

Controlling cholesterol levels naturally: RYR + vitamin E + astaxanthin

- **Monacolin K** from red yeast rice contributes to the maintenance of normal blood **cholesterol levels** with a daily intake of 10 mg.
- **Hydroxytyrosol** is a polyphenol from olive oil that helps to protect the blood lipids, especially **LDL cholesterol, against oxidative stress**. This beneficial effect occurs with a daily dose of at least 5 mg hydroxytyrosol or 22 ml high quality olive oil.

Typical indications for red yeast rice (RYR):

Hypercholesterolemia
Increased LDL cholesterol
Alternative for statin-intolerant individuals

Typical indications for hydroxytyrosol, vitamin E and astaxanthin:

Protection against oxidized cholesterol
Increase of HDL cholesterol thanks to astaxanthin
Potential in the prevention of thrombosis (and microthromboses)
Oxidative stress of different origins (e.g. induced by blood sugar dysregulation or intensive physical training, ...)

Interactions and precautions

Avoid concomitant use of grapefruit, pomelos, tangelos and Seville oranges. These citrus fruits inhibit the hepatic degradation of monacolins, causing elevated blood levels.

Scientific information

Cholesterol lowering action of Red Yeast Rice

Red Yeast Rice (RYR) is a **synergetic, cholesterol-lowering** natural product.

Rice is fermented by fungi of the *Monascus* type that synthesize a purple-reddish pigment and up to 14 different monacolins (of which 55-90% is monacolin K).

Monacolins inhibit the activity of the enzyme (**HMG-CoA reductase**) that is crucial to hepatic cholesterol synthesis.

In comparison to statins lower doses of monacolins are needed to obtain a cholesterol-lowering effect. A RYR preparation with 5 mg monacolin K (approx. 10 mg total monacolins) was found equally effective as 20-40 mg lovastatin.¹ This may be due to a synergy between the different components: **fibres, unsaturated fatty acids** (oleic acid, linoleic acid), **phytosterols** (beta-sitosterol, campesterol, stigmasterol, sapogenin) and **monacolins** all contribute to the cholesterol-lowering effect.¹⁻³

During evaluation of 20 placebo-controlled trials in a total of 6663 patients with hyperlipidaemia (meta-analysis of 2015) it was demonstrated that RYR, in a dosage equivalent to 4,8 mg – 24 mg monacolin K per day, could **reduce LDL cholesterol levels by 39 mg/dl (1,02 mmol/l)**.⁴ Red yeast rice is less reliable to raise HDL cholesterol or to lower triglyceride levels.^{1,5-7}

Knowledge about the citrinin content of a dietary supplement based on RYR is desirable since the substance was found to be nephrotoxic in animals. Citrinin is a mycotoxin that may be synthesized by the *Monascus* fungus. According to European guidelines (EU Nr. 212/2014) the citrinin level in RYR supplements should not exceed 2 mg per kg.⁸

Monacolin K may be present in the lactone and/or hydroxy-acid form. The lactone form is identical to lovastatin (a statin commercialised in the US).²

Why is the hydroxy-acid form best choice?

Thanks to its synergy – and consequently lower dose of monacolins – the probability for a RYR preparation to cause muscle pain is lower than that for statins. Statin-induced muscle pain is indeed dose-dependent. Red yeast rice has already been successfully used as an alternative to statins in patients with statin-induced muscle pain.⁹⁻¹⁴ A RYR supplement that contains monacolin K in mainly the hydroxy-acid form is intended to reduce muscle pain even more. The hydroxy-acid form allows available co-enzyme Q10 to be used in cellular energy production most optimally. This is not the case with the lactone form.

Coenzyme Q10 deficiency is not the only reason for statin-induced muscle pain

Inhibition of the HMG-CoA-reductase enzyme by statins not only inhibits the synthesis of cholesterol but also blocks the formation of coenzyme Q10.¹⁵ This is why coenzyme Q10 deficiency has been considered a possible reason for the muscle pain. While earlier intervention studies with coenzyme Q10 showed positive results¹⁶⁻¹⁸, a meta-analysis from 2015 suggested that supplementation with coenzyme Q10 did not provide significant benefits for reducing statin-induced muscle pain.¹⁹ Hence, other mechanisms should also play a role in muscle pain development.

Lactone form inhibits optimal coenzyme Q10 activity

In vitro research on mice myoblasts, which are **muscle cell** precursors, showed that the **lactone forms** of statins (e.g. lovastatin = monacolin K) were **more toxic** to myoblasts than the hydroxy-acid forms. The lactone form binds to sites of complex III that are involved in the transfer of electrons from coenzyme Q10 to cytochrome c. Both the lactone form and coenzyme Q10 (ubiquinol) compete for the same binding site. By doing this the lactone form prevents the optimal use of coenzyme Q10 (ubiquinol) in cellular energy production, which is why an “excess of the lactone form” is currently put forward as possible cause for the muscle pain.²⁰

LDL protective hydroxytyrosol

In a placebo-controlled trial a combination product of RYR (equivalent to 5,88 mg monacolin K/day) and olive fruit extract (equivalent to 9,32 mg hydroxytyrosol/day) was shown to induce a 24% reduction in LDL cholesterol levels and a 20% decline in oxidized LDL cholesterol in patients with metabolic syndrome after 8 weeks of use. In the placebo group LDL cholesterol levels and oxidized LDL cholesterol increased with 1% and 5%, respectively.²¹

Oxidized LDL cholesterol causes atherosclerosis. **Extra virgin olive oil** containing high amounts of polyphenols such as **hydroxytyrosol protects** against the **oxidation of LDL cholesterol**^{22,23}, and thus offers a valuable potential in the prevention of atherosclerosis. Studies showed clear benefits with a daily use of at least 9.15-14.6 mg total polyphenols and 5-10 mg hydroxytyrosol.²⁴⁻²⁶

Hydroxytyrosol is a powerful antioxidant and mild inhibitor of platelet aggregation.^{27,28} The latter characteristic is useful in the **prevention of thrombosis (and microthromboses)**.²⁸ Hydroxytyrosol induces a reduction in thromboxane. This has been observed in vivo in a test group of diabetes type 1 patients taking 25 mg hydroxytyrosol during the first day, followed by 12.5 mg of hydroxytyrosol for 3 consecutive days. Their serum thromboxane B₂ was reduced by 46%.²⁹

Antioxidative astaxanthin

Astaxanthin is the pinkish-red pigment found in salmon, trout, lobster and shrimp, but also in unicellular microalgae. It is a powerful antioxidant and anti-inflammatory agent.³⁰ Astaxanthin supplementation also offers cardiovascular benefits. In patients (n = 61) with mild hypertriglyceridemia (TG up to 200 mg/dl) supplementation with astaxanthin (6 mg/day) induced a significant 10% **increase in HDL cholesterol** after 12 weeks of use.³¹ A trial in football players (n = 40) showed that a 3 months' supplementation with astaxanthin (4 mg/day) increased paraoxonase 1 activity significantly. Paraoxonase is the antioxidant enzyme present on HDL cholesterol particles that **protect LDL cholesterol** particles **against oxidation**.³²

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