Comparison of Red Yeast Rice With Placebo in Statin-Intolerant Adult Patients With Hyperlipidemia

Mercedes Serrano
Pacific University

Follow this and additional works at: http://commons.pacificu.edu/pa

Recommended Citation
Comparison of Red Yeast Rice With Placebo in Statin-Intolerant Adult Patients With Hyperlipidemia

Abstract
Background: Hyperlipidemia is a very common condition as it affects millions of people globally. With approximately 20% of the U.S. population having a total serum cholesterol levels above 240 mg/dL. Red yeast rice has been used as a natural alternative to statins, Red Yeast Rice (RYR) is a fermented biproduct of rice where the yeast, monascus purpureus, is grown. The components that makes RYR effective at lowering cholesterol are monacolin K.

Methods: A search of the literature published in the last twelve years was conducted using Medline, CINAHL, and ISI Web of Science. The terms researched were: Red Yeast Rice, monascus purpureus, LDL-C, LDL, hyperlipidemia, statin myalgias. A manual search was performed using references from the articles retrieved which yielded additional studies to be considered. Studies were eligible for inclusion only if they met all of the following criteria: statin intolerant adults with statin-induced myalgias resolved after discontinuation of statin drug. All other studies focusing on other products besides RYR were excluded.

Results: All three studies used for this systematic review demonstrated significant decreases in LDL-C in comparison to placebo and lifestyle modifications. Study 1 showed a decrease of 43 mg/dL from baseline LDL at week 12 and a drop of 35 mg/dL at week 24, compared to the placebo group whose LDL cholesterol decreased 11mg /dL at week 12, and by 15 mg/dL at week 24. Study 2: This 12 week study showed the mean LDL cholesterol concentration in RYR was 135 compared to 175 mg/dL in the placebo treated group, this was an overall reduction in 39 points from LDL in the placebo group compared to a 5 point drop in the placebo group. Study 3: This 8 week study showed that LDL levels dropped significantly for the Went RYR group whole LDL decreased by 27.7% compared to placebo which dropped by 1.5 % after the 8 weeks.

Conclusion: Red Yeast Rice has been seen to reduce low density lipoprotein cholesterol by significant amounts in comparison to a placebo group. With patients requiring multiple lipid lowering medications, and many failing the generic and inexpensive lovastatin, it is necessary for studies to continue to prove the safety and efficacy of Red Yeast Rice as a replacement for statin drugs such as pravastatin, simvastatin, atorvastatin or fluvastatin.

Degree Type
Capstone Project

Degree Name
Master of Science in Physician Assistant Studies

First Advisor
Dr. Mark Pedemonte, MD

Second Advisor
Annjanette Sommers MS, PAC

This capstone project is available at CommonKnowledge: http://commons.pacificu.edu/pa/197
Third Advisor
Rob Rosenow PharmD, OD

Keywords
Red yeast rice, Statin intolerant, Hyperlipidemia, LDL-C, SAM

Subject Categories
Medicine and Health Sciences

Rights
Terms of use for work posted in CommonKnowledge.

This capstone project is available at CommonKnowledge: http://commons.pacificu.edu/pa/197
Copyright and terms of use

If you have downloaded this document directly from the web or from CommonKnowledge, see the “Rights” section on the previous page for the terms of use.

If you have received this document through an interlibrary loan/document delivery service, the following terms of use apply:

Copyright in this work is held by the author(s). You may download or print any portion of this document for personal use only, or for any use that is allowed by fair use (Title 17, §107 U.S.C.). Except for personal or fair use, you or your borrowing library may not reproduce, remix, republish, post, transmit, or distribute this document, or any portion thereof, without the permission of the copyright owner. [Note: If this document is licensed under a Creative Commons license (see “Rights” on the previous page) which allows broader usage rights, your use is governed by the terms of that license.]

Inquiries regarding further use of these materials should be addressed to: CommonKnowledge Rights, Pacific University Library, 2043 College Way, Forest Grove, OR 97116, (503) 352-7209. Email inquiries may be directed to: copyright@pacificu.edu

This capstone project is available at CommonKnowledge: http://commons.pacificu.edu/pa/197
NOTICE TO READERS

This work is not a peer-reviewed publication. The Master’s Candidate author of this work has made every effort to provide accurate information and to rely on authoritative sources in the completion of this work. However, neither the author nor the faculty advisor(s) warrants the completeness, accuracy or usefulness of the information provided in this work. This work should not be considered authoritative or comprehensive in and of itself and the author and advisor(s) disclaim all responsibility for the results obtained from use of the information contained in this work. Knowledge and practice change constantly, and readers are advised to confirm the information found in this work with other more current and/or comprehensive sources.

The student author attests that this work is completely his/her original authorship and that no material in this work has been plagiarized, fabricated or incorrectly attributed.
Comparison of Red Yeast Rice With Placebo in Statin-Intolerant Adult Patients With Hyperlipidemia

Mercedes Serrano

A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
Pacific University
Hillsboro, OR
For the Masters of Science Degree, [August 14, 2010]

Faculty Advisor: Dr. Mark Piedemonte, MPAS
Clinical Graduate Project Coordinators: Annjanette Sommers MS, PAC & Rob Rosenow PharmD, OD
Biography

Mercedes moved to Portland, Oregon in 1994 with her family at the age of 12. She is a family oriented and a very happy individual. She has been blessed with the best family in the world, and with a loving and caring husband. Mercedes was born and raised in Lima, Peru and moved to the US at the age of 7. She grew up in Southern California, and continued to grow and love Portland, Oregon. She went to Portland State University and received a Bachelor of Science in 2004 and a Bachelors degree in Microbiology in 2005. Mercedes is an active member in her community and has many years of volunteer experience with the uninsured and underserved communities around Portland and Hillsboro, Oregon.
Abstract

**Background:** Hyperlipidemia is a very common condition as it affects millions of people globally. With approximately 20% of the U.S. population having a total serum cholesterol levels above 240 mg/dL. Red yeast rice has been used as a natural alternative to statins, Red Yeast Rice (RYR) is a fermented biproduct of rice where the yeast, monascus purpureus, is grown. The components that makes RYR effective at lowering cholesterol are monacolin K.

**Methods:** A search of the literature published in the last twelve years was conducted using Medline, CINAHL, and ISI Web of Science. The terms researched were: Red Yeast Rice, monascus purpureus, LDL-C, LDL, hyperlipidemia, statin myalgias. A manual search was performed using references from the articles retrieved which yielded additional studies to be considered. Studies were eligible for inclusion only if they met all of the following criteria: statin intolerant adults with statin-induced myalgias resolved after discontinuation of statin drug. All other studies focusing on other products besides RYR were excluded.

**Results:** All three studies used for this systematic review demonstrated significant decreases in LDL-C in comparison to placebo and lifestyle modifications. Study 1 showed a decrease of 43 mg/dL from baseline LDL at week 12 and a drop of 35 mg/dL at week 24, compared to the placebo group whose LDL cholesterol decreased 11mg /dL at week 12, and by 15 mg/dL at week 24. Study 2: This 12 week study showed the mean LDL cholesterol concentration in RYR was 135 compared to 175 mg/dL in the placebo treated group, this was an overall reduction in 39 points from LDL in the placebo group compared to a 5 point drop in the placebo group. Study 3: This 8 week study showed that LDL levels dropped significantly for the Went RYR group whole LDL decreased by 27.7% compared to placebo which dropped by 1.5 % after the 8 weeks.

**Conclusion:** Red Yeast Rice has been seen to reduce low density lipoprotein cholesterol by significant amounts in comparison to a placebo group. With patients requiring multiple lipid lowering medications, and many failing the generic and inexpensive lovastatin, it is necessary for studies to continue to prove the safety and efficacy of Red Yeast Rice as a replacement for statin drugs such as pravastatin, simvastatin, atorvastatin or fluvastatin.

**Keywords:** Red yeast rice, Statin intolerant, Hyperlipidemia, LDL-C, SAM.
Acknowledgements

To all my family, who have supported my dreams and helped me accomplish so much in this world. To my loving husband, without you I do not know where my mind would be, your love, your humor, your character and your support have made me the happiest woman in the world, even through this last year, when we were apart. And finally to my nieces who have brought me so much joy on my worst days, no words can describe the love that I feel for you two, Hailey and Mailey. And lastly, to the staff at Pacific University who has been supportive and understanding. Thank you all very much.
# Table of Contents

Biography ..................................................................................................................1

Abstract ....................................................................................................................2

Acknowledgements .................................................................................................3

Table of Contents .....................................................................................................4

List of Tables ...........................................................................................................5

List of Abbreviations ...............................................................................................5

Background .............................................................................................................6

Methods ...................................................................................................................10

Results .....................................................................................................................11

Discussion ..............................................................................................................18

Conclusion .............................................................................................................19

References .............................................................................................................21

Tables .....................................................................................................................23
List of Tables

Table 1: Classification of LDL-C levels
Table 2: Summary Matrix of Review articles

List of Abbreviations

LDL-C…………………………………………………Low Density Lipoprotein Cholesterol
CAD………………………………………………………………Coronary Artery Disease
CPK………………………………………………………………Creatine Phosphokinase
AST………………………………………………………………Aspartate Aminotransferase
ALT………………………………………………………………Alanine Aminotransferase
HDL-C………………………………………………...High Density Lipoprotein Cholesterol
RYR …………………………………………………………Red Yeast rice
FDA …………………………………………………………Food and Drug Administration
CHD ………………………………………………………..Coronary Heart Disease
SAM……………………………………………………….Statin Associated Myalgias
Comparison of Red Yeast Rice With Placebo in lowering LDL-C in Statin-Intolerant Adult Patients With Hyperlipidemia

BACKGROUND

Diagnosis of Hyperlipidemia

Hyperlipidemia is a very common condition as it affects millions of people globally. It is a group of disorders characterized by an excess of lipids in the bloodstream. Lipids are transported in the blood as large lipoproteins. Lipoproteins have five major classes all based on density, these are chylomicrons, very low density lipoproteins (VLDL), intermediate density lipoproteins (IDL), low density lipoproteins (LDL), and high density lipoproteins (HDL). Most triglyceride is transported in chylomicrons or VLDL and most cholesterol is carried in LDL and HDL. Hyperlipidemia is a major risk factor for atherosclerosis and coronary heart disease (CHD). Lowering cholesterol levels has been shown to prevent coronary artery disease in people with hypercholesteremia, as well as decrease the risk of recurrent coronary events and procedures in patients with coronary artery disease (CAD). A study published in 2001 has shown evidence of regression of atherosclerotic lesions in patients whose lipid levels are lowered.¹

Hyperlipidemia is a common problem, with approximately 20% of the U.S. population having a total serum cholesterol levels above 240 mg/dL.² Diet and exercise are the foundation of any treatment and should be emphasized in all patients who have hyperlipidemia. Unfortunately, as valuable as diet and exercise can be, they often will not bring the patient's LDL-C to goal.³ Statins are usually the medication of choice in patients with a high risk of coronary artery disease, coronary artery bypass surgery, or angioplasty.
Red Yeast Rice has been used as a natural alternative to statins, because of this; RYR has become so popular in western society that demand has affected the purity of the components that were traditionally found to lower cholesterol. Toxins have been found in RYR which is known to be nephrotoxic. Critinin is a toxin of Menascus Purpureus which has been found in larger amounts due to the inappropriate fermenting of RYR.

**Recommendations**

In diagnosing for hyperlipidemias, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III Guidelines suggests that for primary prevention of cardiovascular disease, all adults over the ages of 20-35 should have a fasting lipoprotein profile and evaluation of risk factors every 5 years if they are at high risk for cardiovascular disease. Lipoprotein analysis should be performed on serum obtained after a 12 hour fast.\(^2\) LDL-C is calculated using the Friedewald formula, by subtracting the level of HDL cholesterol from the total level of cholesterol.\(^4\) The initial classification is based on an LDL cholesterol level which will be the primary target for therapy (see Table 1).

**Common Treatment**

The use of statin medication has been shown to decrease low density lipoprotein cholesterol (LDL) and therefore lowers negative cardiovascular effects by blocking 3-hydroxy-3 methylglutaryl Coenzyme A reductase, thus inhibiting the liver’s ability to produce LDL cholesterol. This causes an increase in the number of LDL receptors on the surface of the liver resulting in more cholesterol being removed from the blood stream.\(^5\)
There are many statin drugs on the market, most of which have been derived from Aspergillus.\textsuperscript{6} Because of the risk of side effects from statins, which are seen in 10\% of patients on statin therapy, these drugs are not available over the counter and require a prescription. The most common side effects of these drugs are myalgias, rhabdomyolysis, nephrotoxicity, and hepatotoxicity.\textsuperscript{7}

**Red Yeast Rice**

Red Yeast Rice (RYR) is a fermented biproduct of rice where the yeast, *Monascus purpureus*, is grown. Red Yeast Rice contains multiple strains, all of which are being studied further for decreasing lipids. In China, RYR has been used for centuries, dating back to the Ming Dynasty (1368-1644) for medicinal purposes, food coloring, food preservative, spice and general cuisine\textsuperscript{8} The components that makes RYR effective at lowering cholesterol are monacolin K, monacolin J, monacolin M, dihydromevinolin, polyketide monacolins, and saturated fatty acids, all of which are known to inhibit cholesterol synthesis. Monacolin K is a potent 3-Hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor, and it is also known as mevinolin or lovastatin. Due to the monacolin K content (lovastatin) found in some strains of RYR, side effects such as rhabdomyolysis and hepatotoxicity can be seen when high or uncontrolled doses of RYR are administered.\textsuperscript{9}

**Purpose of the Study**

The question of using Red Yeast Rice in individuals who are intolerant of statin therapy is important, as studies have shown that reducing cholesterol ratios decreases coronary artery disease (CAD) and cardiovascular compromise.\textsuperscript{10} With this being stated,
there is a continuous debate as to the use of RYR in comparison to statins in decreasing low density lipoproteins due to the safety and efficacy of RYR as it is not bound by FDA regulations. The issue is one of cost effectiveness since RYR can be obtained at much lower prices than some of the non-generic formulations of statins. Since many individuals lack insurance coverage and many require other statin medications besides the generic lovastatin, it is crucial that medical facilities aid in giving their patients the best medication and resources for their money and their health. In this society, if people are able to pay less for a medication that can act the same as a prescribed one costing hundreds of dollars, the patient will be a compliant one.

**Clinical Question**

Several studies have compared the use of Menascus Purpureus, a strain of RYR, and its efficacy with other herbal medications to reduce overall lipid profile, while others have compared its efficacy to statins.\textsuperscript{11} A systematic review of the literature was performed to determine whether RYR has the same LDL lowering capabilities as prescription statin medication. The main goal is to see if a significant conclusion can be drawn as to whether RYR lowered LDL levels to a degree comparable or better than prescription statins, and if there is a decrease of intolerable myalgias.
METHODS

Search Strategy

A systematic review examines original studies which may aid in the contribution to medical communities in the understanding of the risks and benefits of the use of Red Yeast Rice in decreasing Low Density Lipoprotein Cholesterol, particularly if the previous use of a statin produced intolerance in the patient. Only studies published in the last twelve years comparing the effects of Red Yeast Rice with placebo in reducing LDL were included. Randomized control trials, cohort studies, and case control studies, both prospective and retrospective were included. Meta-analyses and Systematic reviews are not addressed.

A search of the literature published in the last twelve years was conducted using Medline database, CINAHL and the ISI Web of Science (science citation index, current contents) from 1998 through 2010 using the Medical Subject Headings of the National Library of Medicine (MeSH). The terms researched were: Red Yeast Rice, Monascus Purpureus, LDL-C, LDL, Hyperlipidemia, and statin myalgias. A manual search was performed using references from the articles retrieved and provided additional studies to be considered.

Eligibility Criteria

Studies were judged suitable for this systematic review and were eligible for inclusion only if they met all of the following criteria: statin intolerant adults with statin-induced myalgias resolved after discontinuation of statin drug, Red Yeast Rice versus placebo, and decreasing LDL-C. Outcomes beyond the use of Red Yeast Rice to lower LDL, such as the
use of fish oil or niacin were excluded. Studies that did not include a comparison of RYR to placebo were excluded.

Only results fully reported in journal articles were considered. The methodological quality and validity of the selected studies was assessed using the Jadad scale with scores ranging from zero to five. Higher scores were given to randomized and/or double blinded studies, and if the studies included an appropriate method for randomization. If a study did not include methods of randomization but otherwise stated that they were randomized, one point was deducted and lower points were given. This method of validity score did not eliminate any of the three studies from the review.

RESULTS

Sixteen articles were found, after applying the eligibility criteria only three purported to compare the role of Red Yeast Rice in lowering LDL in statin intolerant patients. All three studies were Randomized placebo controlled trials, and two articles are double blind studies. (see Table 2). Most studies focused specifically on the relationship between Red Yeast Rice decreasing low density lipoprotein cholesterol in conjunction with lifestyle modification and weight loss. These studies further compare the effects of RYR against placebo and the drop in LDL-C.

Study 1

Becker et al\textsuperscript{12} performed a randomized controlled trial of a population consisting of adults with dyslipidemia with a history of discontinuation of statin therapy due to myalgias.
The baseline patient characteristics found in this study were similar for both treatment vs. placebo group. Mean age in both groups were 60.5 and 61.5 respectively (P=0.44), race, ethnicity and co morbidities were similar in both groups. Mean weight ranged from 81.0 in the treatment group, and 81.9 in placebo group. BMI in treatment was 28.8 versus 29.2 in placebo.12

**Exclusion criteria for study**

The randomization process started in September 2006 and March 2007. A total of 174 patients were screened who had known hypercholesterolemia and had discontinued at least 1 statin because of myalgias, with resolution of muscle pain when the medication was discontinued. A total of 112 patients were ineligible for the study for multiple reasons including recent use of statin drug or RYR, history of myositis, rhabdomyolysis, chronic pain, and inability to exercise, had a previous myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting within the last 6 months. Among the inclusion criteria, abnormal baseline lab results such as LDL <100 mg/dL, triglycerides levels > 400 mg/dL, CPK levels of > 500 U/L, aspartate transferase or alanine transferase levels > 1.5 times the upper limit of normal and abnormal thyroid hormone levels. Sixty two patients were randomly assigned to receive three 600 mg capsules of RYR or 3 placebo capsules twice daily for 24 weeks, totaling 1.8 grams of RYR daily. Patients were randomly assigned to receive these pills. The study included a table of the components which made up the formulation of the RYR used, which included 1.02 mg per capsule of Monacolin K (lovastatin), 0.0120 of Monacolin JA, 0.0186 of monacolin J, 0.0080 of Monacolin XA, 0.607 of Monacolin KA.12
Randomization of study

Sixty two patients were randomly assigned to blocks of 4 and placed into 4 categories. These categories included LDL cholesterol level < 150mg/dL, LDL cholesterol level > 150mg/dL, body mass index less than 27 kg/m^2, and body mass index of 27 kg/m^2 or greater. A random assignment list was generated on a computer using the blockrand library with a fixed blocked option. 13 The Red Yeast Rice and placebo used were purchased and made from the same manufacturer (Sylvan Bioproducts, Kittanning, Pennsylvania). The two capsules were identical in size, shape, and color. All of the patients received a 30 day supply during their follow up visits. All patients also participated in a 12 week therapeutic lifestyle change program.12

Results of study

Of the 62 participants, the LDL-C in the Red Yeast Rice group decreased by 43 mg/dL from baseline at week 12 and by 35 mg/dL at week 24, compared to the placebo group whose LDL cholesterol decreased by 11mg/dL at week 12, and by 15 mg/dL at week 24. Low density lipoprotein was significantly lower in the Red Yeast Rice group than the placebo group at both weeks.12

The LDL levels of each group were measured at baseline, 12 weeks, and 24 weeks. The RYR group baseline LDL cholesterol level were 163 mg/dL, 120mg/dL at week 12, and 128 mg/dL at week 24, compared to the placebo group mean LDL cholesterol level of 165 mg/dL at baseline, 154 mg/dL at week 12, and 149.8 mg/dL at week 24. At week 24, 9 out of 30 patients in the RYR group achieved an LDL <100mg/dL compared to 2 out of 29 in the placebo group.12
Study 2

Heber et al\textsuperscript{14} demonstrated through a double blind, placebo-controlled, prospective randomized 12 week controlled trial comparing Red Yeast Rice, to placebo, showed that LDL cholesterol concentrations differed significantly between the red yeast rice group and placebo (P<0.001) Subjects were recruited through newspapers and announcements. Seven hundred and twenty eight potential participants were interviewed and screened. A total of 238 were asked for a visit and fasting blood sample taken for lipid panel. Subjects with LDL cholesterol > 161 mg/dL and triglycerides concentrations < 261 mg/dL in the screening sample were sent to an outside reference laboratory and entered into the run in phase. These subjects have not been treated previously for hypercholesterolemia, and had to have normal liver and renal function tests at baseline to participate in the study.\textsuperscript{14}

**Exclusion criteria for study**

Subjects who were taking lipid regulating drugs, hormone replacement therapy, immunosuppressive agents, or any drug that affects lipid concentrations, or drugs associated with rhabdomyolysis, including erythromycin, and cyclosporine, and those taking insulin, or hypoglycemic agents, or known to have an endocrine disease leading to a lipid abnormality were excluded from the study. A total of 83 subjects, 46 men and 37 women, entered the trial.\textsuperscript{14}

**Randomization of study**

All 83 subjects were given a screening physical exam and had fasting blood drawings on 2 occasions. Blood samples were analyzed in a biomarker laboratory of UCLA center for human nutrition. During week 1, placebo capsules were given to both groups to assess
compliance with pill taking. Food frequency questionnaires (FFQ) were completed before the randomization, and subjects were given an American Heart Association pamphlet instructing them in the step I diet (< 30% of energy from fat, and < 10% of energy from saturated fat, and < 300 mg cholesterol/d). Subjects were then assigned in a double blind fashion to receive capsules containing either rice powder placebo or 2.4 g of Red Yeast Rice daily. Placebo capsules resembled the RYR dietary supplement. The treatment group was given 600 mg of pulverized fermented RYR in a gelatin capsule by Pharmanex, Inc, Simi Valley CA.14

This study was double blind and randomized with 88 white subjects assigned to 2 treatment groups, focusing on lipid and nutrition. Lipid data was gathered twice at baseline and at weeks 8,9,11, and 12. The first 80 subjects were selected through the use of a random permuted block design; the remaining 8 subjects were randomly assigned by staff following the same randomized methods used for the first 8 subjects in the group of 80. The subjects who participated in the study had the following baseline characteristics, treatment group had a total of 42 individuals with an average triglyceride content of 133mg/dL in the treatment group compared to 143mg/dL in the placebo group. HDL in the treatment group was 50mg/dL compared to the HDL levels in the control group of 46mg/dL. LDL levels in the treatment group were 174mg/dL compared to LDL levels in the placebo group of 181mg/dL. Dietary intake was monitored through a food frequency questionnaire, which was reviewed at each visit. Dietary intake forms were used and gathered at each visit to determine the role of diet in conjunction with RYR to lower LDL. In the treatment group, baseline intake total energy in KJ was 6611, 6443 at week 8, and 5607 in week 12. The control group baseline total energy intake was 7448 at baseline, 6987 at week 8, and 6694 at week 12. The following were total fat (g/d) measured at baseline, week 8, and week 12 for the treatment
Results of study

The study demonstrated significant outcomes at week 8 and 12 in the RYR group (P<0.001). At the twelfth week, the mean LDL cholesterol concentration in RYR was 135 mg/dL compared to 175 mg/dL in the placebo treated group. The overall difference in LDL points dropped in the RYR group was 39 ± 19mg/dL, compared to the placebo group which dropped 5± 22 mg/dL. No side effects were noted for the Red Yeast Rice group. Dietary influences did not play a role in decreasing LDL levels as total energy intake and total fat consumption between the two groups were similar at baseline and week 8. Blood lipid differences between RYR and control group were evident at week 8. With this finding, the study concluded that differences in dietary intake cannot account for the decrease in cholesterol concentrations. There were no abnormal liver or renal function test results at any time for any subject under the study.14

Study 3

Lin et al15 conducted a study, demonstrating the effects of 1.2 grams of Monascus Purpureus Went Red Yeast Rice compared to placebo in an 8 week randomized, double blind, placebo controlled trial. The participants in each group constituted of male and females with equal percentages in both groups, mean age for all participating subjects were 46 years old, ranging from 23-65years. More than 80% of the participants had never smoked, and a high percentage of these participants had never had alcohol. Both groups had comparable BMI ranging from 23.4 kg/m^2 for the placebo group, and 24.3kg/m^2 for the
treatment group. Labs were drawn at baseline, and at each follow up visits. The labs drawn included LDL, HDL, triglycerides, apolipoproteins A-I and apolipoprotein B. These showed no significant differences between both groups during baseline

**Randomization**

Seventy nine patients (39 in treatment and 40 in placebo) were randomly assigned to groups, using the permuted-block randomization to categorize the subjects into two different groups. Each subject in each group received either Monascus Purpureus Went rice or placebo. The sample size was based on the efficacy outcome, and the standard deviation obtained from the change of LDL-C from both groups from baseline to week 8. Assumptions were made based on a two sided alpha (type I error) at 0.05 and the beta (type II error) at 0.10. With these values, an assumption was made that approximately 17 subjects in each group was needed to see a difference of 1mmol/L in mean LDL-C.

All individuals in this study participated in a 4 week trial of the American Heart Association step I diet. All 79 patients were instructed to continue this diet through the study, and were randomly assigned to 8 weeks of treatment with rice powder placebo or monascus purpureus Went rice. All patients received instructions from a registered dietician at every visit and all were contacted by phone weekly during the study. Participants were reviewed every 4 weeks and blood samples obtained. This study was double blind as the lab staffs were blinded to treatment, and received all blood samples labeled with name codes and dates.

The treatment group in this study received pulverized monascus purpureus Went rice placed in capsules by Y & B Pharmaceuticals Co. Ltd, Taipei, Taiwan. The study also demonstrated the composition of monascus purpureus used in the study. The placebo capsule
was made from grounded rice with food coloring to mimic the appearance of the RYR. Both RYR and placebo capsules were dispensed by the hospital pharmacy in identical containers marked with the participants name codes. All participants were instructed to take one capsule of 600 mg RYR or placebo twice daily, 30 minutes after breakfast and dinner for 56 days and to return the containers for capsule counts on each clinic visit.15

**Results of study**

This study focused on safety and efficacy by drawing labs every 4 weeks which included AST, ALT and CPK. After 4 weeks, the RYR group showed a 30.6% decrease in LDL compared to the placebo group which was less than a 1.5% drop. At 8 weeks, LDL levels for the Went RYR group were 27.7%, placebo was 1.5 %. Not only were LDL levels significantly decreased, but total cholesterol was reduced by 21% and triglycerides by 15.8 %. The study also focused on the negative side effects that were reported by each participant, and 21 of the 37 participants in the placebo group had adverse effects during the study. Only 3 of the 21 were non fatal drug related adverse effects. No fatal side effects were noted for the RYR treatment group.15

**DISCUSSION**

Of the studies reviewed, Red Yeast Rice has been seen to reduce low density lipoprotein cholesterol by significant amounts in comparison to a placebo group. All three studies reviewed emphasized lifestyle modifications in conjunction with Red Yeast Rice and the placebo groups. With these findings, it is clear that lifestyle modifications are needed to maximize the effects of RYR in its role to decrease LDL-C; however, each treatment group demonstrated significant decreases of LDL-C in comparison to their corresponding placebo
groups. An assumption can be made that the placebo groups accounted for dietary or lifestyle modifications alone. This finding within each study is sufficient in proving that dietary modification alone is not enough to lower LDL-C.

All three studies provided information regarding the components of the RYR used in their studies, and this is important as over the counter RYR found in the US and worldwide can have components which are similar if not identical to Lovastatin. Future studies need to focus on implementing the main components needed to lower LDL-C and specifications need to be made as to what these components are. So far, these have been characterized as 10 compounds of monacolin K.16

Each study included a chart reviewing the components of the Red Yeast Rice that was used during the specific study. Comparing all three studies and their treatment components, Becker’s study (study 1) demonstrated the highest percentage of monacolin K at 1.02 mg /capsule. Heber’s study compared a monacolin K content of 0.2% = 5 mg of RYR. In the study, this is equivalent to or comparable to 20-40 mg of lovastatin. Heber continues to explain that this minimal amount causes a dramatic and significant drop in cholesterol, therefore; it is not only the menacolin K content found, but rather, a combination of actions of multiple monacolins, with other substances found within the Red Yeast Rice.17

CONCLUSION

The question of whether Red yeast Rice is a suitable alternative to lower LDL-C in statin intolerant adults is an important and practical one for all health care providers. The current standard of care entails treating each patient with the best medical knowledge and with suitable resources where the patient will be able to afford medications. With patients
requiring multiple lipid lowering medications, and some failing the generic and inexpensive 
lovastatin, it is necessary for studies to continue to prove the safety and efficacy of Red Yeast 
Rice as a replacement for statin drugs such as pravastatin, simvastatin, atorvastatin or 
fluvastatin. It is in the best interest of the public to recommend a drug such RYR under the 
supervision of a physician who can routinely monitor liver enzymes and creatinine kinase 
levels to prevent myalgias and rhabdomyolysis.

Based on the results demonstrated by all studies reviewed in this paper, and the 
positive effects seen with the use of RYR for lowering LDL-C, further and larger sample size 
studies are clearly warranted. This topic is of great interest to our health care system as 
multiple co-morbidities are starting to arise in infancy, and young adults that are now 
w warranting the use of statins in younger generations. Statin induced myalgias are a serious 
clinical problem as more clinicians will continue to administer statins as first line treatment 
to prevent cardiovascular disease in patients with hyperlipidemia. Studies should focus on 
specifying the concentrations of RYR needed to adequately and safely decrease cholesterol 
without compromising the cholesterol lowering effects of RYR, as this is still a confusing 
factor for many individuals. Furthermore, more RTC need to be conducted that compare 
RYR to statins directly. For instance, one recent randomized, double blind trial study\textsuperscript{18} has 
demonstrated the comparison of pravastatin versus Red Yeast Rice in a population with statin 
induced myalgias, The results showed that RYR was as well tolerated as pravastatin in 
patients with a history of SAM (statin associated myalgias), both also showed similar levels 
of LDL-C reduction, and similar reduction rates of recurrent myalgias.
REFERENCES


### Tables

#### Table 1: Classification of LDL-C

<table>
<thead>
<tr>
<th>Initial classification</th>
<th>Total cholesterol and HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal LDL-C</td>
<td>Desirable total cholesterol</td>
</tr>
<tr>
<td></td>
<td>&lt;200 mg/dL</td>
</tr>
<tr>
<td>Near or above optimal LDL-C</td>
<td>Borderline high blood cholesterol</td>
</tr>
<tr>
<td></td>
<td>200-239 mg/dL</td>
</tr>
<tr>
<td>Borderline high – LDL-C</td>
<td>High blood cholesterol</td>
</tr>
<tr>
<td></td>
<td>&gt;240 mg/dL</td>
</tr>
<tr>
<td>Very high LDL –C</td>
<td>Low HDL – C</td>
</tr>
<tr>
<td></td>
<td>&lt;40 mg/dL – counted as a risk factor</td>
</tr>
<tr>
<td></td>
<td>High HDL – C</td>
</tr>
<tr>
<td></td>
<td>&gt;60 negative risk factor</td>
</tr>
</tbody>
</table>
### Table 2. Summary Matrix of Review articles

<table>
<thead>
<tr>
<th>Study</th>
<th>Yr. published</th>
<th>Patients/Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome(s)</th>
<th>Study type</th>
<th>Validity (Jadad score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker et al(^{12})</td>
<td>2009</td>
<td>Patients with dyslipidemia intolerant to statins due to myalgias</td>
<td>Red Yeast Rice</td>
<td>Placebo</td>
<td>Lowering of LDL cholesterol</td>
<td>Randomized controlled trial</td>
<td>4</td>
</tr>
<tr>
<td>Heber et al(^{14})</td>
<td>1999</td>
<td>American population consuming a similar diet to the American Heart Association.</td>
<td>Red Yeast Rice, diet providing 30% of energy from fat, &lt;10% sat fat, &lt;300 mg cholesterol daily.</td>
<td>Placebo</td>
<td>Total cholesterol, triacylglycerol, HDL, LDL cholesterol.</td>
<td>Double blind, placebo controlled porspective randomly randomized 12 week controlled trial</td>
<td>4</td>
</tr>
<tr>
<td>Lin et al(^{15})</td>
<td>2005</td>
<td>Adult patients with dyslipidemia.</td>
<td>Monascus Purpureus Went rice</td>
<td>Placebo</td>
<td>Lipid lowering effects on serum lipids LDL-C, total cholesterol, triglycerides and apolipoproteins B, HDL</td>
<td>Randomized double blind, placebo controlled study</td>
<td>3</td>
</tr>
</tbody>
</table>