yeast Rice

### Common Indications:

- Therapeutic choice for statin- intolerant hypercholesterolemic individuals
- Reducing serum LDL and total cholesterol
- Reducing serum triglycerides
- Improving HDL-cholesterol
- Blood pressure lowering
- Reduce vascular plaque adherence and migration in atherosclerosis
- May help with prostate disorder including prostate cancer
- Stimulating bone formation

### General Comments:

*Monascus purpureus* 'Went' sp. is a mold that grows on starch and silage and is also known as angkak rice mold, corn silage mold, maize silage mold, and rice kernel discoloration. Red yeast rice is traditionally prepared by fermenting boiled, non-glutinous rice with red wine mash, natural juice of *Polygonum* grass, and alum water. In practice, the fungus is cultivated on rice and then ground into a powder. Red yeast rice has been used for centuries in the making of rice wine, as a food preservative, and for its medicinal properties. It is used today in traditional Chinese medicine and as a food coloring. Until recently, the nutritional and medicinal properties of red yeast rice were not fully appreciated by the Western world.

The lipid balancing properties of red yeast rice were explained in the late 1970s, when lovastatin was being isolated from *Aspergillus sp.* and *Monascus sp.* to make the pharmaceutical drug lovastatin (Mevacor). It was determined that lovastatin was identical to monacolin K, commonly found in red yeast rice fermentation products.<sup>1</sup> Biochemical and pharmacological studies have reported red yeast rice as a beneficial supplement for maintaining a healthy balance of cholesterol and related lipids in the body. Clinical studies report lowering of total and LDL cholesterol and triglycerides while increasing HDL cholesterol, without the side effects associated with the statins, including myopathy, rhabdomyolysis and hepatotoxicity.

### Benefits & Mechanism of Action:

#### Cholesterol Lowering and Cardiovascular

Fermented red yeast rice contains 9 compounds called monacolins. Monacolins have HMG-CoA reductase activity, considered the mechanism of action of red yeast rice its use in

hypercholesterolemia. Lovastatin and its hydroxy acid form are typically the predominant monacolins in red yeast rice. The hypocholesterolemic “statin” drugs are manufactured from the isolated monacolin K. Red yeast rice supplements also contain sterols (including beta-sitosterol, campesterol, stigmasterol, sapogenin), isoflavones, monosaturated fatty acids and GABA.

Although levels of lovastatin vary in the product, 2.4 g of red yeast rice daily may contain about 4.8 mg of lovastatin, or 0.2% of the total dose.<sup>2</sup> Amounts of 5- 18 mg of lovastatin have also been reported in red yeast rice supplements that have been used in recent clinical studies, including in China. Supplements tested in the US by Consumerlab.com were found to contain 0 – 13.6 mg lovastatin per day. However, the amount of lovastatin used in the pharmaceutical drug for hypercholesterolemia is 20-80 mg daily, significantly more than that found in red yeast rice supplements.

In 2001 the FDA ruled that the red yeast rice supplements on the market were drugs and not supplements because they contained high levels of lovastatin. The FDA required companies marketing red yeast rice in the United States to remove lovastatin in their products, where only trace amounts were detectible.

Clinical studies support the efficacy of *M. purpureus* red yeast rice as an HMG-CoA reductase inhibitor and as an adjunct in cholesterol therapy. A meta-analysis in 2006 looked at ninety-three randomized trials (9625 participants) using red yeast rice supplements for cholesterol health. The study reported that red yeast rice treated individuals had significantly lower LDL (lowered by an average 28mg/dl) and total cholesterol levels (lowered by an average 35mg/dl), lower triglyceride levels (lowered by an average 35mg/dl) and higher HDL levels (raised by an average 6mg/dl) than untreated individuals.<sup>3</sup> The lipid modification effects appeared to be similar to the “stain” drugs, including pravastatin, simvastatin, lovastatin, atorvastatin, or fluvastatin. Compared with non-statin lipid lowering agents, the red yeast rice preparations appeared superior to nicotinate and fish oils, but equal to or less effective than fenofibrate and gemfibrozil.

A 2010 clinical study published in the American Journal of Cardiology reported that in 43 adults with dyslipidemia, treatment with red yeast rice (2,400mg twice daily) decreased the LDL-C by 30% compared to pravastatin (20mg twice daily) at 27%.<sup>4</sup> Of note was incidence of withdrawal from the study due to myalgia was 5% (1 of 21) in the red yeast rice group and 9% (2 of 22) in the pravastatin group.

A Chinese clinical study lasting 4.5 years in approximately 5,000 individuals having a previous myocardial infarction reported those with previous heart attack had a significant decrease in recurrent heart attacks, heart attack-related deaths, and the need for angioplasty or heart surgery.<sup>5</sup> A 20% decrease in LDL cholesterol and a 4% increase in HDL cholesterol was also observed.

Red yeast rice supplements have also been reported useful in improving the lipid profiles in children.<sup>6</sup>

In a 2007 randomized clinical trial red yeast rice extract was found to significantly reduce C-reactive protein and other inflammatory markers and prolong exercise tolerance and time.<sup>7</sup>

#### Anticancer

Red yeast rice is also reported in laboratory animal studies to be beneficial against tumor growth in prostate and breast cancer.<sup>8,9</sup>

#### Bone Support

Red yeast rice has been shown to stimulate bone formation by stimulating cell proliferation and preventing osteoporosis.<sup>10,11</sup>

#### GABA Increase

Fermentation red yeast rice contains varying levels of GABA (gamma-aminobutyric acid). Based on the GABA content, red yeast rice supplements may also help in improving levels of GABA.

#### Potential Concerns with Using Red Yeast Rice Supplements:

The clinical evidence strongly suggests that red yeast rice is an effective natural dietary supplement for controlling serum cholesterol, and that the product is well-tolerated in humans. The isolated monacolin HMG-CoA reductase inhibitor drugs are widely known to cause myopathies in certain individuals, with some myopathies leading to rhabdomyolysis. However, the rate of myalgias when using the more balanced monacolin red yeast rice supplements are reported much lower than the incidence reported using statins. The incidence of statin-induced myalgias is estimated at 9-20%, where only a few isolated case reports of red yeast rice leading to myalgias.

A study of using red yeast rice for hypercholesterolemia in statin-intolerant patients reported that the incidence of myalgias was not increased over a 24-week period.<sup>12</sup> Another study in 2010 reported similar results when using red yeast rice in statin-intolerant patients.<sup>13</sup>

The mechanism behind the reduction in myalgias when using red yeast rice can be related to the mixture of monacolins in the supplement vs. a single monacolin K in the pharmaceuticals. This mixture of compounds may lead to a reduction in the depletion of mevalonate metabolites distal to HMG-CoA reductase, including intracellular isoprenoids such as ubiquinone (CoQ10) and guanosine triphosphate-binding regulatory proteins, which are reported to mediate statin-induced muscle injury.<sup>14</sup>

**Dose:**

- 600-1,200 mg, 2 -4 times a day with food.
- Although research on red yeast rice and coenzyme Q10 depletion has not been reported, HMGCoA Reductase inhibitors are reported to reduce the production of CoQ10 and potentially lead to myalgias and rhabdomyolysis. It may be best to also use coenzyme Q10 (Co10) concurrently with red yeast rice supplementation> Dose of 50 - 150mg daily is most common.

**Cautions & Side Effects:**

- Red yeast rice supplements are reported generally safe in recommended doses. Only a few mild side effects associated with red yeast rice are reported with using red yeast rice supplements, including heartburn, abdominal flatulence, and dizziness. The frequency of these effects is extremely low (less than 2%).
- There are no reports of red yeast rice supplements interacting with other pharmaceutical drugs, dietary supplements or foods, although the possibility of hepatic effects and/or myalgias increase when using more than one agent, i.e. a cyclosporin plus red yeast rice.
- Although the incidence of myalgias are much lower when using red yeast rice in comparison to statins, there are a few reports of increases in creatine phosphokinase with resulting symptomatic myopathies in several individuals and 1 case report of rhabdomyolysis in a renal transplant recipient.<sup>15-19</sup> However, in several case reports patients were taking other dietary supplements and/or pharmaceuticals such as cyclosporine, which can interfere with the metabolism of HMG-CoA reductase inhibitors including red yeast rice.<sup>16</sup> The adulteration of red yeast rice supplements manufactured in other countries with lovastatin cannot be ruled out as a causative factor for these results.
- A Chinese study lasting 4.5 years in 5,000 cardiac patients who were taking a number of pharmaceutical drugs but NOT a statin reported only minor occasional and transient increases in serum transaminase and creatine kinase in patients taking red yeast rice and placebo.<sup>5</sup>
- If the process of culturing and fermenting red yeast rice is not carefully controlled, a compound called citrinin can form. Citrinin has been reported to cause kidney failure in experimental animals and genetic damage in human cells. In a 2011 analysis of red yeast rice products sold as dietary supplements, 4 of 11 products were found to contain this contaminant. There are no government standards or guidelines for citrinin content in red yeast rice; however, the generally recognized standard in the industry is less than 1 part per million, but high quality supplements can be as low as 0.05 parts per million, which is less than 1/20th of that standard.

- Hepatotoxicity is not reported as a common problem when using quality red yeast rice supplements. However, there have been 2 isolated case reports of hepatic effects when using red yeast rice. One case report described a case of hypertransaminasemia in a 63 y/o female who had been taking a combination of red yeast rice and guggul (*Commiphora mukul*), also used to help lower cholesterol levels.<sup>20</sup>
- Quality of the red yeast rice supplement should be taken into consideration, as red yeast rice supplements have been reported to be adulterated with lovastatin, which stresses the responsible choice of a quality red yeast rice supplement. When taking a quality red yeast rice supplement, use only those supplements tested for monacolin content and for citrinin content.
- Red yeast rice is contraindicated in individuals who are hypersensitive or allergic to rice or yeast.

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### General Role and Cardiovascular

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## Bone Support

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## Potential Concerns

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## Cautions and Side Effects

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