Metabolites of Monascus ruber in silages.

Schneweis I, Meyer K, Hörmansdorfer S, Bauer J.

Source

Lehrstuhl für Tierhygiene, Fakultät für Landwirtschaft und Gartenbau, Technische Universität München, Freising-Weihenstephan, Germany.

Abstract

A total of 233 silages were examined and found that Monascus ruber was present in 43 samples with counts between 1 x 10^3 and 9 x 10^6 colony-forming units (CFU)/g (mean: 2 x 10^5 CFU/g). Monacolin K(L) and the hydroxy acid monacolin K(A) were detected by liquid chromatography-mass spectrometry in 45 and 50 of 233 samples at levels ranging from 25-15 600 and 28-65 400 microg/kg, respectively. Citrinin was found with high-performance liquid chromatography-fluorescence detection (FLD) in 14 (6%) samples, the concentrations varied between 2.4 and 64.2 microg/kg. The concentrations of citrinin were low and toxic effects are not anticipated. Monacolin K(A) and monacolin K(L) occur frequently and in considerable amounts in silages. These metabolites are believed to influence the metabolic activity of rumen anaerobic fungi resulting in a poorer digestion of crude fibre.

Monacolin M, a new inhibitor of cholesterol biosynthesis.

Endo A, Komagata D, Shimada H.

Abstract

Monacolin M, a new specific inhibitor of cholesterol biosynthesis structurally related to monacolin K (mevinolin), was isolated from cultures of a strain of Monascus ruber. The structure of monacolin M was determined to be beta-hydroxybutyryl ester of monacolin J by a combination of physical techniques. It was suggested that monacolin M is derived from monacolin J via a synthetic pathway distinct from that for the synthesis of monacolin K, alpha-methylbutyryl ester of monacolin J. The inhibitory effect of monacolin M on beta-hydroxy-beta-methylglutaryl-CoA reductase was slightly lower than that of monacolin K.

Tolerability of red yeast rice (2,400 mg twice daily) versus pravastatin (20 mg twice daily) in patients with previous statin intolerance.


Source

Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA.

Abstract
Currently, no consensus has been reached regarding the management of hyperlipidemia in patients who develop statin-associated myalgia (SAM). Many statin-intolerant patients use alternative lipid-lowering therapies, including red yeast rice. The present trial evaluated the tolerability of red yeast rice versus pravastatin in patients unable to tolerate other statins because of myalgia. The study was conducted in a community-based setting in Philadelphia, Pennsylvania. A total of 43 adults with dyslipidemia and a history of statin discontinuation because of myalgia were randomly assigned to red yeast rice 2,400 mg twice daily or pravastatin 20 mg twice daily for 12 weeks. All subjects were concomitantly enrolled in a 12-week therapeutic lifestyle change program. The primary outcomes included the incidence of treatment discontinuation because of myalgia and a daily pain severity score. The secondary outcomes were muscle strength and plasma lipids. The incidence of withdrawal from medication owing to myalgia was 5% (1 of 21) in the red yeast rice group and 9% (2 of 22) in the pravastatin group (p = 0.99). The mean pain severity did not differ significantly between the 2 groups. No difference was found in muscle strength between the 2 groups at week 4 (p = 0.61), week 8 (p = 0.81), or week 12 (p = 0.82). The low-density lipoprotein cholesterol level decreased 30% in the red yeast rice group and 27% in the pravastatin group. In conclusion, red yeast rice was tolerated as well as pravastatin and achieved a comparable reduction of low-density lipoprotein cholesterol in a population previously intolerant to statins.


Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial.

Becker DJ, Gordon RY, Halbert SC, French B, Morris PB, Rader DJ.

Source
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dbeckerchcardiology@hotmail.com

Abstract

BACKGROUND:
Red yeast rice is an herbal supplement that decreases low-density lipoprotein (LDL) cholesterol level.

OBJECTIVE:
To evaluate the effectiveness and tolerability of red yeast rice and therapeutic lifestyle change to treat dyslipidemia in patients who cannot tolerate statin therapy.

DESIGN:
Randomized, controlled trial.

SETTING:
Community-based cardiology practice.

PATIENTS:
62 patients with dyslipidemia and history of discontinuation of statin therapy due to myalgias.

INTERVENTION:
Patients were assigned by random allocation software to receive red yeast rice, 1800 mg (31 patients), or placebo (31 patients) twice daily for 24 weeks. All patients were concomitantly enrolled in a 12-week therapeutic lifestyle change program.
MEASUREMENTS:

Primary outcome was LDL cholesterol level, measured at baseline, week 12, and week 24. Secondary outcomes included total cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, liver enzyme, and creatinine phosphokinase (CPK) levels; weight; and Brief Pain Inventory score.

RESULTS:

In the red yeast rice group, LDL cholesterol decreased by 1.11 mmol/L (43 mg/dL) from baseline at week 12 and by 0.90 mmol/L (35 mg/dL) at week 24. In the placebo group, LDL cholesterol decreased by 0.28 mmol/L (11 mg/dL) at week 12 and by 0.39 mmol/L (15 mg/dL) at week 24. Low-density lipoprotein cholesterol level was significantly lower in the red yeast rice group than in the placebo group at both weeks 12 (P < 0.001) and 24 (P = 0.011). Significant treatment effects were also observed for total cholesterol level at weeks 12 (P < 0.001) and 24 (P = 0.016). Levels of HDL cholesterol, triglyceride, liver enzyme, or CPK; weight loss; and pain severity scores did not significantly differ between groups at either week 12 or week 24.

LIMITATION:

The study was small, was single-site, was of short duration, and focused on laboratory measures.

CONCLUSION:

Red yeast rice and therapeutic lifestyle change decrease LDL cholesterol level without increasing CPK or pain levels and may be a treatment option for dyslipidemic patients who cannot tolerate statin therapy.
fermentation using Monascus spp. may serve as a multi-functional dietary supplement and can prevent heart disease. In this study, Monascus purpureus CCRC 31615, the strain with the highest amount of monacolin K, was identified from 16 strains using solid fermentation. Its GABA productivity was particularly high. Addition of sodium nitrate during solid-state fermentation of M. purpureus CCRC 31615 improved the productivity of monacolin K and GABA to 378 mg/kg and 1,267.6 mg/kg, respectively. GABA productivity increased further to 1,493.6 mg/kg when dipotassium hydrophosphate was added to the medium.


Medical lipid-regulating therapy: current evidence, ongoing trials and future developments.
Evans M, Roberts A, Davies S, Rees A.

Source
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Abstract
Coronary heart disease (CHD) is a major cause of morbidity and mortality worldwide. Elevated low density lipoprotein-cholesterol (LDL-C) and reduced high density lipoprotein-cholesterol (HDL-C) levels are well recognised CHD risk factors, with recent evidence supporting the benefits of intensive LDL-C reduction on CHD risk. Such observations suggest that the most recent National Cholesterol Education Program Adult Treatment Panel III guidelines, with LDL-C targets of 2.6 mmol/L, may result in under-treatment of a significant number of patients and form the basis for the proposed new joint European Societies treatment targets of 2 and 4 mmol/L, respectively, for LDL and total cholesterol. HMG-CoA reductase inhibitors (statins) reduce LDL-C by inhibiting the rate-limiting step in cholesterol biosynthesis and reduced CHD event rates in primary and secondary prevention trials. The magnitude of this effect is not fully accounted for by LDL-C reduction alone and may relate to effects on other lipid parameters such as HDL-C and apolipoproteins B and A-I, as well as additional anti-inflammatory effects. With increasing focus on the benefits of intensive cholesterol reduction new, more efficacious statins are being developed. Rosuvastatin is a potent, hydrophilic enantiomeric statin producing reductions in LDL-C of up to 55%, with about 80% of patients reaching European LDL-C treatment targets at the 10 mg/day dosage. The Heart Protection Study (HPS) demonstrated that LDL-C reduction to levels as low as 1.7 mmol/L was associated with significant clinical benefit in a wide range of high-risk individuals, including patients with type 2 diabetes mellitus, or peripheral and cerebrovascular disease, irrespective of baseline cholesterol levels, with no apparent lower threshold for LDL-C with respect to risk. Various large endpoint trials, including Treating to New Targets (TNT) and Study of Effectiveness of Additional reductions in Cholesterol and Homocysteine (SEARCH) will attempt to further address the issue of optimal LDL-C reduction. At low LDL-C levels, HDL-C becomes an increasingly important risk factor and is the primary lipid abnormality in over half of CHD patients, with the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study set to assess the effect of raising HDL-C on cardiovascular events in patients with low HDL-C and LDL-C levels below 3 mmol/L. A variety of agents are being developed, which affect both LDL-C and HDL-C metabolism, including inhibitors of acyl-coenzyme A-cholesterol acyl transferase, microsomal transfer protein and cholesterol ester transfer protein, as well as specific receptor agonists. Ezetimibe is a selective cholesterol absorption inhibitor, which produces reductions in LDL-C of up to 25 and 60% reduction in chylomicron cholesterol content with a 10 mg/day dosage. A 1 mmol/L reduction in LDL-C results in a 25% reduction in cardiovascular risk, independent of baseline LDL-C levels. Growing evidence supports the concept that lower is better for LDL-C and that increasing HDL-C represents an important therapeutic target. Furthermore, there is growing appreciation of the role of inflammation in atherogenesis. Consequently, increasing numbers of people should receive lipid-regulating therapy with the development of newer agents offering potential mechanisms of optimising lipid profiles and thus risk reduction. In addition, the pleiotropic anti-inflammatory effects of lipid lowering therapy may provide further risk reduction.
Development of Monascus fermentation technology for high hypolipidemic effect.

Lee CL, Pan TM.

Source
Department of Life Science, National Taitung University, Taitung, Taiwan, Republic of China.

Abstract
Monascus species has been used as the traditional food fungus in Eastern Asia for several centuries. Monascus-fermented products are gradually developed as the popular functional food for the prevention of cardiovascular disease, but we know that culture condition affects the hypolipidemic effect of Monascus-fermented product. In the past, the cholesterol-lowering agent--monacolin K--is regarded as the most important hypolipidemic agent. Two natural yellow pigments--monascin and ankaflavin--are also proven as novel hypolipidemic agents in recent years. However, the hypolipidemic effect of Monascus-fermented product should contribute from monacolin K, monascin, ankaflavin, and other unknown functional ingredients. In addition to hypolipidemic effect, the safety concern of Monascus-fermented product is involved in the levels of mycotoxin--citrinin. The hypolipidemic effect and the production of these functional metabolites or mycotoxin are influenced by many factors such as the choice of culture substrates, carbon and nitrogen source, pH value, extra nutrients, and so on. Therefore, this review focused on the effect of various culture conditions and nutrients on the functional metabolites production, hypolipidemic effect as well as citrinin concentration, and further organized the fermentation technologies used by previous studies for the promotion of hypolipidemic effect and safety.

The effect of red yeast rice (Monascus purpureus) in dyslipidemia and other disorders.

Yang CW, Mousa SA.

Source
The Pharmaceutical Research Institute at the Albany College of Pharmacy and Health Sciences, Rensselaer, NY 12144, USA.

Abstract
BACKGROUND:
Red Yeast Rice (RYR) is a traditional Chinese food that is fermented and obtained after red yeast (Monascus purpureus) is grown on rice. RYR contains Monacolin K (Lovastatin) and other active ingredients that are thought to play a role in the management of cholesterol levels. Recently, many clinical trials have focused on the uses of RYR, including for dyslipidemia, coronary heart disease, diabetes, osteoporosis, cancer, non-alcoholic fatty liver disease, fatigue, and memory.

OBJECTIVES:
The primary objective of this review is to evaluate the effectiveness of RYR on the management of dyslipidemia. The secondary objective is to review studies that focus on the other uses of RYR. The following search terms were used: red yeast rice, Xuezhikang, Hypocol, Cholestin, Monascus purpureus combined with dyslipidemia, hypercholesterolemia, hyperlipidemia, lipid, cardiovascular, coronary, atherosclerosis, diabetes, sugar, bone, osteoporosis, liver, fatigue, memory, Alzheimer's, dementia.

RESULTS:
Studies reviewed show that RYR significantly lowered LDL cholesterol and total cholesterol. Effects on triglycerides and HDL cholesterol were also observed in some studies. Compared with statins, RYR was shown to have an equal efficacy to statins when combined with or without other dietary supplements. RYR also appeared to be superior to placebo in preventing nonfatal myocardial infarction, total coronary heart disease events, and total deaths. On the other hand, information on diabetes, osteoporosis, cancer, non-alcoholic fatty liver disease, fatigue, and memory are currently limited although in vivo and in vitro studies have shown an effect.
CONCLUSION:
Results of RYR clinical trials presented here have limitations and RYR's clinical use should be further investigated before using RYR as one of the alternative treatments for dyslipidemia management, despite the fact that the strongest evidence for RYR use is in dyslipidemia versus other clinical conditions.

Chinese red yeast rice (Monascus purpureus) for primary hyperlipidemia: a meta-analysis of randomized controlled trials.
Source
National Research Centre in Complementary and Alternative Medicine (NAFKAM), University of Tromso, Tromso N-9037, Norway. Jianping.liu@fagmed.uit.no
Abstract
Extracts of Chinese red yeast rice (RYR, a traditional dietary seasoning of Monascus purpureus) contains several active ingredients including lovastatin, and several trials of its possible lipid-lowering effects have been conducted. This meta-analysis assesses the effectiveness and safety of RYR preparations on lipid modification in primary hyperlipidemia. We included randomized controlled trials testing RYR preparation, compared with placebo, no treatment, statins, or other active lipid-lowering agents in people with hyperlipidemia through searching PubMed, CBMdisk, TCMLARS, the Cochrane Library, and AMED up to December 2004. Ninety-three randomized trials (9625 participants) were included and three RYR preparations (Cholestin, Xuezhikang and Zhibituo) were tested. The methodological quality of trial reports was generally low in terms of generation of the allocation sequence, allocation concealment, blinding, and intention-to-treat. The combined results showed significant reduction of serum total cholesterol levels (weighted mean difference -0.91 mmol/L, 95% confidence interval -1.12 to -0.71), triglycerides levels (-0.41 mmol/L, -0.6 to -0.22), and LDL-cholesterol levels (-0.73 mmol/L, -1.02 to -0.043), and increase of HDL-cholesterol levels (0.15 mmol/L, 0.09 to 0.22) by RYR treatment compared with placebo. The lipid modification effects appeared to be similar to pravastatin, simvastatin, lovastatin, atorvastatin, or fluvastatin. Compared with non-statin lipid lowering agents, RYR preparations appeared superior to nicotinate and fish oils, but equal to or less effective than fenofibrate and gemfibrozil. No significant difference in lipid profile was found between Xuezhikang and Zhibituo. RYR preparations were associated with non-serious adverse effects such as dizziness and gastrointestinal discomfort. Current evidence shows short-term beneficial effects of RYR preparations on lipid modification. More rigorous trials are needed, and long-term effects and safety should be investigated if RYR preparations are to be recommended as one of the alternative treatments for primary hyperlipidemia.

NMR evaluation of total statin content and HMG-CoA reductase inhibition in red yeast rice (Monascus spp.) food supplements.
Lachenmeier DW, Monakhova YB, Kuballa T, Löbell-Behrends S, Maixner S, Kohl-Himmelseher M, Waldner A, Steffen C.
Source
Chemisches und Veterinäruntersuchungsamt (CVUA) Karlsruhe, Weissenburger Strasse 3, 76187 Karlsruhe, Germany. lachenmeier@web.de.
Abstract
BACKGROUND:
Red yeast rice (i.e., rice fermented with Monascus spp.), as a food supplement, is claimed to be blood cholesterol-lowering. The red yeast rice constituent monacolin K, also known as lovastatin, is an inhibitor of the hydroxymethylglutaryl-CoA (HMG-CoA) reductase. This article aims to develop a sensitive nuclear magnetic resonance (NMR) method to determine the total statin content of red yeast rice products.
METHODS:
The total statin content was determined by a 400 MHz 1H NMR spectroscopic method, based on
the integration of the multiplet at δ 5.37-5.32 ppm of a hydrogen at the hexahydronaphthalene
moiety in comparison to an external calibration with lovastatin. The activity of HMG-CoA
reductase was measured by a commercial spectrophotometric assay kit.

RESULTS:
The NMR detection limit for total statins was 6 mg/L (equivalent to 0.3 mg/capsule, if two capsules
are dissolved in 50 mL ethanol). The relative standard deviations were consistently lower than 11%.
The total statin concentrations of five red yeast rice supplements were between 1.5 and 25.2 mg per
specified daily dose. A dose-dependent inhibition of the HMG-CoA reductase enzyme activity by
the red yeast rice products was demonstrated.

CONCLUSION:
A simple and direct NMR assay was developed to determine the total statin content in red yeast
rice. The assay can be applied for the determination of statin content for the regulatory control of
red yeast rice products.

Statin alternatives or just placebo: an objective review of omega-3, red yeast rice and garlic in
cardiovascular therapeutics.
Source
HT Ong Heart Clinic, Penang, Malaysia. htyl@stremyx.com

OBJECTIVE:
The aim of this review is to objectively access the trial evidence on the role of omega-3, red yeast
rice and garlic in preventing clinical cardiovascular events. Given the large number of clinical trials
favoring statin use in cardiovascular disease, it is important to see if evidence is available for these
supplements and whether they could replace statin therapy.

DATA SOURCE:
A PubMed search was conducted using the keywords 'trial, omega-3, red yeast rice, xuezhikang,
garlic, cholesterol, cardiovascular, outcomes'; the resulting trials were reviewed together with the
references quoted in the papers obtained.

STUDY SELECTION:
The studies selected are prospective, randomized, placebo-controlled studies with predefined
clinical cardiovascular end-points recruiting at least 2000 patients, with a follow-up over 2 years.

RESULTS:
Modest dose omega-3 fatty acid has been shown in GISSI-P (11 324 patients, follow-up 3.5 years)
to produce a reduction in sudden death of 45%, and in cardiac death of 35%, acting probably via an
anti-arrhythmic effect. In JELIS (18 645 patients, follow-up 4.6 years), high dose omega-3 given to
Japanese patients on a high fish diet and already on statin treatment produced further benefit with a
19% reduction of nonfatal cardiovascular outcomes; fatal cardiac events are not affected. CCSPS
(4870 patients, follow-up 4 years), a secondary prevention trial using xuezhikang, a commercial red
yeast rice preparation, produced a 46% reduction in nonfatal myocardial infarction and coronary
death. There has been no trial to show that garlic reduces clinical cardiovascular outcomes. A
rigorous trial with constant assessment of chemicals in the study material in 192 patients found that
over a 6-month follow-up, raw garlic and 2 commercial preparations do not significantly affect lipid
levels.

CONCLUSIONS:
Omega-3 in modest doses reduces cardiac deaths, and in high doses reduces nonfatal cardiovascular
events. Red yeast rice reduces adverse cardiac events to a similar degree as the statins. It is unlikely
that garlic is useful in preventing cardiovascular disease.
Hypolipidemic and anti-atherogenic effects of long-term Cholestin (Monascus purpureus-fermented rice, red yeast rice) in cholesterol fed rabbits.


Source
Department of Biochemical Pharmacology, School of Pharmaceutical Science, Peking University Health Science Center, Beijing 100083, China.

Abstract
Long-term effects of Cholestin (Monascus purpureus rice; red yeast rice) on serum lipids and severity of atherosclerosis were examined in rabbits fed for 200 days on a semi-purified diet containing 0.25% cholesterol. Serum total cholesterol was 25 and 40% lower, respectively, in rabbits fed 0.4 or 1.35 g/kg/day of Cholestin (Monascus purpureus rice; red yeast rice) compared to controls. This treatment also lowered serum LDL cholesterol. This 200-day treatment significantly reduced serum triglycerides and atherosclerotic index (ratio of non-HDL-cholesterol to HDL-cholesterol). Although similar reductions of total, LDL-cholesterol and triglycerides were observed, a parallel group of rabbits fed lovastatin (0.0024 g/kg/day) failed to reduce the index significantly. Apolipoprotein A(1) was increased and apolipoprotein B was reduced in all treatment groups. Severity of atherosclerosis was reduced significantly in all treatment groups. The sudanophilic area of involvement was 80.6% in controls, and reduced significantly; to 30.1% on the low dose of Cholestin (Monascus purpureus rice; red yeast rice), and 17.2% on the high dose. Lovastatin reduced severity of lesions by 89% (sudanophilia) and 84% (visual). Visual grading of lesion severity showed reduction by 38% and 68%.


Journoud M, Jones PJ.

Source
School of Human Nutrition, Faculty of Agricultural and Environmental Sciences, McGill University, Montreal, Canada.

Abstract
Red yeast rice is a source of fermented pigment with possible bioactive effect. Evidence shows that fermented red yeast rice lowers cholesterol levels moderately compared to other statin drugs, but with the added advantage of underscores its potential as a new alternative to lipid level control. It is concluded from the present evidence that other types of pigmented rice possess opportunities for development as new functional foods.


Monascus rice products.

Wang TH, Lin TF.

Source
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Abstract
The fermentation products of Monascus, especially those produced by solid-state fermentation of rice, have been used as food and health remedies for over 1000 years in China. Monascus rice products (MRPs) are currently being used as health foods in the United States and many Asian countries such as Japan, Taiwan, China, Korea, Thailand, the Philippines, and Indonesia. Many studies have shown that Monascus spp. produce commercially viable metabolites, including food colorants, cholesterol-lowering agents, and antibiotics. The most important bioactive compound isolated from Monascus is monacolin K, which is identical to the potent cholesterol-lowering, antiatherosclerotic drug lovastatin, a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor. Several species of the genus Monascus also produce citrinin, a mycotoxin harmful to the hepatic and renal systems. Monacolin K and citrinin are polyketide fungal metabolites. The biosynthetic pathways leading to the formation of polyketides, including
monacolin K and citrinin, have been elucidated in Aspergillus and Monascus. The concern for safety is, therefore, high for the development of MRPs as health foods. Other attractive applications for MRPs are likely, as supported by recent studies that indicate that MRPs contain other substances (flavonoids, polyunsaturated fats, phytosterols, pyrroli nic compounds, and others) with a wide variety of biological activities and pharmacological potentials. Their effects in lowering blood sugar and triacylglycerol while raising HDL-C are more pronounced than those of monacolin K alone. Beyond cholesterol lowering, MRP may also be an ideal candidate for the treatment of metabolic syndrome.


Development of Monascus fermentation technology for high hypolipidemic effect.

Lee CL, Pan TM.

Source
Department of Life Science, National Taitung University, Taitung, Taiwan, Republic of China.

Abstract
Monascus species has been used as the traditional food fungus in Eastern Asia for several centuries. Monascus-fermented products are gradually developed as the popular functional food for the prevention of cardiovascular disease, but we know that culture condition affects the hypolipidemic effect of Monascus-fermented product. In the past, the cholesterol-lowering agent--monacolin K--is regarded as the most important hypolipidemic agent. Two natural yellow pigments--monascin and ankaflavin--are also proven as novel hypolipidemic agents in recent years. However, the hypolipidemic effect of Monascus-fermented product should contribute from monacolin K, monascin, ankaflavin, and other unknown functional ingredients. In addition to hypolipidemic effect, the safety concern of Monascus-fermented product is involved in the levels of mycotoxin--citrinin. The hypolipidemic effect and the production of these functional metabolites or mycotoxin are influenced by many factors such as the choice of culture substrates, carbon and nitrogen source, pH value, extra nutrients, and so on. Therefore, this review focused on the effect of various culture conditions and nutrients on the functional metabolites production, hypolipidemic effect as well as citrinin concentration, and further organized the fermentation technologies used by previous studies for the promotion of hypolipidemic effect and safety.