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The effects of nutraceutical combinations based on red yeast rice supplementation on cholesterol levels in adults

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Abstract: **Red yeast rice (RYR) is the fermented functional food with Monacus purpureus onto rice. It includes a multitude of bioactive components monacolins, polyketide pigments, and unsaturated fatty acids. The bioactive ingredient monacolin K of red yeast rice is similar to the synthetic drug lovastatin but has no serious side effects of statins. This mini-review summarizes the effects of RYR on cholesterol levels in patients with hyperlipidemia and statin intolerance.**

Keywords: Red yeast rice; Cholesterol; Nutraceutical

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1. Introduction

Hypercholesterolemia is one of the major risk factors for cardiovascular disease[1]. Statins are the most commonly used drugs for the treatment of hypercholesterolemia. But statins are also associated with a variety of adverse effects, including elevated levels of liver enzymes, gastrointestinal symptoms, and statin-related myalgia, including weakness and muscle aches[2-4].

RYR is a dietary supplement made by fermenting monascus purpureus onto rice. It produces a series of substances called monacolin (lovastatin) which acts as a reversible inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, a key enzyme in cholesterol biosynthesis. In addition to HMG-CoA reductase inhibitors, RYR has been found to contain pigments, sterols, isoflavones, isoflavone glucosides and unsaturated fatty acids, all of which have been shown lowering cholesterol effects [5-7]. RYR has been shown to not only improve lipid metabolism, but also lower blood pressure, and may have antidiabetic, anti-inflammatory, anticancer and osteogenic properties[8-13]. This review summarizes the the effects of nutraceutical combinations based on RYR supplementation on cholesterol levels in adults.

2. Clinical Trial Evidence

The efficacy of red yeast rice has been confirmed by many clinical trials. A pilot randomized trial reported that patients receiving nutraceutical with RYR, Bergavit, Omega-3, and Crominex 3+ can significantly enhance endothelial function and reduce total cholesterol (TC)[14]. RYR combination with phytosterols, and L-tyrosol has been shown to be effective reducing in TC, low density lipoprotein cholesterol (LDL-C), uric acid, liver fat index, systolic blood pressure and significant improving in endothelial function[15]. A randomized, double-blind, placebo controlled study showed 12 weeks of treatment with a new nutritional supplement formula containing compounds with putative complementary cholesterol-lowering properties (chitosan, red yeast rice and berberine) combination lower plasma non-high density lipoprotein cholesterol (non-HDL-C) and LDL-C compared to placebo[16]. The using of joint nutraceutical containing banaba, red yeast rice, and coenzyme Q10, have been proven to be well tolerated in patients with hypercholesterolemia and have been shown to be effective in simultaneously improving more risk factors: dyslipidemia, liver transaminase and high sensitivity C-reactive protein (hsCRP)[17]. Body Lipid (BL), a new food supplement containing red yeast rice, berberine, coenzyme Q10 and hydroxytyrosol, reduces TC, LDL-C in patients with mild to moderate hypercholesterolemia[18]. Arrigo et al.[19] reported that the combination of phytosterols and red yeast rice had a cholesterol-lowering effects. A double-blind, crossover, placebo-controlled randomized clinical trial reported that monacolins combined antioxidants could improve hs-CRP, lipid pattern, and endothelial function[20]. Hyperlipidemia patients were treated with red yeast rice plus Lactobacillus casei and no additional cholesterol-lowering effects were observed compared with RYR plus placebo[21]. Yang et al[22] research works showed that nattokinase combined with RYR has better blood lipid lowering effect than nattokinase alone. Zhao et al[23] reported that RYR had a clear lipid-lowering function in patients with hyperlipidemia and abnormal liver function, and no effect on impaired liver function.

3. Tolerability in Patients with a History of Statin Intolerance

Many clinical trials have shown that RYR is effective in lowering cholesterol in patients who are unable to tolerate statins due to statin-related

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myalgia,gastrointestinal side effects, or elevated levels of transaminases[24,25]. Decrease LDL-C level without increasing pain levels of RYR in statin-intolerant patients was reported[26]. ALP (Armolipid Plus containing RYR, policosanol, berberine, folic acid, astaxanthin, and coenzyme Q10) plus low dose statin in high-dose statin (HDS)-tolerant patients compared with low-dose statin alone are more effective in reducing TC[27,28]. The combination of RYR and olive extract was used in high-risk hypercholesterolemia patients to achieve a significant reduction in LDL-C without inducing new seizures of statin-associated muscle symptoms[29]. One trial evaluated the tolerance of RYR and pravastatin to patients who were unable to tolerate other statins due to myalgia. The results demonstrate that RYR is as tolerant as pravastatin and achieves a significant reduction in LDL-C in previously intolerant to statins[30]. A retrospective observational study of the clinical population showed that treatment with red yeast rice significantly reduced LDL-C in people who were highly intolerant of daily statin use[31]. However, LDL-C lowering effect of RYR is superior to the expected effect of monacolin-K. Therefore, the reduction effect may be caused by the combined action of phytosterols, monacolins, isoflavones and monounsaturated fatty acids[32-34].

4. Conclusion

RYR has a significant cholesterol-lowering effect and does not increase the onset of myalgia in patients with statin intolerance. But there are also many problems. Supplemental formulations vary widely, and ingredients of various doses can be mixed in large amounts. More clinical trials are needed to reveal adverse reactions and drug interactions to determine the safest and most effective RYR supplement formulation. If RYR preparation is used as an alternative treatment for primary hyperlipidemia, its long-term efficacy and safety should be explored.

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