**Polyphenols in Red Wine and Lipid-Lowering Levels**

**Introduction**

Polyphenols are a bioactive food component commonly found in red wines. They are a type of chemical that occurs naturally in plants, and there are over 500 different subcategories of polyphenols. 1 Types of polyphenols include flavonoids, phenolic acids, stilbenes, and ligands.1 Polyphenols can be found in fruits, vegetables, whole grains, nuts, seeds, legumes, beverages, fats, spices and seasonings. Some dietary sources that are a rich source of polyphenols may surprise you. Foods that are high in polyphenols include red wine, dark chocolate, cocoa powder, dried peppermint, spinach, berries, and virgin olive oil.1 Polyphenols play an important role as an antioxidant which protects the body from oxidative stress, inflammation, and cellular damage. As a bioactive component in food, polyphenols can have an effect on genes and gene expression.1 Many Mediterranean diets include a daily glass of red wine. Red wine is commonly known to have greater health benefits than white wine, one of the reasons for this is that the polyphenol concentration of red wine is greater than that of white wine. This is because in the process of making red wine the grape juice is fermented for a maximum of two weeks with the skin and seeds of the grape, while white wine is made by removing the grape juice from the skin and seeds.2 The amount of polyphenols in a wine depends on the type of grape used to make the wine, and the amount of time the grape’s skin is exposed to sunlight.2 The longer the grape is exposed to sunlight, the larger the quantity of polyphenols in the grape’s skin. Therefore, what is the effect of polyphenols from red wine on blood lipid levels? Many studies have followed the properties of polyphenols in red wine and the health benefits they have on the human body in regards to lowering lipid levels and helping prevent cardiovascular disease.

**Review of Literature**

In the first article, “Effects of acute and chronic red wine consumption on lipopolysaccharide concentrations,” there were a total of ten middle- aged male participants in the randomized, crossover, controlled trial.3 The time period of the study was from June 2010 to December 2010. Participants of the study were all adult men ranged from 45-50 years of age who were patients of the studies’ Endocrinology Department. All participants had their anthropometric measurements calculated as well as their glucose, triglycerides, cholesterol, HDL cholesterol, and LDL cholesterol levels. The first part of this study involved a 15- day baseline, washout period where participants were not allowed to consume any alcohol or red wine (RW). The next three parts of the study consisted of 20 days where the participants would drink only 272 mL/day of red wine (RW), 20 days of drinking 272 mL/day of dealcoholized red wine (DRW), and 20 days of drinking 100 mL/day of gin. After the washout period, a dietitian randomly assigned the participants to one of six diet sequences of the three drinks. The participants were not blinded to the beverages they consumed. The participants were randomly assigned to four different treatments. The Fat overload (FO) treatment required the participants to consume 50g of fat. Of the 50g of fat, 10g were saturated, 29.46g were monounsaturated, and 10.625g were polyunsaturated. With the FO treatment, participants were told to consume 272 mL of red wine, 272 mL of dealcoholized red wine, and 100 mL of gin with fat. After a baseline of three hours post consumption, a blood test was taken from the participants. The blood test analyzed cholesterol, triglycerides, and HDL cholesterol in a Dimension autoanalyzer. LDL cholesterol was calculated by using Friedewald’s formula. In addition, 24-hour urine samples were obtained from the patients in order to measure resveratrol metabolites to determine a biomarker of DRW and RW. The composition of the RW and DRW was the same. They were both made from Merlot grapes, both RW and DRW had the same polyphenolic compounds, except that DRW only had 0.42% ethanol. HPLC determined the phenolic profiles of both wines. The results of this study showed that there was not a significant difference the polyphenols of either wine. The researchers concluded that chronic consumption of RW (containing alcohol) leads to lower serum lipopolysaccharide concentrations (LPS) in men aged 45- 50 years. The study did not prove to show any evidence supporting that acute intake of red wine, dealcoholized red wine, or gin modified the LPS increased concentration induced by FO treatment.

 This article was thorough in design and explanation of how they conducted their study. The article had a detailed abstract that was concise, clearly stated the objective of the study, and gave a clear background of the information being studied. In addition, information was given to the reader in both table, and graph form. Despite the strengths of this article, there were many weaknesses that rendered it a rating of a weak or negative article. The study did not have a control group, had a significantly small sample size of 10 men, there was no blinding of the participants or researchers of the study, and only half of the references used for the study were up to date. Along with this, other weaknesses were that the conclusion was very confusing, and there should have been more washout periods in between each cross over to avoid carryover effects (however no carryover effect was reported). For these reasons, I gave this article a negative rating rendering it a weak article.

 In the second article, “Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: a randomized clinical trial,” there were a total of 67 male participants in the randomized, crossover trial.4 The duration of this trial extended from January 2008 to December 2010. All participants of the trial were adult men who consume moderate amounts of alcohol and were between the ages of 55 and 75 years, and who were at a high risk of getting cardiovascular disease. All participants were outpatients of the clinic of International Medicine Department of the study’s institution. The participants would not be allowed in the trial if they already had cardiovascular disease (CVD), human immunodeficiency virus infection, chronic liver disease, malnutrition, neoplastic or acute infectious diseases, and customary use of vitamins and supplements. Two weeks prior to the study the participants were advised to maintain their usual diet, and stop consuming alcoholic beverages. The dietitian then randomly assigned each patient to a specific diet intervention. The participants were informed to consume 100 mL/day of gin (containing 30g of ethanol), 272 mL/day of RW (containing 30g of ethanol, and 798mg of total polyphenols), or 272 mL/day DRW (containing1.14g of ethanol and 733mg of total polyphenols). The phenolic content of the beverages was measured using the Folin-Ciocalteu method, and the phenolic profile was determined by HPLC-DAD. The phenolic content of RW and DRW were the same. Gin contained no phenolic content. Fasting blood levels and 24-hour urine samples were taken and analyzed after each diet intervention. Participants had to fill out a 7-day food record that was analyzed by using ESHA in order to assess the nutrient intake of each subject. The results of the study showed that in regards to the lipid profile of the participants, the mean LDL-C concentrations decreased by 4.5% from baseline after the RW diet intervention. HDL-C concentrations increased from baseline after RW (+7%) and gin (+5%) diet interventions as compared to the DRW diet intervention. The research showed that LDL was decreased after the RW and gin dietary interventions. The mean lipoprotein concentration decreased by 12% after RW consumption compared to DRW and gin consumption. The evidence of this study supported the claim that a moderate intake of RW (containing alcohol-ethanol) has a beneficial effect on lipid and lipoprotein metabolism in men between the ages of 55 and 75 who are at a high risk of getting CVD.

 This article was very clear and specific in detail. Strengths of this article were that the sample size was big enough to promote validity, the information was presented in both table and text form, the limitations and potential conflicts of the study were discussed, and at least half of the references were up to date. Although the participants were not blinded to the study, the clinical investigators and laboratory technicians were. There was no wash out period but the researchers noted that there was no carry over effects in between diet interventions. The weaknesses of this article would be that there was no washout period and that there was a potential conflict of interest, however the article states that neither affected the study in any way. Overall this was a very strong article and I am rating it as positive.

 In the third article, “Changes in LDL Oxidative Status and Oxidative and Inflammatory Gene Expression after Red Wine Intake in Healthy People: A randomized Trial,” the main focus of the study was to compare the effects of LDL oxidative status after a consuming a McDonald’s meal (McDM), alone or consuming the McDM with 250 mL non-pruned vineyard red wine (NPVRW) that contained 30g of alcohol.5 The time line of this study is not listed. The 30 participants of this study were all healthy patients of the Section of Clinical Nutrition and nutrigenomic at the University of Rome between the ages of 18 and 65. The inclusion criteria which made the subjects eligible to be a part of this study required them to have a BMI of ≥ 19 Kg/m2. Participants were not allowed to participate in the study if they were pregnant, an active smoker, had arterial hypertension, a BMI > 30 kg/m2, acute or chronic diseases, autoimmune disease HIV/AIDS, neoplastic disease, intestinal disorders, vegetarianism, or use of antioxidants or vitamin supplement or any medication that could influence inflammation and oxidative stress. Participants of the study were not allowed to consume alcohol 15 days prior to the first diet intervention. At a baseline, the participants had their anthropometric and body composition measured and assessed by DXA. The bromatological composition of McDM was analyzed by a diet analyzer software package Dietosystem. The first part of the study focused on assessing the oxidative LDL levels after consuming 250 mL of NPVRW (containing 30g alcohol) alone or paired with a McDM. The second part of the study focused on assessing the changes of gene expression levels of 75 genes that were related to oxidative stress pathways (HOSp), 72 genes of human inflammation pathways (Hip), and 61 genes of Human Drug Metabolism (HDM) under the same conditions. This was controlled by repeating the analysis again after participants consumed 250 mL of NPVRW (containing 30g alcohol), with respect to baseline. There were 4 total sections of the study: baseline, McDM, McDM + 250 mL NPVRW, and 250 mL NPVRW. After each section of the study was complete, it was followed by a three- week washout period. Blood samples (10 mL) were taken at baseline and measured fasting glucose, HDL cholesterol, LDL cholesterol, triglycerides, aspartate aminotransferase (AST), alanine transaminase (ALT), creatinine, fibrinogen, and C-reactive protein (CRP) levels. Oxidative LDL levels in the blood were measured by enzyme linked immunosorbent assay. The results of the study showed that there was a decrease in oxidative LDL levels after consuming the beverages containing polyphenols, there were higher amounts of trans-resveratrol after consuming NPVRW, and after consuming McDM with RPVRW there was a statistically significant decrease in oxidative LDL levels than after consuming McDM alone. The results of this study concluded that consuming red wine (enriched with resveratrol) leads to lower postprandial oxidative LDL levels and lowers inflammation and oxidative stress related genes in healthy people.

 This article had an equal amount of strengths and weaknesses, therefore, I rated this article as Neutral. The main strengths of this article was that the information was presented in multiple formats including, text, graphs, diagrams, and tables. The information was very thorough and detailed, especial when explaining how they took specific measurements, such as anthropometric measurements, from the participants. The study could easily be duplicated because of how precise and detailed the article was. Another strength was that the study talked about their limitations and mentioned how they did not affect the outcome of the study. Some neutral aspects of the article were that half of the references were up to date for the study, the sample size was 30 participants which is just big enough to promote validity. The weaknesses of the study were that the abstract was confusing to read and understand, it was difficult to find the final conclusion of the study, the sample of participants was too generalized in both age and gender, and the duration of the study is unclear.

 In the fourth article, “A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis: results from a randomized controlled trial,” was an un-blinded trial that studied the effect red wine had on lipid-lowering levels in 108 carotid atherosclerosis patients from June 4th, 2009 to October 10th 2011.6 The participants of this study were all out-patients of the Neurology department of the Centre Hospitalier de Luxembourg who had received carotid and intracranial bi-temporal color coded duplex sonography using an Antares system. The participants of the study were between the ages of 37 and 83, of which 36 were women and 72 were men. In order to be a part of the study the participants had to be over 30 years of age, and had plaques or stenosis without hemodynamic compromise in at least one common carotid artery, the carotid bifurcation, or the internal carotid artery. Participants were not allowed to participate in the study if they had a history of ocular or cerebral ischemia, atrial fibrillation, or if they did not give informed consent. The participants were randomly assigned to different “life style” groups. The first group did not receive any lifestyle counseling (LC) and therefore did not change their daily routine (this was the control group), while the second group had lifestyle counseling at the beginning of the trial, and again after week 1,2,3, and 4. The participants of group that had lifestyle counseling were randomly assigned to either consume 1 glass of any red wine of their choosing, or to avoid consuming alcohol completely. The lifestyle counseling was performed by a dietitian who advised the participants on eating healthy based off of the Mediterranean diet, and physical activity. Anthropometric measurements of each participant were recorded, and physical activity was measured using a questionnaire. Blood samples, of the participants, were taken at a baseline of 4 and 20 weeks. A Modular P module was used to measure and analyze total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. Enzymatic colorimetric assays were used to determine total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides. The results of the study showed that after 20 weeks, LDL levels were significantly lowered by 7%, LDL/HDL ratio was lowered by 8%, red wine independently was lowered by 13%, total cholesterol was lowered by 6%, and triglycerides were lowered by 13% in the LC group as compared to the group with no lifestyle counseling. The study concluded that lifestyle changes including a modified Mediterranean diet and physical activity as well as a daily glass of red wine improve independently the LDL/ HDL ratio in patients who suffer from carotid arteriosclerosis.

 This article was outstanding compared to the other three that I reviewed. It was written clearly and concisely, and presented information in the form of text, diagram, table, and graphs. The diagrams in this article were extremely clear and easy to understand, but were not lacking in information. Other strengths of this article were that the abstract was clearly written out and the conclusion was direct and concise. The sample size of this article was large enough to promote validity. Every part of this article was written out clearly and meticulously. The Limitations of the article were discussed and the researchers noted that the potential limitations would have no effect on the study, overall. The only weakness I can report for this article was that there was no blinding used. Therefore, I am positively rating this article as exceptionally strong.

**Summary and Conclusion**

Polyphenols are a bioactive food component found in foods such as red wine, dark chocolate, and certain vegetables.1 The articles that I reviewed focused on the polyphenols that come specifically form red wine and how they effected human lipid levels. From the articles I reviewed, the research expanded on the idea that polyphenols in red wine can lower blood lipid levels. The first article found that chronic consumption of RW, that contains alcohol, leads to lower serum lipopolysaccharide concentrations in men between the ages of 45 and 50.3 The second article found that a moderate intake of red wine, that contained alcohol (ethanol), had a beneficial effect on lipid and lipoprotein metabolism in men between the ages of 55 and 75 who are at a high risk for getting CVD.4 The third article found that consuming red wine, that was enriched with resveratrol, leads to lower postprandial oxidative LDL levels and lowers inflammation and oxidative stress related to genes in healthy people.5 Finally, the fourth article found that lifestyle changes including a modified Mediterranean diet and physical activity as well as a daily glass of red wine improve independently the LDL/HDL ratio in patients who suffer from carotid arteriosclerosis.6 Overall the evidence showed that polyphenols in red wine do have a beneficial impact on lowering lipid levels in adults. More research is needed on this topic in order to generalize the statement to all people instead of certain groups of people who were tested in these studies.

 After gathering information from my background research and the four articles that I reviewed, I found that these articles supported my thesis stating that the polyphenols in red wine have a beneficial effect on lowering blood lipid levels. The benefit of consuming polyphenols (specifically from red wine) in relation to genes, is that it lowers oxidative stress markers, inflammation, and lowers LDL cholesterol levels.5 This results in a lowered risk of getting CVD. However, a risk of consuming polyphenols from red wine, is that if heavily overconsumed, because of the alcohol contend of red wine, it can lead to alcoholism. Overall, the information from the trials that I reviewed had enough information to support the claim that all adult people should be consuming polyphenols from at least one glass of red wine daily in order to help prevent CVD by decreasing lipid levels in the blood.

**References**

1. Ware, M. Why are polyphenols good for you. Medical News Today Website. <https://www.medicalnewstoday.com/articles/319728.php>. Updated October 18, 2017. Accessed 3 April, 2018.

2. Cordova, A.C., & Sumpio, B.E. (2009). Polyphenols are medicine: Is it time to prescribe red wwwwwine for our patients? *The International Journal of Angiology: Official Publication of wwwwthe International College of Angiology, Inc, 18*(3), 111-117.

3. Clemente-Postigo M, Queipo-Ortuño MI, Boto-Ordoñez M, et al. Effect of acute and chronic red wine consumption on lipopolysaccharide concentrations. *Am J Clin Nutr.*2013;97(5):1053-1061.

4. Chiva-Blanch G, Urpi-Sarda M, Ros E, et al. Effects of red wine polyphenols and alcohol on glucose metabolism and the lipid profile: a randomized clinical trial. *Clin Nutr.*2013;32(2):200-206.

5. Di Renzo L, Marsella LT, Carraro A, et al. Changes in LDL Oxidative Status and Oxidative and Inflammatory Gene Expression after Red Wine Intake in Healthy People: A Randomized Trial. *Mediators Inflamm.*2015;2015:317348.

6. Droste DW, Iliescu C, Vaillant M, et al. A daily glass of red wine associated with lifestyle changes independently improves blood lipids in patients with carotid arteriosclerosis: results from a randomized controlled trial. *Nutr J.*2013;12(1):147.