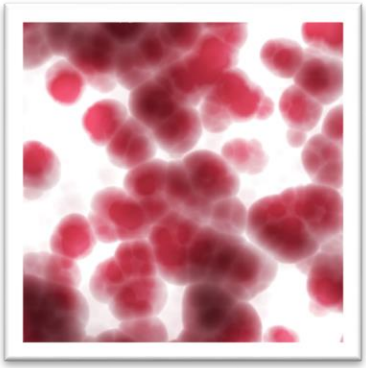
Red Yeast Rice and Cholesterol

General Information:



- **Active component[s]:** 14 monocolin compounds [monacololin K (Mevinolin), J,L,X, M] and their hydroxy acid form, compactin, dehydromonacolin K, dihydromonacolin L, 3α-hydroxy-3,5-dihydromonacolin L.
- **Source material:** *Monascus purpureus* or *Monascus yeast.*
- **Dosage route:** Oral.
- **Directions of use:** Take with food to reduce risk of stomach upset.
- **Duration of use:** usually 6-24 weeks, but up to 4.5 years (Lu et al., 2008).
- **Risk Information:**
  - Dizziness, low appetite, alopecia, arthralgia, back pain, dyspepsia, fatigue, fracture, headache, bloating, muscular weakness, decrease in motor coordination in left hand, nausea, stomach-ache, abdominal dissention, diarrhoea, increased serum blood urea nitrogen and alanine aminotransferase [ALT] levels, influenza, back pain, Crohn's disease, increase in creatine kinase, general discomfort, musculoskeletal symptoms, increased transaminase levels, heart burn, chest pain, rash, pneumonia (Becker et al., 2008; Bogsurd et al., 2010; Halbert et al., 2010; Heber et al., 1999; Lu et al., 2008; Lui et al., 2006).
  - Avoid grapefruit when using statins such as those found in red yeast rice [lovastatin] (Stump et al., 2006).

Human Health Indications:

Recommended Use or Purpose	
General	**Adults**
For the maintenance of blood cholesterol.	*600-4800 mg/d RYR extract containing 5mg and no more than 15 mg monacolin K per day.

* Efficacious dose based on values found in literature (Becker et al., 2009; Becker et al., 2008; Bogsrud et al., 2010; Borden et al., 2010; Halbert et al., 2010; Herbert et al., 1999; Lu et al., 2008; Lui et al., 2006; Wang et al., 1997; Zhao et al., 2004).

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RED YEAST RICE AND CHOLESTEROL

Red yeast rice [RYR], also known as hong qu, is the fermented by-product of red yeast cultured with rice (Becker et al., 2008; Ong and Cheah, 2008). It has traditionally been used in Chinese societies as a food flavouring and as a medicinal ingredient for its lipid-lowering effects (Becker et al., 2008; Ong and Cheah, 2008; Wang et al., 1997). The active medicinal ingredient is thought to be monacolin K [also known as mevinolin and lovastatin] which acts as hydroxy-3-methylglutaryl coenzyme A [HMG-CoA] reductase inhibitor (Borden, 2010; Heber et al., 1999; Lu et al., 2008). However, the alcohol extract of RYR – xuezhikang – which contains a fraction of monacolin K also seems to exhibit cardio-protective effects, likely due to a synergistic effect of other monacolin species and other nutrients within the product matrix (Ong and Cheah, 2008). The RYR dietary supplement Cholestin and the Chinese proprietary medicines Xuezhikang and Zhibituo have all been included in this literature review.

Clinical trials have highlighted significant improvements in the plasma lipid profile including decreases in LDL-Cholesterol [LDL-C], total cholesterol [TC] and triglyceride [TG] levels and at times increases HDL-cholesterol [HDL-C] (Becker et al., 2009; Becker et al., 2008; Bogsrud et al., 2010; Borden et al., 2010; Halbert et al., 2010; Herber et al., 1999; Lu et al., 2008; Lui et al., 2006; Wang et al., 1997; Zhao et al., 2004). Study dosages range from 1200-3600mg and last 6-24 weeks; however one administered a dose of 600mg Xuezhikang for an average of 4.5years (Lu et al., 2008). Red yeast rice appears to be most effective in those who are at the highest risk for heart disease. Improvements in the lipid profile can are usually most dramatic in those with *high* baseline cholesterol values (Becker et al., 2009; Mayoclinic, 2010). Some studies show significant improvements in HDL-C levels (Lu et al., 2008; Lui et al., 2006; Wang et al., 1997; Zhao et al., 2004) and an improvement in the TC to HDL-C ratio which is a strong indicator of cardiac risk (Becker et al., 2008). However, study design should not be overlooked. Some studies mentioned above incorporate lifestyle changes such as exercise and nutritional / dietary advice which has been shown to positively modulate the blood lipid profile (Borden et al., 2010; Becker et al., 2009; Becker et al., 2008; Halbert et al., 2010).

Pharmaceutical statin drugs like Pravastatin, Simvastatin, Lovastatin, Atorvastatin, and Fluvastatin elicit the similar effects on the lipid profile as those seen by RYR; however, these drugs run the risk of statin associated myalgias [SAM] (Border et al., 2010; Liu et al., 2006). Halbert et al., saw a 30% reduction in LDL-C in both the RYR group [containing less than 10 mg lovastatin per day] compared to 40mg pravastatin per day (Halbert et al., 2010). The RYR group had a lower incidence of recurrent intolerable myalgia; however, there was no significant difference between both groups – likely the result of low dose pravastatin (Halbert et al., 2010). The use of RYR in the treatment of hypercholesterolemia/ hyperlipidemia may provide a natural medicinal alternative for patients who are prone SAM; however more clinical studies are warranted as some case reports have noted the recurrence of SAM after switching from statins to RYR (Muller, 2006; Vercelli et al., 2006).

A meta-analysis comparing the effects of Cholestin, Xuezhikang and Zhibituo to statin drugs and non-statin alternatives on modulating the lipid profile showed that various RYR treatments appeared to be significantly better than fish oils and inositol nicotinate but equal to or less effective than fenofibrate and gemfibrozil (Lui et al., 2006). Moreover, no significant differences in the lipid profile were found between both Xuezhikang and Zhibituo (Liu et el., 2006)

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A limitation in RYR literature is the nondisclosure of monacolin *species*, respective *quantities*, *active form* and other nutrients which may work synergistically to modulate the lipid profile. Monacolin K/lovastatin can exist in a lactone form or the active hydroxyl-acid form after bioconversion; however, both forms seem to be well absorbed (Bogsrud et al., 2010). Some studies suggest that the effects seen by RYR containing low lovastatin quantities [10 to 15 mg/day] compared o the established therapeutic dose of 20-40 mg are not sufficient to independently lower lipid levels (Heber et al., 1999; Lu et al., 2008). Heber et al., proposes that the lipid lowering effects of RYR are likely the result of the combination of monacolin species (Heber et al., 1999) and thus acknowledging them and perhaps designing future studies to reflect varying levels of monacolin species on lipid endpoints are warranted. Furthermore, Zhao et al., states that statins in RYR exert potent anti-inflammatory effects aside from their lipid-lowering effects (Zhao et al., 2004) and others acknowledge nutrients such as sterols [b-sitosterol, campesterol, stigmasterol, sapogenin], isoflavones / isoflavone glycosides, monounsaturated fatty acids [MUFA] found in RYR preparations as modulators of the lipid-profile (Heber et al., 1999; Lu et al., 2008).

Overall, the use of RYR dietary supplements [i.e. Cholestin] or proprietary blends like Xuezhikang and Zhibituo can gravely vary in their monacolin and ingredient quantity and content (Gordon et al., 2010). Studies that have disclosed the contents of various RYR supplement have found traces of citrinin – a potent nephrotoxin – and arsenic, cadmium, lead and mercury (Halbert et al., 2010; Heber et al., 2001) which presents a potential safety hazard and draw back to RYR supplementation. However, the literature seems to show that RYR intake can be useful in improving the lipid-profile in patients who are hyperlipidemic and therefore standardizing supplements to remove toxins might be beneficial for the promotion of RYR use.

SAFETY AND TOXICITY:

RYR has been associated with hyper-creatinekinase-emia, and/or muscle weakness and pain which tends to subside upon cessation of treatment (Muller, 2006; Smith and Olive, 2003; Vercelli et al., 2006). Prasad et al. noted rhabdomyolysis in a renal transplant patient taking RYR for post-transplant hyperlipidemia (Prasad et al., 2002). Authors hypothesized that this adverse effect was brought on by a possible interaction between RYR and cyclosporine (Prasad et al., 2002). Other safety issues documented in another case study noted hepatitis and symptoms of nausea, vomiting, diarrhea, chills, and daily fever which improved clinically after RYR termination (Roselle et al., 2008). Another case report noted decreased levels of Coenzyme Q_{10} and increased creatine kinase in one patient taking RYR for 3 months after cessation of statin-theapy due to S-adenosylmethionine [SAMe] (Vercelli et al., 2006). A randomized control trial provided RYR at 4.8 grams per day compared to 40mg of Pravastatin and reported no difference in the adverse events between both groups [muscular weakness, abdominal gas, bloating, alopecia, arthralgia, back pain, diarrhea, dizziness, dyspepsia, fatigue, fracture, headache, decreased motor coordination in L hand] (Halbert et al., 2010). However, there is great variability in RYR content depending on proprietary preparation. An analysis of 9 RYR preparations by Heber et al. reported differences in monacolin content as well as measureable concentrations of citrinin [a potent nephrotoxin] in 7 or the 9 preparations alluding to potential safety issues (Heber et al., 2001). To complement this finding, Becker et al. and Halbert et al. also found trace amounts of citrinin in their administered

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proprietary blends, and Halbert et al. also detected trace amounts of arsenic, lead, cadmium and mercury (Becker et al., 2008; Halbert et al., 2010).

Health Canada has issued a Foreign Product Alert advising Canadians not to consume products that contain red yeast rice (Health Canada, 2007). These products are not authorized for sale in Canada sue to their lovastatin content which is a public safety issue.

Cautions, Warnings, Contraindications and Interactions

Consult a health care practitioner prior to use if you have a pre-existing medical condition, are taking prescription medications, or are pregnant or breastfeeding.

A clinical literature search did not yield any results with regards to bitter melon and interactions with food ingredients.

Drug	Interaction with RYR
Drug	A clinical literature search did not yield any results with regards to RYR and interactions with drugs.

Natural Health Products [NHP] Substances	Interaction with RYR
Coenzyme Q10	Supplementation with coenzyme Q_{10} in combination with red yeast can potentially result in a reduction in serum coenzyme Q_{10} levels (Reilly, 2003).

Food	Interaction with RYR
Grape Fruit	Do not consume grapefruit when taking RYR as grapefruit is extensively metabolized through the same enzyme as the statin active [lovastatin] in RYR. Consumption of grapefruit while taking RYR can result in altered metabolism of the statin whereby its blood levels are elevated for a longer period of time [i.e., increased effectiveness of RYR] (Stump et al., 2006).

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