

INTERNATIONAL TREE NUT COUNCIL
NUTRITION RESEARCH & EDUCATION FOUNDATION

LISTING OF TREE NUT RESEARCH REFERENCES

(Last updated 9-18-08)

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MIXED TREE NUT REFERENCES

CANCER AND ANTIOXIDANT ACTIVITY

American Institute for Cancer Research, 1997. World Cancer Research Fund. **Food, Nutrition and the Prevention of Cancer: A Global Perspective. Nuts and Seeds.** 450-1.

Since the early '80s, a number of expert reports have reviewed the literature on diet and cancer and made recommendations designed to reduce the risk of cancer. The report, of which this is a summary, builds on that earlier work. The experts recommend that populations consume nutritionally adequate and varied diets, based primarily on foods of plant origin. They specifically recommend that the public choose predominantly plant-based diets rich in a variety of vegetables and fruits, legumes and minimally processed starchy staple foods. The report notes, "While there are as yet no useful epidemiological data on nuts and seeds, it is biologically plausible that diets high in specific nuts and seeds or these foods as a whole, protect against cancers."

Bruce, B., G.A. Spiller, L.M. Klevay, S.K. Gallagher, 2000. **A diet high in whole and unrefined foods favorably alters lipids, antioxidant defenses and colon function.** *J Clin Nutr.* 19(1): 61-7.

Diets rich in whole and unrefined foods such as nuts, contain high amounts of antioxidant phenolics, fibers and numerous other phytochemicals that may be protective against chronic diseases. This study compared the effects of a phytochemical-rich diet to a refined-food diet on lipoproteins, antioxidant defenses and colon function. Twelve hyperlipidemic women followed 2 diets for 4 weeks starting with a refined-food diet, and then crossing over directly to the phytochemical-rich diet. Fasting serum lipids and antioxidant enzymes were measured at the end of each period. The results showed that total calories and fat intake were similar in both diet periods, but saturated fat decreased by 61%, total cholesterol by 13% and LDL by 16% in the phytochemical-rich diet group. Dietary fiber, vitamin E, vitamin C and carotene intakes were 160%, 145%, 160% and 500% more, respectively, than during the refined-food diet period. In conclusion, a diet high in phytochemical-rich foods positively affected lipoproteins, decreased the need for oxidative defense mechanisms and improved colon function.

Hebert, J.R., T.G. Hurley, B.C. Olendzki, J. Teas, Y. Ma, J.S. Ha, 1998. **Nutritional and socioeconomic factors in relation to prostate cancer mortality: a cross-national study.** *J Natl Cancer Inst.* 90:1637-47.

This study included data for men ages 45-74 years from 59 countries. As the consumption of nuts and oilseeds increased, prostate cancer mortality decreased.

Jain, M.G., G.T. Hislop, G.R. Howe, P. Ghadirian, 1999. **Plant foods, antioxidants and prostate cancer risk: findings from case-control studies in Canada.** *Nutr and Cancer.* 34(2):173-84.

This study, which looked at data from three case-control studies involving 1,253 subjects followed for five years, revealed a decreased risk for prostate cancer with an increased intake of beans/lentils/nuts. The inverse effect of the latter may be due to their phytoestrogen content.

Jenab, M., et al., 2004. **Association of nut and seed intake with colorectal cancer risk in the European prospective investigation into cancer and nutrition.** *Cancer Epidemiol Biomarkers Prev.* 13(10):1595-603.

This study looked at the effect of nut and seed intake on colorectal cancer in men and women. Total nut intake was determined from country-specific dietary questionnaires for 855 (327 men, 528 women) colon cancer cases, 474 (215 men, 259 women) rectal cancer cases, and 478,040 (141,988 men, 336,052 women) total subjects. Division of the data into colon and rectal cancers showed a significant protective effect of nut intake on colon cancer in females at the highest quintile of intake, which was greater than six grams daily. The results showed a significant protective effect of increased nut intake on colon cancer in women, with no effects on rectal cancer for either gender.

Kune, S., G.A. Kune, L.F. Watson, 1987. **Case-control study of dietary etiological factors: the Melbourne colorectal cancer study.** *Nutr Cancer.* 9:21-42.

This study compared 715 cases with 727 age- and sex-matched community controls. The combination of a high-fiber and high-vegetable intake was found to be protective against large bowel cancer as well as colon and rectal cancers. Pulses, nuts and seeds were one of the groups analyzed and shown to have possible protective effects.

Mills, P.K., W.L. Beeson, R.L. Phillips, G.E. Fraser, 1989. **Cohort study of diet, lifestyle, and prostate cancer in Adventist men.** *Cancer.* 64:598-604.

In a 6-year prospective study researchers looked at the effect of diet and lifestyle on the incidence of prostate cancer in a cohort of approximately 14,000 Seventh-day Adventist men. Strong protective relationships were seen with increasing consumption of dried beans, lentils, fresh citrus fruit, raisins, dates and other dried fruit, nuts and tomatoes.

Pickle, L.W., M.H. Greene, R.G. Ziegler, A. Toledo, R. Hoover, H.T. Lynch, J.F. Fraumeni, Jr., 1984. **Colorectal cancer in rural Nebraska.** *Cancer Research.* 44:363-9.

A case-control interview study of colorectal cancer was conducted in eastern Nebraska to determine reasons for the elevated colon cancer mortality rates during 1950 to 1969. Information provided by 86 colorectal cancer cases was compared to 176 matched controls. The data suggest ancestry and certain dietary patterns may be associated with the colon cancer in this region. Nuts and legumes were associated with a lower incidence of colon cancer.

Singh, P.N., G.E. Fraser, 1998. **Dietary risk factors for colon cancer in a low-risk population.** *Am J Epidemiol.* 148:761-74.

In a 6-year prospective study, researchers looked at the relation between diet and incidence of colon cancer in 32,051 non-Hispanic white cohort members of the Adventist Health Study who, at baseline, had no documented or reported history of cancer. Those who ate nuts more than 4 times per week had a lower incidence of colon cancer than those who never ate nuts or ate them 1-4 times per week.

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CARDIOVASCULAR

Abbey, M., M. Noakes, G.B. Belling, P.J. Nestel, 1994. **Partial replacement of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol.** *Am J Clin Nutr.* 59:995-9.

This study involved 16 normolipidemic men in a consecutive, supplemental field study that lasted for three, 3-week dietary periods. During the first three weeks, subjects consumed a reference diet that included a background diet supplemented with 50g/day of peanuts, 40g/day of coconut, and 50g/day of a coconut confectionary bar. During the second three weeks, subjects consumed the background diet supplemented with almonds (84g/day) and during weeks 7-9, subjects consumed the background diet supplemented with walnuts (68g/day). The almond diet lowered total cholesterol by 7% and LDL by 10%, while the walnut diet lowered total cholesterol by 5% and LDL by 9%. Neither diet had a significant effect on HDL or triglycerides.

Albert, C.M., M. Gaziano, W.C. Willett, J.E. Manson, 2002. **Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study.** *Arch. Intern. Med.* 162:1382.

This study, with 21,454 male participants enrolled in US Physicians' Health Study, prospectively assessed whether increased frequency of nut consumption, as ascertained by an abbreviated food frequency questionnaire at 12 months of follow-up, was associated with a lower risk of sudden cardiac death and other coronary heart disease end points. Compared with men who rarely or never consumed nuts, those who consumed nuts 2 or more times per week had a 47 percent lower risk of sudden cardiac death and a 30 percent lower risk of total coronary heart disease death.

Appel, L.J., et al., 1997. **A clinical trial of the effects of dietary patterns on blood pressure.** *NEJM.* 336:1117-24.

In this study, Dietary Approaches to Stop Hypertension (DASH), researchers looked at the effects of dietary patterns on blood pressure in 459 adults with systolic blood pressures less than 160 mm Hg and diastolic blood pressures of 80 to 95 mm Hg. For three weeks subjects were fed a control diet that was low in fruits, vegetables and dairy products, with a fat content typical of the average US diet. They were then randomly assigned to receive the control diet, a diet rich in fruits and vegetables, or a "combination" diet rich in fruits, vegetables and low-fat dairy products and with reduced saturated fat and total fat. Sodium intake and body weight were maintained at constant levels. The results showed that a "combination" diet rich in fruits,

vegetables and low-fat dairy foods, and with reduced total and saturated fat can significantly lower blood pressure.

One and one-half ounces of nuts, or 1/3 cup, are recommended 4-5 times per week (as part of the nuts, seeds and legumes group) in the DASH eating plan, primarily due to the fact that they are rich sources of energy, magnesium, potassium, protein and fiber.

Berry, E.M., S. Eisenberg, Y. Friedlander, D. Haratz, N.A. Kaufmann, Y. Norman, Y. Stein, 1992. **Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins – the Jerusalem Nutrition Study. II monounsaturated fatty acids vs. carbohydrates.** *Am J Clin Nutr.* 56:394-403.

Seventeen male students were randomly assigned to a crossover study with two 12-week dietary periods of monounsaturated fatty acids (MUFA) versus a carbohydrate (CHO)-rich diet, while polyunsaturated (PUFA) and saturated fatty acids (SFA) were kept similar. (Nuts are rich in MUFAs and PUFAs).

Berry, E.M., S. Eisenberg, D. Haratz, Y. Friedlander, Y. Norman, N.A. Kaufmann, Y. Stein, 1991. **Effects of diets rich in monounsaturated fatty acids on plasma lipoproteins – the Jerusalem Nutrition Study: high MUFAs vs. high PUFAs.** *Am J Clin Nutr.* 53:899-907.

The Jerusalem Nutrition Study was a randomized, controlled crossover study involving 18 young men that examined the effects of a high mono-unsaturated fat (MUFA) diet (including almonds, olive oil and avocado) versus a high polyunsaturated fat (PUFA) diet (including walnuts, safflower and soy oils) during two 12-week dietary periods. The MUFA diet lowered total cholesterol by approximately 10% and LDL by 14% compared to baseline values, while the PUFA diet lowered total cholesterol by 16% and LDL by 21%. There were no significant effects on HDL or triglycerides.

Bruce, B., G.A. Spiller, 1997. **Nuts and healthy diets.** *Veg Nutr: An Int J.* 1(1):12-16.

Since ancient times, nuts and seeds have been considered healthful foods worldwide. This paper looks at the history and composition of a variety of nuts, and their effects on health, particularly heart disease. According to the authors, “nuts are an under-recognized and under-consumed food in modern diets.” Nuts provide a variety of nutrients and can play an important role in the diet, especially for those who are eating a more plant-based diet.

Bruce, B., G.A. Spiller, L.M. Klevay, S.K. Gallagher, 2000. **A diet high in whole and unrefined foods favorably alters lipids, antioxidant defenses, and colon function.** *J Am Coll Nutr.* 19(1):61-7.

This study involved 12 hyperlipidemic women in a crossover design that lasted for two 4-week periods. Subjects first consumed a refined-food diet and then switched to a phytochemical-rich diet primarily consisting of whole grains, legumes, fruits, vegetables, seeds and two tablespoons of almonds, hazelnuts or pecans per day. Compared to the refined-food diet, the phytochemical-rich diet lowered total cholesterol by 13% and LDL by 16% with no significant changes in HDL or triglycerides.

Bruce, B., G.A. Spiller, J.W. Farquhar, 1997. **Effects of a plant-based diet rich in whole grains, sun-dried raisins and nuts on serum lipoproteins.** *Veg Nutr.* 1(2):58-63.

After four weeks of a diet rich in whole grains, sun-dried raisins and nuts, researchers saw an improvement in total and LDL cholesterol levels in 15 adults with elevated blood lipids. Both improved colon function and increased feelings of fullness were also seen with this plant-based diet containing unrefined, minimally processed foods. Further research is needed to identify additional positive effects of this diet on heart disease risk factors.

Colquhoun, D.M., 2000. **Food for prevention of coronary heart disease: Beyond the low fat, low cholesterol diet.** *Asia Pacific J Clin Nutr.* 9(suppl):S86-90.

Coronary heart disease (CHD) is now the single major cause of death worldwide. A low fat diet is almost universally recommended throughout the world. However, the most successful secondary prevention diet trials have used modification of fat, rather than just a decrease in total fat. For example, the Mediterranean-type diet, rich in antioxidants, fiber, nuts and wine, has been shown to help decrease LDL oxidation and improve endothelial function over the NCEP Step 2 diet. Therefore, until more research is done, the author recommends giving patients the choice of alternatives to a low fat diet, such as healthy cardioprotective cuisines from Greece, Spain, southern Italy, etc.

Cooke, J.P., P. Tsao, A. Singer, B.Y. Wang, J. Kosck, H. Drexler, 1993. **Anti-atherogenic effect of nuts: is the answer NO?** *Arch Intern Med.* 153:896, 899, 902.

In a commentary regarding the Seventh Day Adventist study, the authors highlight the fact that frequent nut consumption reduced the risk of experiencing fatal or nonfatal heart attacks by 50%. A possible explanation for the protective effect may be that nuts are high in arginine, a basic amino acid that is a precursor to nitric oxide (NO). The latter is known to inhibit plaque formation, or atherogenesis, which can lead to heart attacks. Studies have shown that people with hypercholesterolemia have reduced activity of NO. Adding arginine-rich nuts to the diet may help increase NO activity and thereby reduce the risk of heart attacks.

de Lorgeril et al, 1994. **Mediterranean alpha-linolenic acid-rich diet in secondary prevention of heart disease.** *Lancet.* 343(8911):1454-9

This study, also known as the Lyon Heart Study, is a prospective, randomized single-blinded secondary prevention trial with 605 subjects. The results showed essential fatty acids (EFAs) in the blood reduce clotting and inflammation, cutting risk for sudden heart attack and clogging of the arteries. Two grams of alpha-linolenic acid on a modified Crete Mediterranean diet reduced total death by 70%.

de Lorgeril, M., P. Salen, J-L. Martin, I. Monjaud, J. Delaye, N. Mamelle, 1999. **Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction. (Final report of the Lyon diet heart study.)** *Circulation.* 99:779-85.

This study presents findings from an extensive follow-up to the Lyon Diet Heart Study, a randomized secondary prevention trial that looked at whether a Mediterranean type diet (which

included nuts) could reduce the rate of recurrence after a first heart attack. An intermediate analysis showed a positive effect after 27 months of follow-up, this study looked at a mean of 46 months of follow-up per patient. The results showed a protective effect of the Mediterranean diet up to 4 years after the first heart attack. Major traditional risk factors, such as high blood pressure and high cholesterol, were shown to be independent and joint predictors of recurrence, indicating that the Mediterranean diet did not alter, qualitatively, the usual relationships between major risk factors and recurrence. The researchers concluded that a comprehensive strategy to decrease risk of cardiovascular morbidity and mortality should include a cardioprotective diet. This should be associated with other means (i.e., medications) aimed at reducing modifiable factors.

de Lorgeril, M., P. Salen, F. Laporte, F. Boucher, J. De Leiri, 2001. **Potential use of nuts for the prevention and treatment of coronary heart disease: From natural to functional foods.** *Nutr Metab Cardiovasc Dis.* 11:362-71.

This editorial discusses the research on nuts and coronary heart disease (CHD) and suggests that before using food technology to develop new and artificial foods to help patients follow what they think would be an “optimal diet,” scientists and physicians should first refer to the traditional diets of populations with low CHD rates. Studying the effect of natural or whole foods, such as nuts, should be a priority. According to the authors, natural foods are still the preferred functional foods because they may provide a better nutrient profile than any recomposed food, and the proportions of the various nutrients and non-nutrients are the result of a natural, and biologically compatible, evolution and not of an industrial process.

Dreher, M. L., Maher, C. V., Kearney, P. 1996. **The traditional and emerging role of nuts in healthful diets.** *Nutrition Reviews* 54:241.

This paper reviews the role of nuts throughout history and highlights the nutritional benefits of nuts, as well as the connection between frequent nut consumption and reduced incidence of coronary heart disease.

Durlach, J., Y. Rayssiquier, 1993. **Fatty acid profile, fiber content and high magnesium density may protect against risk of coronary heart disease events.** *Magnes Res.* 6:191-2.

Ellsworth, J.L., L.H. Kushi and A.R. Folsom, 2001. **Frequent nut intake and risk of death from coronary heart disease and all causes in postmenopausal women: The Iowa Women’s Health Study.** *Nutr Metab Cardiovasc Dis.* 11:372-7.

This study looked at whether or not the risk of death due to coronary heart disease (CHD) and all causes is reduced in postmenopausal women who frequently consume nuts. In 1986, 34,111 postmenopausal women with no known cardiovascular disease reported the frequency of their consumption of nuts and other foods. After 12 years of follow-up, there was an inverse but not statistically significant association between frequent nut consumption (2 or more 1-ounce servings per week compared with less than one serving per month) and death from CHD. There was also a weak inverse association between frequent nut intake and all-cause mortality. In conclusion, frequent nut consumption may offer modest protection against the risk of death from all causes and CHD in postmenopausal women.

Estruch, R., M.A. Martínez-González, D. Corella, J. Salas-Salvadó, V. Ruiz-Gutiérrez, M.I. Covas, M. Fiol, E. Gómez-Gracia, M.C. López-Sabater, E. Vinyoles, F. Arós, M. Conde, C. Lahoz, J. Lapetra. G. Sáez, E. Ros for the PREDIMED Study, 2006. **Effects of a Mediterranean-style diet in cardiovascular risk factors: A randomized trial.** *Annals of Internal Medicine.* 145:1-11.

This substudy of a multicenter, randomized, primary prevention trial of cardiovascular disease compared the short-term effects of 2 Mediterranean diets versus those of a low-fat diet on intermediate markers of cardiovascular risk. Participants (772 asymptomatic persons 55 to 80 years of age at high cardiovascular risk) were assigned to a low-fat diet (n=257) or to 1 of 2 Mediterranean diets. Those allocated to Mediterranean diets received nutritional education and either free virgin olive oil, 1 liter per week (n=257), or free nuts, 30 g/d (n=258). The authors evaluated outcome changes at 3 months: body weight, blood pressure, lipid profile, glucose levels, and inflammatory molecules. The results showed that compared with the low-fat diet, the 2 Mediterranean diets produced beneficial changes in most outcomes. Compared with the low-fat diet, the mean changes in the Mediterranean diet with olive oil group and the Mediterranean diet with nuts group were -0.39 mmol/L (95% CI, -0.70 to -0.07 mmol/L) and -0.30 mmol/L (CI, -0.58 to -0.01 mmol/L), respectively, for plasma glucose levels; -5.9 mm Hg (CI, -8.7 to -3.1 mm Hg) and -7.1 mm Hg (CI, -10.0 to -4.1 mm Hg), respectively, for systolic blood pressure; and -0.38 (CI, -0.55 to -0.22) and -0.26 (CI, -0.42 to -0.10), respectively, for the cholesterol–high-density lipoprotein cholesterol ratio. The Mediterranean diet with olive oil reduced C-reactive protein levels by 0.54 mg/L (CI, 1.04 to 0.03 mg/L) compared with the low-fat diet. Limitations: This short-term study did not focus on clinical outcomes and the nutritional education about low-fat diet was less intense than education about Mediterranean diets. The researchers concluded that compared with a low-fat diet, Mediterranean diets supplemented with olive oil or nuts have beneficial effects on cardiovascular risk factors.

Fitó, M., M. Guxens, D. Corella, G. Sáez, R. Estruch, R. de la Torre, F. Francés, C. Cabezas, M. del C. López-Sabater, J. Marrugat, A. García-Arellano, F. Arós, V. Ruiz-Gutierrez, E. Ros, J. Salas-Salvadó, M. Fiol, R. Solá, M.I. Covas; for the PREDIMED Study, 2007. **Effect of a traditional Mediterranean diet on lipoprotein oxidation: a randomized controlled trial.** *Arch Intern Med.* 167:1195-203.

A total of 372 subjects at high cardiovascular risk (210 women and 162 men; age range, 55-80 years), who were recruited into a large, multicenter, randomized, controlled, parallel-group clinical trial (the Prevenció n con Dieta Mediterrá nea [PREDIMED] Study) directed at testing the efficacy of the traditional Mediterranean diet (TMD) on the primary prevention of coronary heart disease, were assigned to a low-fat diet (n=121) or one of 2 TMDs (TMD + virgin olive oil or TMD + nuts). The TMD participants received nutritional education and either free virgin olive oil for all the family (1 L/wk) or free nuts (30 g/d). Diets were ad libitum. Changes in oxidative stress markers were evaluated at 3 months. The results after the 3-month interventions showed mean (95% confidence intervals) oxidized low-density lipoprotein (LDL) levels decreased in the TMD + virgin olive oil (-10.6 U/L [-14.2 to -6.1]) and TMD + nuts (-7.3 U/L [-11.2 to -3.3]) groups, without changes in the low-fat diet group (-2.9 U/L [-7.3 to 1.5]). Change in oxidized LDL levels in the TMD + virgin olive oil group reached significance vs that of the low-fat group (P=0.02). No changes in serum glutathione peroxidase activity were observed. The researchers concluded that individuals at high cardiovascular risk who improved their diet toward a TMD pattern showed significant reductions in cellular lipid levels and LDL oxidation. Results provide further evidence to recommend the TMD as a useful tool against risk factors for CHD.

Fraser, G.E., 1999. **Nut consumption, lipids and risk of a coronary event.** *Clin Cardiol.* 22(suppl. III):11-5.

The author gives an overview on the benefits of consuming nuts stating, “Four of the best and largest cohort studies in nutritional epidemiology have now reported that eating nuts frequently is associated with a decreased risk of coronary heart disease of the order of 30-50%.” He explains that possible mechanisms include the reduction of LDL cholesterol, the effects on the endothelium and platelet function of higher levels of nitric oxide, as well as the antioxidant properties of vitamin E.

Fraser, G.E., 1994. **Diet and coronary heart disease: beyond dietary fats and low-density-lipoprotein cholesterol.** *Am J Clin Nutr.* 59(suppl):1117S-23S.

For years researchers have been studying the effects of dietary fats and cholesterol on blood cholesterol levels, particularly LDL cholesterol levels. However, little attention has been given to the possible protective effect of specific foods. For example, nuts are high in unsaturated fats, which can lower total blood cholesterol and improve the lipoprotein profile; vitamin E in almonds and hazelnuts may prevent oxidation of LDL cholesterol (oxidized LDL can increase the risk of heart disease); fiber and plant sterols in nuts may lower LDL cholesterol; and magnesium and copper in nuts may also protect against heart disease.

Fraser, G.E., J. Sabaté, W.L. Beeson, T.M. Strahan, 1992. **A possible protective effect of nut consumption on risk of coronary heart disease.** *Arch Intern Med.* 152:1416-24.

This cohort investigation with 31,208 Seventh-day Adventists, which began in 1974, included detailed investigation of diet. Subjects who consumed nuts more than four times per week experienced substantially fewer definite fatal CHD events and definite nonfatal heart attacks than those who consumed nuts less than once per week. The results showed that nut consumption may reduce the risk of both fatal and nonfatal coronary heart disease.

Hu, F.B., 2003. **Plant-based foods and prevention of cardiovascular disease: an overview.** *Am J Clin Nutr.* 78:544S-51S.

This article highlights the benefits of plant foods, particularly nuts, in the prevention of heart disease. Nuts are high in unsaturated fats as well as important vitamins and minerals, which may provide the protective effects.

Hu, F.B., M.J. Stampfer, 1999. **Nut consumption and risk of coronary heart disease: a review of epidemiologic evidence.** *Current Atherosclerosis Reports.* (1):205-10.

This article proved an overview of the epidemiologic studies done on nuts and coronary heart disease. Given the strong evidence of the beneficial effects of nuts, the author recommends moving nuts to a “more prominent place” in the USDA Food Guide Pyramid.

Hu, F.B., M.J. Stampfer, J.E. Manson, E.B. Rimm, G.A. Colditz, B.A. Rosner, F.E. Speizer, C.H. Hennekens, W.C. Willett, 1998. **Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study.** *British Med J.* 317:1341-5.

In this study, investigators analyzed links between diet and heart disease that showed up between 1980 and 1990, among 86,000 female nurses, ages 34-59. The researchers found that those who ate more than five ounces of nuts per week had one-third fewer heart attacks than those who rarely or never ate nuts. These data, and those from other epidemiological and clinical studies, support a role for nuts in reducing the risk of coronary heart disease. Preliminary results from the companion Physician's Health Study suggest that frequent nut consumption may provide similar benefits to men.

Jenkins, D.J.A., D.G. Popovich, C.W.C. Kendall, E. Vidgen, N. Tariq, T.P.P. Ransom, T.M.S. Wolever, V. Vuksan, C.C. Mehling, D.L. Boctor, C. Bolognesi, J. Huang, R. Patten, 1997. **Effect of a diet high in vegetables, fruit, and nuts on serum lipids.** *Metabolism.* 46(5):530-7.

This study involved 10 adults in a randomized crossover design that lasted for two 2-week periods. The control diet was the subjects' habitual diet. The study diet consisted of mainly vegetables, fruit, avocados and nuts (limited to 60-120g/day, average consumption was 100g/day). Compared to the control diet, total cholesterol was reduced by approximately 25%, LDL by 33% and triglycerides by 20%, with no significant change in HDL.

Jiang, R., D.R. Jacobs, Jr., E. Mayer-Davis, M. Szkio, D. Herrington, N.S. Jenny, R. Kronmal, R. G. Barr, 2006. **Nut and seed consumption and inflammatory markers in the multi-ethnic study of atherosclerosis.** *Am J Epidemiol.* 163:222-231.

Nuts and seeds are rich in unsaturated fat and other nutrients that may reduce inflammation. Frequent nut consumption is associated with lower risk of cardiovascular disease and type 2 diabetes. The authors examined associations between nut and seed consumption and C-reactive protein, interleukin-6 and fibrinogen in the Multi-Ethnic Study of Atherosclerosis. This 2000 cross-sectional analysis included 6,080 US participants aged 45-84 years with adequate information on diet and biomarkers. Nut and seed consumption was categorized as never/rare, less than once/week, 1-4 times/week and five or more times/week. After adjustments for age, gender, race/ethnicity, site, education, income, smoking, physical activity, use of fish oil supplements, and other dietary factors, mean biomarker levels in categories of increasing consumption were as follows: C-reactive protein-1.98, 1.97, 1.80, and 1.72 mg/liter, interleukin-6 – 1.25, 1.24, 1.21 and 1.15 pg/ml; and fibrinogen-343, 338, 338, and 331 mg/dl (all p's for trend < 0.01). Further adjustment for hypertension, diabetes, medication use, and lipid levels yielded similar results. Additional adjustment for body mass index moderately attenuated the magnitude of the associations, yielding borderline statistical significance. Associations of nut and seed consumption with these biomarkers were not modified by body mass index, waist:hip ratio, or race/ethnicity. Frequent nut and seed consumption was associated with lower levels of inflammatory markers, which may partially explain the inverse association of nut consumption with cardiovascular disease and diabetes risk.

Key, T., G. Fraser, M. Thorogood, 1998. **Mortality in vegetarians and non-vegetarians: a collaborative analysis of 8300 deaths among 76,000 men and women in five prospective studies.** *Pub Health Nutr.* 1(1):33-41.

Klevay, L.M., 1993. **Copper in nuts may lower heart disease risk.** *Arch Intern Med.* 153: 401-2.

In this commentary on the Seventh-Day Adventist study, the author discusses the fact that nuts are relatively high in copper and that this may provide protection against a variety of disorders related to atherosclerosis. Copper deficiency is the only nutritional insult that has been shown to produce abnormal electrocardiograms, glucose intolerance, hypercholesterolemia, hypertension, hyperuricemia, injury by free radicals and thrombosis in animals. More than 31 men and women have responded to diets low in copper with potentially harmful changes in glucose tolerance, blood pressure, blood lipids and electrocardiograms. Copper in these daily diets ranged from 0.65 to 1.02 mg amounts. Eating an ounce of nuts can add approximately 0.37 mg of copper to daily intakes.

Krauss R.M., R.H. Eckel, B. Howard, L.J. Appel, S.R. Daniels, R.J. Deckelbaum, J.W. Erdman, Jr, P. Kris-Etherton, I.J. Goldberg, T.A. Kotchen, A.H. Lichtenstein, W.E. Mitch, R. Mullis, K. Robinson, J. Wylie-Rosett, S. St. Jeor, J. Suttie, D.L. Tribble, T.L. Bazzarre, 2001. **Revision 2000: a statement for healthcare professionals from the Nutrition Committee of the American Heart Association.** *J Nutr.* 131(1):132-46.

This scientific statement provides guidelines for reducing the risk of cardiovascular disease by dietary and other lifestyle practices. One of the guidelines for a desirable blood cholesterol and lipoprotein profile, suggests substituting grains and unsaturated fatty acids from vegetables, fish, nuts and legumes.

Kris-Etherton, P.M., S. Yu-Poth, J. Sabaté, H.E. Ratcliffe, G. Zhao, T.D. Etherton, 1999. **Nuts and their bioactive constituents: effects on serum lipids and other factors that affect disease risk.** *Am J Clin Nutr.* 70 (suppl.):504S-11S.

Researchers looked at the effects of nut-containing test diets on plasma lipids and lipoproteins, and compared the actual cholesterol response to the predicted response derived from the most current predictive equations for blood cholesterol. Results from the comparison showed that individuals who consumed test diets with nuts had a ~25% greater cholesterol-lowering response than predicted by the equations. The results suggest that there are non-fatty components in nuts that have cholesterol-lowering effects.

Kris-Etherton, P.M., G. Zhao, A.E. Binkoski, S.M. Coval, T.D. Etherton, 2001. **The effects of nuts on coronary heart disease risk.** *Nutr Rev.* 59:103.

Epidemiologic studies have shown again and again the beneficial effects of nut consumption on coronary heart disease morbidity and mortality in various population groups. Clinical studies have shown total and low-density lipoprotein cholesterol-lowering effects of nut-containing heart-healthy diets. The beneficial effects of nuts include their fatty acid profile, dietary fiber and other bioactive components that may offer additional cardioprotective effects.

Kushi, L.H., A.R. Folsom, R.J. Prineas, P.J. Mink, Y. Wu, R.M. Bostick, 1996. **Dietary antioxidant vitamins and death from coronary heart disease in postmenopausal women.** *NEJM.* 334:1156-62.

The “Iowa Women’s Health Study” looked at 35,000 postmenopausal women with no cardiovascular disease, over a seven-year period (1986-1992). The researchers observed that women who ate nuts and seeds more than four times a month had a 40% reduction in risk of coronary heart disease compared to those who never ate nuts or seeds.

Lairon, D., N. Arnault, S. Bertrais, R. Planells, E. Clero, S. Hercberg, M.-C. Boutron-Ruault. **Dietary fiber intake and risk factors for cardiovascular disease in French adults.** *Am J Clin Nutr.* 82:1185-94.

This cross-sectional study looked at the relation between the source or type of dietary fiber intake and cardiovascular disease risk factors in a cohort of 2532 adult men and 3429 adult women. The highest total dietary fiber and nonsoluble dietary fiber intakes were associated with a significantly ($P_{0.05}$) lower risk of overweight and elevated waist-to-hip ratio, blood pressure, plasma apolipoprotein (apo) B, apo B:apo A-I, cholesterol, triacylglycerols, and homocysteine. Soluble dietary fiber was less effective. Fiber from dried fruit or nuts and seeds was associated with a lower body mass index, waist-to-hip ratio, and fasting apo B and glucose concentrations. The researchers concluded that dietary fiber intake is inversely correlated with several cardiovascular disease risk factors in both sexes, which supports its protective role against cardiovascular disease and recommendations for its increased consumption.

Lapointe, A., J. Goulet, C. Couillard, B. Lamarche, S. Lemieux, 2005. **A nutritional intervention promoting the Mediterranean food pattern is associated with a decrease in circulating oxidized LDL particles in healthy women from the Québec City metropolitan area.** *J. Nutr.* 135:410-15.

This study evaluated the effect of a Mediterranean diet that included nuts, under free living conditions, on circulating oxidized LDL (ox-LDL) in a group of 71 healthy women. The 12-week intervention included 2 courses on nutrition and 7 individual sessions with a dietitian. Among all women, plasma ox-LDL decreased by 11.3% after 12 weeks of nutritional intervention despite a lack of change in plasma LDL cholesterol. The authors concluded that changes in the food pattern in response to a nutritional intervention promoting the Mediterranean diet were accompanied by beneficial effects in circulating ox-LDL concentrations in healthy women.

Mantzoros, C.S., C.J. Williams, J.E. Manson, J.B. Meigs, F.B. Hu, 2006. **Adherence to the Mediterranean dietary pattern is positively associated with plasma adiponectin concentrations in diabetic women.** *Am J Clin Nutr.* 84:328-35.

In this study, researchers examined the effect of the Mediterranean diet on adiponectin concentrations. Adiponectin is an adipose tissue-secreted cytokine that has been shown to regulate glucose and lipid metabolism, improve insulin sensitivity and have pronounced antiatherosclerotic effects. Researchers evaluated dietary data and plasma adiponectin in 987 diabetic women, with no history of cardiovascular disease, from the Nurses’ Health Study. Women with the greatest adherence to a Mediterranean-type diet had higher plasma adiponectin concentrations than women with the lowest adherence. The data suggested that several

components of the Mediterranean diet (alcohol, nuts and whole grains) showed the strongest association with higher concentrations of adiponectin.

Mukuddem-Petersen, J., W. Oosthuizen, J. C. Jerling. 2005. **A systematic review of the effects of nuts on blood lipid profiles in humans.** *J. Nutrition* 135; 2082-2089.

Medline and Web of Science databases were searched from the start of the database to August 2004 and supplemented by cross-checking reference lists of relevant publications. Human intervention trials with the objective of investigating independent effects of nuts on lipid concentrations were included. From the literature search, 415 publications were screened and 23 studies were included. These papers received a rating based upon the methodology as it appeared in the publication. No formal statistical analysis was performed due to the large differences in study designs of the dietary intervention trials. The results of 3 - 14 - August 2006 almond (50-100 g/d), 2 peanut (35-68 g/d), 1 pecan nut 72 g/d, and 4 walnut (40-84 g/d) studies showed decreases in total cholesterol between 2 and 16% and LDL cholesterol between 2 and 19% compared with subjects consuming control diets. Consumption of macadamia nuts (50-100 g/d) produced less convincing results. In conclusion, consumption of ~50-100 g (~1.5-3.5 servings) of nuts \geq 5 times/wk as part of a heart-healthy diet with total fat content (high in mono- and/or polyunsaturated fatty acids) of ~35% of energy may significantly decrease total cholesterol and LDL cholesterol in normo- and hyperlipidemic individuals.

Nash, S.D., M. Westpfal, 2005. **Cardiovascular benefits of nuts.** *American Journal of Cardiology.* 963-65.

This review article highlights some of the cardiovascular benefits of nuts. The authors conclude by writing, "Simply stated, at a time of spiraling costs for medical care, public and professional concerns about drug safety, and in an age of fad diets, it is reassuring to have a "nutty alternative."

Sabaté, J., 1993. **Does nut consumption protect against ischaemic heart disease?** *Eur J of Clin Nutr.* 47(suppl.1):S71-5.

Results of an epidemiological study conducted among California Adventists provides strong evidence that frequent nut consumption has a protective effect on both fatal and non-fatal ischaemic heart disease. It's plausible, due to the unique composition of nuts, that nuts favorably affect heart disease risk factors and interfere with the process of atherogenesis. Results of human nutritional studies, with varying degrees of methodological rigor all seem to indicate that eating nuts lowers serum cholesterol and favorably modifies the lipoprotein profile.

Sabaté, J., 1999. **Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies.** *Am J Clin Nutr.* 70(suppl):500S.

A number of large epidemiologic studies have shown that frequency of nut consumption has a substantial and significant inverse association with risk of myocardial infarction and death from ischemic heart disease (IHD). In addition, frequency of nut consumption has been found to be inversely related to all-cause mortality in several population groups including the elderly,

blacks and whites. The author concludes that nut consumption may not only offer protection against IHD, but also increase longevity.

Sabaté J., G.E. Fraser, 1994. **Nuts: a new protective food against coronary heart disease.** *Current Opinion in Lipidology.* 5:11-16.

Epidemiological findings indicate that eating nuts frequently may help protect against fatal and non-fatal heart disease, including heart attacks. Although preliminary studies indicate that nut consumption lowers total and LDL cholesterol levels, the unique nutrient composition of nuts may decrease risk of heart disease in other ways too. This article provides a review of the epidemiological evidence linking nut consumption with coronary heart disease, and addresses some of the biological mechanisms by which nut consumption may reduce coronary risk.

Sabaté J., D.G. Hook. **Almonds, walnuts, and serum lipids.** In: Spiller, G.A. *Handbook of Lipids in Human Nutrition.* New York, NY: CRC Press, Inc.; 1996.

This chapter reviews human studies that look at the effects of whole almonds and walnuts on blood lipid levels. Although each of the studies differ in methodology, the overriding consensus is that almonds, walnuts, and possibly other nuts with a similar nutrient composition, have a cholesterol lowering effect. The protective effect of nuts on coronary heart disease may be due to their fatty acid composition (mostly unsaturated fats) and other components in nuts.

Sacks, F.M., L.P. Svetkey, W.M. Vollmer, L.J. Appel, B.A. Bray, D. Harsha, E. Obarzanek, P.R. Conlin, E.R. Miller, D.G. Simons-Morton, N. Karanja, P. Lin, 2001. **Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet.** *NEJM.* 344:3.

Salas-Salvadó, J., A. Garcia-Arellano, R. Estruch, F. Marquez-Sandoval, D. Corella, M. Fiol, E. Gómez-Gracia, E. Viñoles, F. Arós, C. Herrera, C. Lahoz, J. Lapetra, J.S. Perona, D. Muñoz-Aguado, M.A. Martínez-González, E. Ros; for the PREDIMED Investigators, 2008. **Components of the Mediterranean-type food pattern and serum inflammatory markers among patients at high risk for cardiovascular disease.** *European Journal of Clinical Nutrition.* 62, 651–659.

This study evaluated associations between components of the Mediterranean diet and circulating markers of inflammation in a large cohort (339 men and 433 women aged between 55 and 80 years) of asymptomatic subjects at high risk for cardiovascular disease because of presence of diabetes or at least three classical cardiovascular risk factors. Food consumption was determined by a semi-quantitative food frequency questionnaire; and serum concentrations of high-sensitivity C-reactive protein (CRP) were measured by immunonephelometry and those of interleukin-6 (IL-6), intracellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) by enzyme-linked immunosorbent assay. After adjusting for age, gender, body mass index, diabetes, smoking, use of statins, non-steroidal antiinflammatory drugs and aspirin, a higher consumption of fruits and cereals was associated with lower concentrations of IL-6 (P for trend 0.005;both). Subjects with the highest consumption of nuts and virgin olive oil showed the lowest concentrations of VCAM-1, ICAM-1, IL-6 and CRP; albeit only for ICAM-1 was this difference statistically significant in the case of nuts (for trend 0.003) and for VCAM-1 in the case of virgin olive oil (P for trend 0.02). Participants with higher adherence to the Mediterranean-type diet did not show significantly lower concentrations of inflammatory markers

($P < 0.1$ for VCAM-1 and ICAM-1). The consumption of some typical Mediterranean foods (fruits, cereals, virgin olive oil and nuts) was associated with lower serum concentrations of inflammatory markers especially those related to endothelial function, in subjects with high cardiovascular risk living in a Mediterranean country.

Serra-Majem, L., B. Roman, R. Estruch, 2006. **Scientific evidence of interventions using the Mediterranean diet: A systematic review.** *Nutrition Reviews*, 64 (2) S27-S47.

The purpose of this study was to analyze and review the experimental studies on Mediterranean diet and disease prevention. A systematic review was made and a total of 43 articles corresponding to 35 different experimental studies were selected. Results were analyzed for the effects of the Mediterranean diet on lipoproteins, endothelial resistance, diabetes and antioxidative capacity, cardiovascular diseases, arthritis, cancer, body composition, and psychological function. The Mediterranean diet showed favorable effects on lipoprotein levels, endothelium vasodilatation, insulin resistance, metabolic syndrome, antioxidant capacity, myocardial and cardiovascular mortality, and cancer incidence in obese patients and in those with previous myocardial infarction. Results disclose the mechanisms of the Mediterranean diet in disease prevention, particularly in cardiovascular disease secondary prevention, but also emphasize the need to undertake experimental research and systematic reviews in the areas of primary prevention of cardiovascular disease, hypertension, diabetes, obesity, infectious diseases, age-related cognitive impairment, and cancer, among others. Interventions should use food scores or patterns to ascertain adherence to the Mediterranean diet. Further experimental research is needed to corroborate the benefits of the Mediterranean diet and the underlying mechanisms.

Singh, R.B., G. Dubnov, M.A. Niaz, S. Ghosh, R. Singh, S.S. Rastogi, O. Manor, D. Pella, E.M. Berry, 2002. **Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high-risk patients (Indo-Mediterranean Diet Heart Study): a randomized single-blind trial.** *Lancet*. 360:1455-61.

This randomized, single-blind trial in 1000 patients with angina pectoris, heart attack, or surrogate factors for coronary artery disease (CAD), compared an Indo-Mediterranean (IM) diet to the NCEP Step 1 diet. 499 patients were allocated the IM, or intervention diet, which included whole grains, fruits vegetables, walnuts and almonds. 501 controls consumed a local diet similar to the Step 1 diet. Total cardiac endpoints were significantly fewer in the intervention group than in the control group; sudden cardiac deaths were also reduced as were non-fatal heart attacks. There was also a significant reduction in serum cholesterol and other risk factors in both groups, but more so in the intervention group. The results indicate that an Indo-Mediterranean diet may be more effective in primary and secondary prevention of CAD than the conventional Step 1 NCEP diet.

Singh, R.B., S.S. Rastogi, R. Verma, L. Bolaki, R. Singh, 1992. **An Indian experiment with nutritional modulation in acute myocardial infarction.** *Am J Cardiol*. 69:879-85.

This study involved 406 patients who were recruited 24 to 48 hours after having an acute myocardial infarction (MI). The randomized, single-blind intervention study lasted 6 weeks. Subjects were divided into two groups. One group consumed Diet A in which meat and eggs were replaced by fish, vegetarian meat substitutes and nuts (almonds and walnuts). Those following Diet B ate a low-calorie, typical hospital diet, followed by a diet prescribed by their doctors. Those consuming Diet A had a 9% decrease in total cholesterol, 10% decrease in LDL

and 9% decrease in triglycerides. Those following Diet A also had a 36% decrease in cardiovascular events compared to those consuming Diet B.

Svetkey L.P., F.M. Sacks, E. Obarzanek, W.M. Vollmer, L.J. Appel, P.H. Lin, N.M. Karanja, D.W. Harsha, G.A. Bray, M. Aickin, M.A. Proschan, M.M. Windhauser, J.F. Swain, P.B. McCarron, D.G. Rhodes, R.L. Laws, 1999. **The DASH diet, sodium intake and blood pressure trial (DASH-sodium): rationale and design. DASH-sodium collaborative research group.** *J Am Diet Assoc* (8 suppl):S96-104.

Ternus, M., K. Lapsley, K. McMahon, G. Johnson, 2006. **Qualified Health Claim for Nuts and Heart Disease Prevention, Development of Consumer-Friendly Language.** *Nutrition Today.* 41 (2):62-66.

In 2003, the US Food and Drug Administration (FDA) began authorizing qualified health claims for conventional foods. Although the FDA had developed generic qualifying language for these claims, the language had not yet been tested with consumers. A shopping mall intercept was conducted among a random sample of 408 adults. The research tested consumer preference, understanding and believability, and impact on nut consumption of 4 variations of the ‘‘B’’ level qualified health claim for nuts and heart disease. The FDA generic language was used as the control. The results show that one of the alternatives was ranked significantly higher than the FDA generic claim for clarity and understandability but was similar in all other categories, including the scientific uncertainty associated with the claim. This research demonstrates that it is possible to meet FDA’s standards for truthful and not misleading health claims using consumer-friendly language.

Zazpe, I, A. Sanchez-Tainta, R. Estruch, R.M. Lamuela-Raventos, H. Schröder, J. Salas-Salvado, D. Corella, M. Fiol, E. Gomez-Gracia, F. Aros, E. Ros, V. Ruíz-Gutierrez, P. Iglesias, M. Conde-Herrera, M.A. Martinez-Gonzalez, 2008. **A Large Randomized Individual and Group Intervention Conducted by Registered Dietitians Increased Adherence to Mediterranean-Type Diets: The PREDIMED Study.** *J Am Diet Assoc.* 108:7 1134-1143.

This study, a 12-month assessment of a randomized primary prevention trial, looked at the effectiveness of an intervention aimed to increase adherence to a Mediterranean diet. One thousand five hundred fifty-one asymptomatic persons aged 55 to 80 years, with diabetes or ≥ 3 cardiovascular risk factors were randomly assigned to a control group or two Mediterranean diet groups. Those allocated to the two Mediterranean diet groups received individual motivational interviews every 3 months to negotiate nutrition goals, and group educational sessions on a quarterly basis. One Mediterranean diet group received free virgin olive oil (1 L/week), the other received free mixed nuts (30 g/day). Participants in the control group received verbal instructions and a leaflet recommending the National Cholesterol Education Program Adult Treatment Panel III dietary guidelines. The results showed that participants allocated to both Mediterranean diets increased their intake of virgin olive oil, nuts, vegetables, legumes, and fruits ($P < 0.05$ for all within- and between-group differences). Participants in all three groups decreased their intake of meat and pastries, cakes, and sweets ($P < 0.05$ for all). Fiber, monounsaturated fatty acid, and polyunsaturated fatty acid intake increased in the Mediterranean diet groups ($P < 0.005$ for all). Favorable, although nonsignificant, changes in intake of other nutrients occurred only in the Mediterranean diet groups. The researchers concluded that a 12-month behavioral intervention

promoting the Mediterranean diet can favorably modify an individual's overall food pattern. The individual motivational interventions together with the group sessions and the free provision of high-fat and palatable key foods customary to the Mediterranean diet were effective in improving the dietary habits of participants in this trial.

Verschuren, W.M.M., E.M. van Leer, A. Blockstra, J.C. Seidell, H.A. Smit, H.B. Bueno de Mesquita, G.L. Oberman-de Boer, D. Kromhout, 1993. **Cardiovascular disease risk factors in the Netherlands.** *Neth J Cardiol.* 4:205-10.

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DIABETES

American Diabetes Association (ADA). 2007. **Nutrition recommendations and interventions for diabetes (Position Statement).** *Diabetes Care.* 30(suppl.1): S48–61.

This position statement promotes the use of individualized medical nutrition therapy for people with diabetes, with consideration given to each individual's usual food and eating habits, treatment goals, metabolic profile and desired outcomes.

American Diabetes Association (ADA). 2003. **Evidence-based nutrition principles and recommendations for the treatment and prevention of diabetes and related complications (Position Statement).** *Diabetes Care.* 26(suppl.1): S51–61.

This position statement promotes the use of individualized medical nutrition therapy for people with diabetes, with consideration given to each individual's usual food and eating habits, treatment goals, metabolic profile and desired outcomes.

Brand-Miller, J, S. Hayne, P. Petocz, S. Colagiuri, 2003. **Low-glycemic index diets in the management of diabetes.** *Diabetes Care.* 26(8):2261-66.

This meta-analysis of randomized controlled trials, including 14 studies and 356 subjects, compared the use of diets with low glycemic index (GI) to conventional or high-GI diets on overall glycemic control in individuals with diabetes, as assessed by reduced HbA_{1c} or fructosamine levels. The results showed that low GI diets reduced HbA_{1c} by 0.43% points more than the high-GI diets. Looking at HbA_{1c} and fructosamine together, glycated proteins were reduced 7.4% more on the low-GI diet than on the high-GI diet. The researchers concluded that choosing low-GI foods in place of conventional or high-GI foods has a small but useful effect on medium-term glycemic control in diabetics. The incremental benefit is similar to that seen with drugs that also target postprandial hyperglycemia. [While this study does not mention nuts specifically, they are a very low-GI food.]

Garg A., 1998. **High monounsaturated fat diets for patients with diabetes mellitus: a meta-analysis.** *Am J Clin Nutr.* 67(suppl):577s-82s.

A meta-analysis of various studies was conducted to compare either low-saturated fat, high-carbohydrate diets or high-monounsaturated fat diets in patients with Type II diabetes. The results show that the high-monounsaturated fat diets improve lipoprotein profiles as well as the glycemic profile, compared to the low-saturated fat, high-carbohydrate diets. The high-monounsaturated fat diets reduced fasting plasma triacylglycerol and VLDL-cholesterol levels by 19% and 22% respectively, and caused modest increases in HDL-cholesterol without negatively impacting LDL-cholesterol. The high-monounsaturated fat diets may also reduce the susceptibility of LDL particles to oxidation and thereby reduce their atherogenic potential. Moreover, there is no evidence that high-monounsaturated fat diets cause weight gain in patients with diabetes, provided that caloric intake is controlled. The researcher concluded that diets rich in monounsaturated fat can be useful and advantageous for both patients with Type I or Type II diabetes who are trying to lose or maintain weight. [Most nuts are rich in monounsaturated fats.]

García-Lorda, P. I. M. Rangil, J. Salas-Salvadó, 2003. **Nut consumption, body weight and insulin resistance.** *Eur J Clin Nutr.* 57(suppl 1):S8-S11.

Since nuts provide a high amount of fat and calories, there has been some concern that they may have a detrimental effect on body weight and insulin resistance. However, according to the authors, the current data available does not support such a negative effect of nut consumption on the short term or when nuts are included on diets that meet energy needs. There is some evidence that nuts may actually help regulate body weight and protect against Type II diabetes, but more research is needed.

Jenkins, D.J., T.M. Wolever, B. Buckley, et al., 1988. **Low-glycemic-index starchy foods in the diabetic diet.** *Am J Clin Nutr.* 48:248-54.

Eight patients with noninsulin-dependent diabetes were provided, in random order, with carbohydrate foods with either low or high glycemic index (GI) during two, 2-week study periods. While weight loss occurred in both the low- and high-GI periods, only during the low-GI period were significant reductions seen in fasting blood glucose, HbA_{1c}, and urinary c-peptide-to-creatinine ratio. The researchers concluded that inclusion of low-GI foods into diets of patients with diabetes may be an additional measure that favorably influences carbohydrate metabolism without increasing insulin demand. [While this study does not mention nuts specifically, they are a very low-GI food.]

Jenkins, D.J.A., T.M.S. Wolever, R.H. Taylor, et al., 1981. **Glycemic index of foods: a physiological basis for carbohydrate exchange.** *Am J Clin Nutr.* 34:362-6.

In order to determine the effect of different foods on blood glucose levels, groups of 5-10 healthy, fasting volunteers were fed 62 commonly eaten foods, individually. Blood glucose levels were measured over two hours. The largest rises were seen with vegetables, breakfast cereals, cereals and biscuits, followed by fruit, dairy products and dried legumes (including peanuts). There was a significant negative relationship between protein and fat and postprandial glucose rise, but not with fiber or sugar content.

Jiang, R., J.E. Manson, M.J. Stampfer, S. Liu, W.C. Willett, F.B. Hu, 2002. **Nut and peanut butter consumption and risk of type 2 diabetes in women.** *JAMA.* 288:2554-60.

This prospective cohort study looked at 83,818 women from 11 states in the Nurses' Health Study, aged 34-59, with no history of diabetes, cardiovascular disease or cancer. The subjects completed a validated dietary questionnaire at baseline in 1980 and were followed up for 16 years. According to the researchers, the findings suggest potential benefits of higher nut and peanut butter consumption in lowering risk of type 2 diabetes in women. To avoid increasing caloric intake, regular nut consumption can be recommended as a replacement for consumption of refined grain products or red or processed meats.

Lopez-Ridaura, R., W.C. Willett, E.B. Rimm, S. Liu, M.J. Stampfer, J.E. Manson, F.B. Hu, 2004. **Magnesium intake and risk of type 2 diabetes in men and women.** *Diabetes Care.* 27(1): 134-40.

Researchers followed 85,060 women and 42,872 men in the Nurses' Health Study and Health Professionals' Follow-up Study, respectively, with no history of diabetes, cardiovascular disease or cancer at baseline. Magnesium intake was monitored every 2-4 years via a food frequency questionnaire. After 18 years of follow-up in women and 12 years in men, there were 4,085 and 1,333 incident cases of type 2 diabetes, respectively. The results showed a significant inverse association between magnesium intake and diabetes risk. This study supports the recommendation to increase consumption of magnesium-rich foods such as nuts, whole grains and green leafy vegetables.

Luscombe, N., M. Noakes, P. Clifton, 1999. **Diets high and low in glycemic index versus high monounsaturated fat diets: effects on glucose and lipid metabolism in NIDDM.** *Eur J Clin Nutr.* 53:473-8.

This study compared high and low glycemic index (GI) carbohydrates (CHO) and monounsaturated fats (mono) on blood glucose and lipid metabolism in free-living outpatients with non-insulin dependent diabetes mellitus (NIDDM). Each subject consumed three diets: a high-GI diet (53% CHO, 21% fat, 63 GI units); a low-GI diet (51% CHO, 23% fat, 43 GI units); and a high-mono, high-GI diet (42% CHO, 35% fat, 59 GI units) in random order and cross-over fashion for four weeks. Each of the diets contained more than 30 grams of dietary fiber and the high-mono, high-GI diet included almonds. At the end of the study, HDL-cholesterol was higher on the low-GI and high-mono, high-GI diets, compared to the high-GI diet. Saturated fat intake and body weight remained stable between the dietary interventions. The researchers concluded that the high-mono, high-GI and high-CHO, low-GI diets are superior to high-CHO, high-GI diets with respect to HDL metabolism, but there was no effect noted on glucose metabolism in variably controlled NIDDM patients.

Miller, J.C., 1994. **Importance of glycemic index in diabetes.** *Am J Clin Nutr.* 59:747S-52S.

This article reviewed 11 medium to long-term studies that have specifically used the glycemic index (GI) to assess the clinical benefits in diabetes or lipid management. All but one study showed positive results. Overall, low-GI diets lowered glucose, cholesterol and triglycerides in modest amounts. And, unlike high-fiber diets, low-GI diets are "use friendly." According to the author, the time has come to reassess the value of GI in planning meals for diabetics. [While this study does not mention nuts specifically, they are a very low-GI food.]

Mantzoros, C.S., C.J. Williams, J.E.Manson, J.B. Meigs, F.B. Hu, 2006. **Adherence to the Mediterranean dietary pattern is positively associated with plasma adiponectin concentrations in diabetic women.** *Am J Clin Nutr.* 84:328-35.

The purpose of this study was to determine whether adherence to a Mediterranean-type diet is associated with higher plasma adiponectin concentrations. The study was a prospective and cross-sectional evaluation of plasma adiponectin concentrations and dietary data from 987 diabetic women from the Nurses' Health Study who had no history of cardiovascular disease at the time blood was drawn in 1990. Women who scored highest on a 9-point scale that measures adherence to a Mediterranean-type dietary pattern tended to be older, were less likely to be current smokers, had lower body mass indexes and waist circumferences, and had higher total energy intakes, physical activities, and plasma adiponectin concentrations than did women with the lowest scores. Median plasma adiponectin concentrations were 23% higher in women who most closely followed a Mediterranean-type diet than in low adherers after adjustment for age and energy intake ($P < 0.01$). Body composition, lifestyle, and medical history explained some, but not all, of the observed association between diet and adiponectin concentrations because high adherers tended to have greater adiponectin concentrations than did moderate or low adherers, even after adjustment for these variables. The data suggest that, of the several components of the Mediterranean dietary pattern score, alcohol, nuts, and whole grains show the strongest association with adiponectin concentrations. Close adherence to a Mediterranean-type diet is associated with higher adiponectin concentrations.

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GALLSTONES

Tsai, C-J., M.F. Leitzmann, F.B. Hu, W.C. Willett, E.L. Giovannucci, 2004. **Frequent nut consumption and decreased risk of cholecystectomy in women.** *Am J Clin Nutr.* 80:76-81.

Researchers analyzed the potential link between nuts and cholecystectomy, or gallstones, between 1980 and 2000, among 80,718 women from the Nurses' Health Study who were 30-55 years old in 1980 and had no history of gallstone disease. After adjusting for age and other known suspected risk factors, researchers found that women who consumed 5 or more ounces of nuts per week had a significantly lower risk of gallstones than women who rarely or never ate nuts. The authors of the study concluded that frequent nut consumption in women is associated with a reduced risk of cholecystectomy.

Tsai, C-J., M.F. Leitzmann, F.B. Hu, W.C. Willett, E.L. Giovannucci, 2004. **The effect of long-term intake of cis unsaturated fats on the risk of gallstone disease in men.** *Ann Intern Med.* 141:514-22.

This prospective, population-based study involved 45,756 men from the Health Professional's Follow-up Study, who were 40-75 years old in 1986 and had no history of gallstone disease. After 14 years of follow-up those with high intakes of both monounsaturated and polyunsaturated fatty acids had fewer self-reported cases of symptomatic gallstone disease than those with low intakes. The authors concluded that long-term intake of high amounts of cis unsaturated fat seems to be associated with a decreased risk of gallstone disease in men. [While nuts were not mentioned specifically in this study, they are very high in mono- and polyunsaturated fats.]

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GENERAL

Jenab, M., J. Sabate, N. Slimani, P. Ferrari, M. Mazuir, C. Casagrande, G. Deharveng, A. Tjønneland, A. Olsen, K. Overvad, M.-C. Boutron-Ruault, F. Clavel-Chapelon, H. Boeing, C. Weikert, J. Linseisen, S. Rohrmann, A. Trichopoulou, A. Naska, D. Palli, C. Sacerdote, R. Tumino, A. Mattiello, V. Pala, H.B. Bueno-de-Mesquita, M.C. Ocke, P.H. Peeters, D. Engeset, G. Skeie, P. Jakszyn, E. Ardanaz, J.R. Quiros, M.D. Chirlaque, C. Martinez, P. Amiano, G. Berglund, R. Palmqvist, B. van Guelpen, S. Bingham, T. Key, E. Riboli, 2006. **Consumption and portion sizes of tree nuts, peanuts and seeds in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts from 10 European countries.** *British Journal of Nutrition.* 96, Suppl. 2, S12–S23

Tree nuts, peanuts and seeds are nutrient dense foods whose intake has been shown to be associated with reduced risk of some chronic diseases. They are regularly consumed in European diets either as whole, in spreads or from hidden sources (e.g. commercial products). However, little is known about their intake profiles or differences in consumption between European countries or geographic regions. The objective of this study was to analyze the population mean intake and average portion sizes in subjects reporting intake of nuts and seeds consumed as whole, derived from hidden sources or from spreads. Data was obtained from standardized 24-hour dietary recalls collected from 36,994 subjects in 10 different countries that are part of the European Prospective Investigation into Cancer and Nutrition (EPIC). Overall, for nuts and seeds consumed as whole, the percentage of subjects reporting intake on the day of the recall was: tree nuts = 4.4%, peanuts = 2.3% and seeds = 1.3%. The data show a clear northern (Sweden: mean intake = 0.15 g/d, average portion size = 15.1 g/d) to southern (Spain: mean intake = 2.99 g/d, average portion size = 34.7 g/d) European gradient of whole tree nut intake. The three most popular tree nuts were walnuts, almonds and hazelnuts, respectively. In general, tree nuts were more widely consumed than peanuts or seeds. In subjects reporting intake, men consumed a significantly higher average portion size of tree nuts (28.5 v. 23.1 g/d, $P < 0.01$) and peanuts (46.1 v. 35.1 g/d, $P < 0.01$) per day than women. These data may be useful in devising research initiatives and health policy strategies based on the intake of this food group.

Knoops, K.T.B., L.C.P.G.M. de Groot, D. Kromhout, A-E. Perrin, O. Moreiras-Varela, A. Menotti, W.A. van Staveren, 2004. **Mediterranean diet, lifestyle factors, and 10-year mortality in elderly men and women.** *JAMA.* 292:1433-39.

In this study of Europeans, aged 70-90 years, adherence to a Mediterranean diet (that included nuts) and healthful lifestyle (moderate alcohol, physical activity and no smoking) was associated with more than a 50% lower rate of all-causes and cause-specific mortality.

Lin, B.H., E. Frazao, J. Allhouse, 2001. **U.S. consumption patterns of tree nuts.** *Food Review* 24(2):54-8.

Lino, M., K. Marcoe, J.M. Dinkins, H. Hiza, R. Anand, 2000. USDA Center for Nutrition Policy and Promotion. **The role of nuts in a healthy diet.** *Insight* 23, December.

Mann, J.I., 2000. **Optimizing the plant-based diet.** *Asia Pacific J Clin Nutr.* 9(suppl):S60-4.

This review looks at the major health benefits of plant-based diets, the specific foods which provide the potential benefits and potential nutrient deficiencies. According to the author, of all the individual potential protective foods from studies to date, consumption of nuts is of particular interest. Nuts appear to provide identical protective effects to both vegetarians and non-vegetarians and seem to be inversely related to all-cause mortality, thus possibly promoting longevity as well as reducing cardiovascular risk. The possible mechanisms by which nuts may protect against heart disease include a favorable fatty acid profile, their cholesterol lowering potential and the presence of a wide range of bioactive compounds.

Noah, A., A.S. Truswell, 2001. **There are many Mediterranean diets.** *Asia Pacific J Clin Nutr.* 10(1):2-9.

This paper provides an overview of the various Mediterranean diets from 20 to 30 years ago. Interestingly, not all Mediterranean countries consume the same foods or the same amounts of foods. In the case of nuts, almonds were consumed 3-5 times per week in Italy and Morocco, but 6-7 times per week in Lebanon and Turkey. Pistachios were consumed rarely in Italy, but 3-5 times per week in Lebanon and 6-7 times per week in Turkey. The authors conclude that there is no single Mediterranean diet and nutritionists who use the concept should qualify the individual country and the time in history of their “model” Mediterranean diet.

Oldways, 1995. **Tree nuts, health and the Mediterranean diet.** A summary report. Boston, USA. 51 pages.

Rainey, C., L. Nyquist, 1997. **Nuts – nutrition and health benefits of daily use.** *Nutrition Today.* 32(4):157-63.

This article dispels many of the myths about the role of nuts in the diet and provides a nice overview on the nutritional benefits and uses of nuts.

Spiller, G.A., B. Bruce, 1997. **Nuts and healthy diets.** *Vegetarian Nutrition: An International Journal.* 1(1):12-16.

This paper examines the history and composition of a variety of nuts from around the world and concludes that nuts are under-consumed in modern diets. Nuts provide an abundance of nutritional value and can play an important role as individuals move from animal-based diets to plant-based diets.

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MENARCHE

F.J. Soriguer, S. Gonzalez-Romero, I. Esteva, J.A. Garcia-Arnes, F. Tinahones, M.S. Ruiz De Adana, G. Oliveira, I. Mancha, F. Vazques, 1995. **Does the intake of nuts and seeds alter the appearance of menarche?** *Acta Obstet Gynecol Scand.* 74:455-61.

A cross-sectional study of 777 schoolgirls in Spain, ages 8-16 years, found that in girls 12-years or older, the age of menarche was essentially related to the intake of nuts and seeds. The study concluded that girls who eat larger amounts of nuts and seeds tend to have their menarche delayed.

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WEIGHT CONTROL

Kirkmeyer, S.V, R.D. Mattes, 2000. **Effects of food attributes on hunger and food intake.** *Int J Obesity.* 24:1167-75.

Preloads of almonds, peanuts, peanut butter, chestnuts, chocolate, rice cakes and pickles were consumed in random order at weekly intervals by 12 male and 12 female healthy, normal weight adults. Hunger was assessed after consumption of 500 calories of a particular preload over the subsequent three hours. The researchers concluded that energy content of a preload may exert a stronger influence on hunger, in the subsequent 180 minutes, than the food's energy density, macronutrient profile, fiber content, weight, volume, rheology or sensory properties.

McManus, K., L. Antinoro, F. Sacks, 2001. **A randomized controlled trial of a moderate fat, low energy diet compared with a low fat, low energy diet for weight loss in overweight adults.** *Int J Obesity.* 25:1503-11.

In this randomized, parallel study, 101 overweight adults were followed for 18 months. Subjects were divided into two groups and consumed one of two study diets, both of which were calorie controlled (1200 kcal/day for women; 1500 kcal/day for men). The low-fat diet (LF) had a total of 20% calories from fat, while the high-unsaturated fat diet (UNSAT) consisted of 35% total fat and included tree nuts, peanuts, canola and olive oils.

After six months the average weight loss was comparable in both groups. However, there was a significant difference at the end of the 18 months in participation rates. In the LF group, only 20% were still actively participating in the study compared to 54% of the UNSAT group. One factor which may contribute to the greater participation rate, is that a moderate fat diet may induce the feelings of satiety after a snack or meal. In addition, the participants in the UNSAT group reported that they did not feel like they were "dieting" and therefore, did not feel deprived.

Piers, L.S., K.Z. Walker, R.M. Stoney, M.J. Soares, K. O'Dea, 2003. **Substitution of saturated with monounsaturated fat in a 4-week diet affects body weight and composition of overweight and obese men.** *British Journal of Obesity.* 90:717-27.

This randomized crossover study tried to determine whether or not substituting saturated fat (SF) with monounsaturated fat (MUFA) affects body weight and composition. Eight overweight or obese men followed two diets for four weeks each. The MUFA diet included nuts, olive oil and avocado, while the SFA diet was rich in milk, butter, cream, cheese and fatty meat. At the end of the study the men had lost more weight and fat mass on the MUFA diet than on the SFA diet. The researchers concluded that substituting SFA with unsaturated fats, particularly MUFA, can result in a small but significant loss of body weight and fat mass without a significant change in fat intake or total calories.

Sabaté, J., 2003. **Nut consumption and body weight.** *Am J Clin Nutr.* 78(suppl):647S-50S.

According to the author, the available data demonstrate that nut consumption among free-living individuals is not associated with higher BMI compared with non-nut consumers despite the fact that nuts are fat- and energy-dense foods. Isocaloric replacement of nuts for other food in the diet does not increase weight. While more research is needed in this area, the current data do not indicate that free-living people on self-selected diets including nuts frequently have a higher BMI or increased body weight.

Sabaté, J., G. Blix, 2001. **Vegetarian diets and obesity prevention:** In: Sabaté, J., (ed.), *Vegetarian Nutrition.* CRC Press, Boca Raton, 91-107.

St-Onge, M.P., 2005. **Dietary fats, teas, dairy, and nuts: potential functional foods for weight control?** *Am J Clin Nutr.* 81:7-15.

Nuts are one of the foods highlighted in this review paper on functional foods and weight control. While few studies have been conducted specifically on nuts and weight control, a number of supplementation studies looking at nuts and lipid profiles have not found negative effects on body weight. In fact, a majority of the papers reviewed here show no weight gain despite the additional calories from nuts. The author concludes that although more research is needed, nuts may play a role in weight maintenance via increased satiety levels, increased resting energy expenditure or energy malabsorption.

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NUTRIENT COMPOSITION

Borchers, A., 2001. **Review of the Scientific Literature on Phenolic Compounds and Phytosterols in Tree Nuts.** (Unpublished 28-page report for INC with 279 references.)

Numerous epidemiological studies suggest that higher consumption of plant products (fruits, vegetables, nuts and grains) is associated with a decreased risk of heart disease, cancer, and possibly other chronic diseases. There are many indications that, in addition to antioxidant vitamins, a variety of phytochemicals may contribute to these health benefits of plant-derived foods. There are a variety of candidates – including fiber, arginine, the lysine:arginine ratio, copper, magnesium, phenolic compounds, and phytosterols. Similarly, phenolic compounds as well as phytosterols are thought to be among the plant constituents that play a role in lowering the risk of various cancers.

This report consists of two major sections, I) phenolic compounds in tree nuts and II) phytosterols in tree nuts, followed by several appendices summarizing information on dietary sources and intake of phenolic compounds, their bioavailability and their metabolism.

Chai, W., M. Liebman, 2005. **Oxalate content of legumes, nuts and grain-based flours.** *Journal of Food Composition and Analysis*. 18:723-29.

This study looked at the oxalate content of legumes, nuts and grain-based flours since dietary oxalate can make a significant contribution to urinary oxalate levels, which can lead to kidney stones. The range of total oxalate of the nuts tested was 42-469 milligrams per 100 grams of nuts—making nuts a rich source of oxalate.

Drewnowski, A., 2005. **Concept of a nutritious food: toward a nutrient density score.** *Am J Clin Nutr*. 82:721-32.

This paper tries to define “nutrient density” and what makes a food nutrient dense. It reviews a number of different types of scoring systems including the “naturally nutrient rich” (NNR) score. The latter is a nutrients-to-calories ratio which looks at the average of percent Daily Values for 16 key nutrients. The author states, “Focusing attention on the nutrient-to-calorie ratio, the NNR score allows consumers to identify the more nutrient-dense foods within each food group and make their food selections accordingly. Adherence to a naturally nutrient-rich diet requires the consumption of more colorful fruit and vegetables, whole grains, lean meats, seafood, eggs, beans and nuts, and low-fat and nonfat dairy products.”

Hopper, K., B. Lampi, E. O’Grady, 1994. **Biotin content in vegetables and nuts available on the Canadian market.** *Food Research International*. 27:495-7.

The mean total biotin levels for nuts and seeds varied from 0.7 to 91.1 micrograms/100 grams.

Gu, L., M.A. Kelm, J.F. Hammerstone, G. Beecher, J. Holden, D. Haytowitz, S. Gebhardt, R.L. Prior, 2004. **Concentrations of proanthocyanidins in common foods and estimations of normal consumption.** *J Nutr*. 134:613-17.

Proanthocyanidins (PAs) have been shown to have potential health benefits, however, until now no data existed concerning their dietary intake. This study analyzed the PAs in common and infant foods in the U.S. Tree nuts were found to contain a substantial amount of PAs. The results showed that PAs account for a major fraction of the total flavonoids ingested in Western diets. More research is needed to study the association between varying amounts of PAs and their effects on different diseases.

Kornsteiner, M., K.H. Wagner, I. Elmadfa, 2005. **Tocopherols and total phenolics in 10 different nut types.** *Food Chemistry*. 98:381-87.

Kornsteiner et al. (2005) looked at tocopherols and total phenolics in 10 different types of nuts. Almonds and hazelnuts had the highest concentrations of α -tocopherol and pistachios had the only detectable levels of carotenoids. The mean content of total phenolics ranged from 32 milligrams of gallic acid equivalents/100 grams of pine nuts, to 1,625 milligrams in walnuts. The researchers concluded that due to the heterogenic amounts of antioxidants in nuts, it's best to consume a variety of mixed nuts.

Venkatachalam, M., S.K. Sathe. 2006. **Chemical Composition of Selected Edible Nut Seeds.** *J Agric Food Chem.* 54, 4705-4714.

Commercially important edible nut seeds were analyzed for chemical composition and moisture sorption. Moisture (1.47-9.51%), protein (7.50-21.56%), lipids (42.88-66.71%), ash (1.16-3.28%) total soluble sugars 0.55-3.96%), tannins (0.01-0.88%) and phytate (0.15-0.35%) contents varied considerably. Regardless of the seed type, lipids were mainly composed of mono- and polyunsaturated fatty acids (>75% of the total lipids). Fatty acid composition analysis indicated that oleic acid was the main constituent of monounsaturated lipids in all seed samples. With the exception of macadamia, linoleic acid (C18:2) was the major polyunsaturated fatty acid. In the case of walnuts, in addition to linoleic acid (58.79%) linolenic acid also significantly contributed toward the total polyunsaturated lipids.

Wu, X., Beecher, G.R., Holden, J.M., Haytowitz, D.B., Gebhardt, S.E., R.L. Prior, 2004. **Lipophilic and hydrophilic antioxidant capacities of common foods in the United States.** *J Agric Food Chem.* 52:4026-37.

This paper looks at the lipophilic and hydrophilic ORAC_{FL} values for over 100 common foods in the U.S., including nuts. Total phenolic concentrations were also measured. The authors note that nuts are an important source of dietary lipids and have been suggested as a potential source of dietary antioxidants on the basis of recent epidemiological and cohort studies. While more research is needed, this paper gives a nice overview of both the antioxidant capacity and phenolic content of nuts.

Wu, X., Beecher, G.R., Holden, J.M., Haytowitz, D.B., Gebhardt, S.E., R.L. Prior, 2006. **Concentrations of anthocyanins in common foods in the United States and estimation of normal consumption.** *J. Agric. Food Chem.* 54:4069-75.

Anthocyanins (ACNs) are water-soluble plant pigments that have important functions in plant physiology as well as possible health effects. Over 100 common foods were screened for ACNs, and 24 of them were found to contain ACNs—including pistachios. Concentrations of total ACNs varied considerably from 0.7 to 1480 mg/100 g of fresh weight in gooseberry and chokeberry, respectively. Not only does the concentration vary, but the specific anthocyanins present in foods are also quite different. Only six common aglycones, delphinidin, cyanidin, petunidin, pelargonidin, peonidin, and malvidin, were found in all of these foods. However, their sugar moieties and acylation patterns varied from food to food. Results from this study will add to the available data for the USDA Nutrient Database of flavonoids. On the basis of the concentration data and updated food intake data from NHANES 2001-2002, the daily intake of ACNs is estimated to be 12.5 mg/day/person in the United States.

Wu, X., R.L. Prior, 2005. **Identification and characterization of anthocyanins by**

high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry in common foods in the United States: vegetables, nuts, and grains. *J Agric Food Chem.* 53:3101-13.

Anthocyanins in common foods in the United States, other than fruits and berries, were identified and characterized by high-performance liquid chromatography (HPLC)-electrospray ionization-tandem mass spectrometry coupled with diode array detection. Of all of the 40+ vegetables, nuts, and grains screened, seven vegetables, one nut, and one grain were found to contain anthocyanins; the number of anthocyanins detected varied from two in pistachio nuts (cyanidin 3-galactoside and cyanidin 3-glucoside) to 34 in red radishes.

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ALMOND REFERENCES

Acosta, M.R., K.H. Roux, S.S. Teuber, S.K. Sathe, 1999. **Production and characterization of rabbit polyclonal antibodies to almond (*Prunus amygdalus* L) major storage protein.** *J Agric Food Chem.* 47: 4053-9.

The results of this study demonstrate the feasibility of developing an immunobased assay to detect the presence of small amounts of almonds in food products. The researchers believe that when further developed, this assay will be of value to the food industry and allergic individuals for the detection of almond contamination in foods.

Ahrens, S., M. Venkatachalam, A.M. Mistry, K. Lapsley, S.K. Sathe, 2005. **Almond (*Prunus dulcis* L.) protein quality.** *Plant Foods for Human Nutrition.* 60: 123–128.

Three varieties of almonds; Carmel, Mission, and Nonpareil; were analyzed for proximate composition and protein nutritive quality. Amino acid analyses indicated the sulfur amino acids (methionine + cysteine), lysine, and threonine to be the first, second, and third limiting amino acids in almonds when compared to the FAO recommended amino acid pattern for children 2–5-year old. However, compared to the recommended amino acid pattern for adults, sulfur amino acids were the only limiting amino acids in almonds tested. True Protein Digestibility values for Carmel, Mission, and Nonpareil were 88.55 ± 1.26 , 92.25 ± 1.05 , and 82.62 ± 1.47 , respectively.

Amarowicz, R., T. Agnieszka, A. Troszynska, F. Shahidi. 2005. **Antioxidant activity of almond seed extract and its fractions.** *J. Food Lipids.* 12:344-358.

In this study, phenolic compounds were extracted from defatted almond seeds. Phenolic compounds present in the crude extract and its fractions showed antioxidant and antiradical properties as revealed following studies using a β -carotene-linoleate model system, total antioxidant activity (TAA) method, 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity and reducing power evaluation. Results of these assays showed highest values when tannins (fraction II) were tested. The content of total phenolics in fraction II was the highest (80.4

mg/g). The content of tannins in this fraction determined using the vanillin method and expressed as absorbance units at 500 nm per 1 g was 2436. The high-performance liquid chromatography (HPLC) analysis of almond seed crude extract showed the presence of phenolic compounds, namely vanillic, caffeic, p-coumaric, ferulic acids (after basic hydrolysis), quercetin, kaempferol and isorhamnetin (after acidic hydrolysis), delphinidin and cyanidin (after n-butanol-HCl hydrolysis) and procyanidin B2 and B3.

Burton-Freeman, B., P.A. Davis, B.O. Schneeman, 2004. **Interaction of fat availability and sex on postprandial satiety and cholecystokinin after mixed-food meals.** *Am. J. Clin. Nutr.* 80:1207-14.

The satiety response to a dietary fat provided as almond oil or whole almonds was influenced by sex and appeared to be dependant on the availability of the fat to stimulate CCK release in women but not in men. The effect of fat availability appears to be less important to satiety-related processes in men. These data support the need for continued research in this area to better understand sex-specific differences mechanistically and outcomes behaviorally in order to design diets that provide optimal food intake control and satiety.

Chen, C.-Y.O., J.B. Blumberg, 2008. **In vitro activity of almond skin polyphenols for scavenging free radicals and inducing quinone reductase.** *J. Agr. Food Chem.* 56:4427-4434.

Almond skins are rich in polyphenols (ASP) that may contribute to these almond oxidant defense benefits. The in vitro effect of ASP extracted with methanol (M) or a gastrointestinal juice mimic (GI) alone or in combination with vitamins C (VC) or E (VE) (1-10 $\mu\text{mol/L}$) on scavenging free radicals and inducing quinone reductase (QR) were tested to assess their potential mechanisms of action. Flavonoid profiles from ASP-M and -GI extracts were different from one another. ASP-GI was more potent in scavenging HOCl and ONOO- radicals than ASP-M. In contrast, ASP-M increased and ASP-GI decreased QR activity in Hepa1c1c7 cells. Adding VC or VE to ASP produced a combination-and dose-dependent action on radical scavenging and QR induction. In comparison to their independent actions, ASPM plus VC were less potent in scavenging DPPH, HOCl, ONOO-, and O₂ - •. However, the interaction between ASPGI plus VC promoted their radical scavenging activity. Combining ASP-M plus VC resulted in a synergistic interaction, inducing QR activity, but ASP-GI plus VC had an antagonistic effect. On the basis of their total phenolic content, the measures of total antioxidant activity of ASP-M and -GI were comparable. Thus, in vitro, ASP act as antioxidants and induce QR activity, but these actions are dependent upon their dose, method of extraction, and interaction with antioxidant vitamins.

Chen, C.-Y., K. Lapsley and J.B. Blumberg, 2006. **A nutrition and health perspective on almonds.** *J Sci Food Agric.* 86:2245-2250.

Almonds provide a nutrient-dense source of vitamin E, manganese, magnesium, copper, phosphorus, fibre, riboflavin, monounsaturated fatty acids and protein. Habitual almond consumption does not lead to weight gain, and their inclusion in low-calorie diets appears to promote more weight loss than a comparable carbohydrate-based low-calorie diet. Also, almonds have a low glycemic index and do not adversely impact insulin sensitivity. Almonds are an excellent source of bioavailable alpha-tocopherol, and increasing their intake enhances the resistance of LDL against oxidation. In addition, the polyphenolic constituents of almonds have been characterized recently and found to possess antioxidant actions. Further research is required to achieve a better understanding of the role that the bioavailability and bioaccessibility of almond constituents and the synergy between them play in their associated health outcomes.

Chen, C.-Y., P.E. Milbury, S.-K. Chung, J. Blumberg, 2007. **Effect of Almond Skin Polyphenols and Quercetin on Human LDL and Apolipoprotein B-100 Oxidation and Conformation.** *J. Nutr. Biochem.* 18 (12):785-794.

Almond skin polyphenols (ASP) and vitamins C or E inhibit the copper-induced generation of conjugated dienes in human low density lipoprotein (LDL) in a synergistic manner. However, the mechanism(s) by which this synergy occurs is unknown. As modification of apolipoprotein (apo) B-100 is an early, critical step in LDL oxidation, the effects of combining ASP or quercetin and antioxidant vitamins on the oxidation of this moiety as well as on the alteration of LDL conformation and electronegativity was examined. In a dose-dependent manner, ASP (0.12-2.0 $\mu\text{mol/L}$ gallic acid equivalents, GAE) decreased tryptophan oxidation by 6.7-75.7%, increased the generalized polarity (Gp) of LDL by 21.0-81% at 90 min, and reduced the ratio of LDL- to total LDL (tLDL) by 38.2-84% at 5 h. The actions of ASP on these parameters were generally additive to those of vitamins C and E. However, a 10-25% synergy of ASP plus vitamin C in protecting apo B-100 tryptophan against oxidation may result from their synergistic interaction in prolonging the lag time to oxidation. ASP and vitamin E acted in synergy to reduce LDL-/tLDL by 24 -43%. The actions of quercetin were similar to ASP, though more potent in inhibiting Trp oxidation. Thus, ASP and quercetin reduce the oxidative modification of apo B-100 and stabilize LDL conformation in a dose-dependent manner, acting in an additive or synergistic fashion with vitamins C and E.

Chen, C.-Y., P.E. Milbury, K. Lapsley and J.B. Blumberg, 2005. **Flavonoids from almond skins are bioavailable and act synergistically with vitamins C and E to enhance hamster and human LDL resistance to oxidation.** *J. Nutr.* 235:1366-1373.

Flavonoids, found predominantly in the skin of almonds, may contribute to their health benefit, but their bioactivity and bioavailability have not previously been studied. Almond skin flavonoids (ASF) were extracted and their content of catechins and flavonols identified by HPLC with electrochemical detection. ASF bioactivity was assessed in vitro by their capacity to increase the resistance of human LDL to oxidation with the lag time to LDL oxidation increasing in a dose-dependent manner. Combining ASF with vitamin E or ascorbic acid extended the lag time >200% of the expected additive value. The bioavailability and in vivo antioxidant activity ASF were examined in hamsters. Peak plasma concentrations of catechin, epicatechin, and flavonols (quercetin, kaempferol and isorhamnetin) occurred at 60, 120 and 1890 min, respectively. The concentration of isorhamnetin was significantly elevated in liver at 180 min. Absorbed ASF enhanced the ex vivo resistance of hamster LDL collected at 60 min to oxidation by 18.0%. ASF possesses antioxidant capacity in vitro; they are bioavailable and act in synergy with vitamins C and E to protect LDL against oxidation in hamsters.

Davis, P.A., and C.K. Iwahashi, 2001. **Whole almonds and almond fractions reduce aberrant crypt foci in a rat model of colon carcinogenesis.** *Cancer Letters.* 165:27-33.

A research study in rats showed that almond consumption may provide a measure of protection from the risk of developing colon cancer. The findings that almonds might provide a measure of protection from the risk of chronic diseases suggests a need to reassess the current view that intake of high fat foods invariably has deleterious health effects. This suggests that almonds might have chemopreventive agents against colon carcinogenesis.

Davis, P., C.K. Iwahashi, W. Yokoyama, 2003. **Whole almonds activate gastrointestinal (GI) tract anti-proliferative signaling in APC^{min} (multiple intestinal neoplasia) mice.** *FASEB Journal*. 17(5):A1153.

Most recently, researchers used a genetic mouse model and examined the effects of whole almonds versus almond-component-containing diets on the APC^{min} mouse. Whole almonds activated GI tract anti-proliferative signaling, which might give a mechanistic explanation of almonds' chemo-protective effect.

Dourado, F., A. Barros, M. Mota, M.A. Coimbra, F.M. Gama. **Anatomy and cell wall polysaccharides of almond (*Prunus dulcis* D.A. Webb) seeds.** *J Agric Food Chem*.52:1364-1370.

Portuguese almond seed anatomy was analyzed by various staining techniques and light microscopy. The almonds seed coat is thin and structurally complex, with lignified cellulosic tissue. The almond kernel cell walls are rich in arabinose (45%) glucose (23%) uronic acids (12%) and xylose (12%).

Ellis, P.R., Kendall, C.W.C., Ren, Y., Parker, C., Pacy, J.P., Waldron, K.W., D.J.Q. Jenkins, 2004. **Role of cell walls in the bioaccessibility of lipids in almond seeds.** *Am J Clin Nutr*. 80:604-13.

The role that cell walls play in influencing the bioaccessibility of intracellular lipids from almonds kernels was investigated. The cell walls were found to be rich in non-starch polysaccharides and a high concentration of phenolics was detected. During disruption by chewing or mechanical means only the surface layer of cells was ruptured and lipids released. In fecal samples collected from subjects on an almond diet, intact cell walls were found, indicating that not all lipids are available for digestion.

Fraser, G.E., H.W. Bennett, K.B. Jaceldo, J. Sabaté, 2002. **Effect on body weight of a free 76 kilojoules (320 calorie) daily supplement of almonds for 6 months.** *J Am Coll Nutr*. 21(3): 275-83.

A one-year clinical study evaluating the long-term effect of eating almonds daily on dietary patterns, displacement of foods and selected nutrients and satiety, concluded that adding a modest quantity of almonds (approximately 2 ounces) to the diet regularly resulted in increased unsaturated fat intake with no significant changes in body weight. Long-term daily consumption of almonds also improved micronutrient profiles and eating patterns of free-living healthy individuals. The lack of weight gain was especially evident in more obese subjects, and some actually lost small amounts of weight. Food records from participants showed that almonds replaced less healthy high calorie snacks in their diets.

Frecka, J.M., J.H. Hollis, R.D. Mattes, 2007. **Effects of appetite, BMI, food form and flavor on mastication: almonds as a test food.** *Eur. J. Clin. Nutr*. doi. 10.1038/sj.ejcn.1602838.

The purpose of this study was to investigate the effects of appetitive sensations, body mass index (BMI) and physical/sensory properties of food (almonds) on masticatory indices and resultant pre-swallowing particle size. Twelve lean (BMI = 22.2 +/- 0.3) adults were studied. After collecting appetitive ratings, electromyographic recordings were used to assess participants'

microstructure of eating for five almond products (raw, dry unsalted roasted, natural sliced, roasted salted and honey roasted) under fasted and satiated conditions. Duplicate samples were masticated to the point of deglutition and then were expectorated and size sorted. No statistically significant effects of BMI were detected for any of the mastication measures. Maximum and mean bite forces were greater under the fasted condition. Sliced almonds required a significantly lower bite force than did the other almond varieties. The pre-swallowing particle sizes were significantly greater for the sliced almonds than all other varieties. Both the number of chews and mastication time were negatively correlated with particle size. There were no significant effects of almond form or flavor on particle size. These results do not support innate differences in masticatory function between lean and obese individuals, nor effects of sensory properties. Instead, the physical form of foods as well as an individual's appetitive state may have a greater influence on masticatory behavior. The health implications of these observations warrant further investigation.

Frison-Norrie, S.L., P. Sporns, 2002. **Identification and quantification of flavonol glycosides in almond seedcoats using MALDI-TOF MS.** *J Agri Food Chem.* 50:2782-7.

The importance of flavonol glycosides, a subclass of flavonoids, has led to the development of a number of methods for identification and quantification. Traditionally, flavonol glycosides have been characterized using paper chromatography, thin-layer chromatography, and UV spectroscopy. Recently the application of high-performance liquid chromatography (HPLC) for their separation and quantification has become predominant. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is a new analytical technique first introduced in 1987, and it offers several advantages over other methodologies including ease of sample preparation, rapid generation of spectra, tolerance of impurities, and minimal fragmentation allowing direct access to molecular weight. The objectives of the current research were to develop and validate a MALDI-TOF MS methodology for qualitative and quantitative analysis of flavonol glycosides in almond seedcoats. The four flavonol glycosides identified in almond seedcoats for the first time were: isorhamnetin rutinoside, isorhamnetin glucoside, kaempferol rutinoside, and kaempferol glucoside.

Frison-Norrie, S.L., P. Sporns, 2002. **Variation in the flavonol glycoside composition of almond seedcoats as determined by MALDI-TOF Mass Spectrometry.** *J Agric Food Chem.* 50:6818-22.

Seedcoats of 16 almond varieties were screened for flavonol glycosides. Each of the 16 seedcoat samples exhibited a unique composition. In all almond varieties, isorhamnetin rutinoside was the most abundant flavonol glycoside, and the total content ranged from 75 to 250 $\mu\text{g/g}$.

Fulgoni, V.L., M. Abbey, P. Davis, D. Hyson, D. Jenkins, J. Lovejoy, M. Most, J. Sabaté, G. Spiller, 2002. **Almonds lower blood cholesterol and LDL-cholesterol but not HDL-cholesterol or triglycerides in human subjects: results of a meta-analysis.** *FASEB J.* 16(5): A981.

A meta-analysis of seven studies was conducted to determine the effects of almond consumption on blood total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C) and triglycerides (TG). Data from 146 individuals with normal, mild or moderate

hypercholesterolemia were included in the meta-analysis. The results showed that almonds significantly reduced TC and LDL-C with no effect on HDL-C or TG.

Gigleux, I., D.J.A. Jenkins, C.W.C. Kendall, A. Marchie, D.A. Faulkner, J.M.W. Wong, R. de Souza, A. Emam, T.L. Parker, E.A. Trautwein, K.G. Lapsley, P.W. Connelly, B. Lamarche, 2007. **Comparison of a dietary portfolio diet of cholesterol-lowering foods and a statin on LDL particle size phenotype in hypercholesterolaemic participants.** *Brit. J. Nutr.* 98(6):1229-1236.

This study examined the effect of diet versus statins on LDL particle size as a risk factor for CVD. The impact of a dietary portfolio of cholesterol-lowering foods and a statin on LDL size electrophoretic characteristics were compared in 34 subjects. LDL electrophoretic characteristics were measured by non-denaturing polyacrylamide gradient gel electrophoresis of fasting plasma at 0, 2 and 4 weeks of each treatment. The reductions in plasma LDL-cholesterol levels with the dietary portfolio and with statins were comparable and were largely attributable to reductions in the estimated concentration of cholesterol within the smallest subclass of LDL (portfolio 20·69 (SE 0·10) mmol/l, statin 20·99 (SE 0·10) mmol/l). These were significantly greater ($P, 0·01$) than changes observed after the control diet (20·17 (SE 0·08) mmol/l). The pronounced reduction in cholesterol levels within the small LDL fraction may provide additional cardiovascular benefit over the traditional low-fat diet of National Cholesterol Education Program Step II.

Harrison, K., L.M. Were, 2007. **Effect of gamma irradiation on total phenolic content yield and antioxidant capacity of almond skin extracts.** *Food Chem.* 102:932-937.

Almond (*Prunus amygdalus*) skins are agricultural by-products that are a source of phenolic compounds. Phenolic compounds from gamma-irradiated almond skins were extracted with 40% ethanol. Total phenolic content was determined using the Folin–Ciocalteu (F–C) method. Almond skin extracts (ASE): soybean oil (1:4 v/v) mixtures containing 0.08% FeCl₃ were prepared. Antioxidant activity was determined by conjugated dienes and trienes (CD and CT, respectively) measurements, peroxide value (PV), Trolox[®] equivalent antioxidant capacity (TEAC) and Photochemiluminescence (PCL). Phenolic content yield ($p < 0.05$) was higher in ASE irradiated at doses greater than 4 kGy (trial I) or 12.7 kGy (trial II) compared to the control. Increased antioxidant activity was observed in TEAC assay and PCL with lipid-soluble antioxidant capacity reagents in ASE irradiated above 4 kGy (trial I) and 12.7 kGy (trial II) compared to 0 kGy. Gamma irradiation of almond skins thus increased the yield of total phenolic content as well as enhanced antioxidant activity of extracts.

Hollis, J., R. Mattes, 2007. **Effect of chronic consumption of almonds on body weight in healthy humans.** *Brit. J. Nutr.* 98:651-656.

Small changes of diet may reduce CVD risk. One example is the inclusion of nuts, which are rich in fiber, unsaturated fatty acids and phytonutrients. However, their fat content and energy density raise concerns that chronic consumption will promote weight gain. Randomized intervention studies are required to evaluate whether this concern is well founded. This study's aim was to determine if the inclusion of a 1440 kJ serving of almonds in the daily diet results in positive energy balance, and body composition change. During a 23-week cross-over design study, participants were required to consume almonds for 10 weeks and were provided no advice on how to include them in their diet. For another 10 weeks (order counter-balanced), participants followed their customary diet and there was a 3-week washout between. A study group of twenty women was used. Potential mechanisms of energy dissipation were measured. Ten weeks of daily

almond consumption did not cause a change in body weight. This was predominantly due to compensation for the energy contained in the almonds through reduced food intake from other sources. Moreover, inefficiency in the absorption of energy from almonds was documented (P,0.05). No changes in resting metabolic rate, thermic effect of food or total energy expenditure were noted. A daily 1440 kJ serving of almonds, sufficient to provide beneficial effects on cardiovascular risk factors, may be included in the diet with limited risk of weight gain. Whether this can be generalized to other high-fat energy dense foods warrants evaluation.

Hyson, D., B.O. Schneeman, P.A. Davis, 2002. **Almonds and almond oil have similar effects on plasma lipids and LDL oxidation in healthy men and women.** *J Nutr.* 132(4):703-7.

Scientists compared the effects of whole almonds vs. almond oil consumption on plasma lipids and reduced cardiovascular risk in healthy men and women. They found that with either whole almonds or almond oil there was a 54% increase in monounsaturated fat in diet, decreased saturated fat and cholesterol intake, and no significant changes in total energy, total or polyunsaturated fat intake. They concluded that whole almonds and almond oil did not differ in their beneficial effects suggesting that the favorable effect is due to components in the almond oil fraction.

Jaceldo-Siegl, G.E. Fraser, J. Sabaté, 2001. **Effect of almond supplementation on eating patterns, and micronutrient and fatty acid intake profile in free-living healthy adults.** *Ann Nutr Metab.* 45(1):152.

In this study, long-term daily consumption of almonds improved the fatty acid and micronutrient profile, and eating patterns of free-living healthy individuals. The researchers concluded that regular nut intake can be considered as part of a nutrition-related behavior change to improve cardiovascular health in adults.

Jaceldo-Siegl, K., J. Sabate, S. Rajaram, G.E. Fraser, 2004. **Long-term supplementation without advice on food replacement induces favourable nutrient modifications to the habitual diets of free-living individuals.** *Brit. J. Nutr.* 92:533-540.

Researchers found that an iso-energetic addition of 320 calories of almonds to a daily diet to 81 people over a one-year period did not significantly increase body weight. Recalls and diaries indicate that the energy for almonds was substituted in place of other foods without weight gain while simultaneously improving nutrient intake of such nutrients as vitamin E, magnesium and dietary fiber.

Jambazian, P. R., E. Haddad, S. Rajaram, J. Tanzman, J. Sabaté, 2005. **Almonds in the Diet Simultaneously Improve Plasma Alpha-Tocopherol Concentrations and Reduce Plasma Lipids.** *J. Am. Diet. Assoc.* 105:449-454.

The study objective was to assess the dose response effect of almond intake on plasma and red blood cell tocopherol concentrations in healthy adults while enrolled in a randomized crossover feeding trial. Participants were 16 men and women, aged 41 +/- 13 years. Incorporating almonds into the diet helped meet the revised Recommended Dietary Allowance of 15 mg/day alpha tocopherol and increased lipid adjusted plasma and red blood cell alpha tocopherol

concentrations in a dose response fashion. The USDA recommended serving size of one ounce of almonds daily can be isocalorically substituted for white bread, crackers, chips and similar refined products to provide 7.4 mg alpha tocopherol vitamin E.

Jenkins, D.J.A., C.W.C. Kendall, D.A. Faulkner, T. Kemp, A. Marchie, T.H. Nguyen, J.M.W. Wong, R. de Souza, A. Emam, E. Vidgen, E.A. Trautwein, K.G. Lapsley, R.G. Josse, L.A. Leiter, W. Singer, 2008. **Long-term effects of a plant-based dietary portfolio of cholesterol-lowering foods on blood pressure.** *Eur. J. Clin. Nutr.* 62:781-788.

For 1 year, 66 hyperlipidemic subjects were prescribed diets high in plant sterols (1.0 g/1000 kcal), soy protein (22.5 g/1000 kcal), viscous fibers (10 g/1000 kcal) and almonds (22.5 g/1000 kcal). There was no control group. Seven-day diet record, blood pressure and body weight were monitored initially monthly and later at 2-monthly intervals throughout the study. Fifty subjects completed the 1-year study. When the last observation was carried forward for non-completers (n=9) or those who changed their blood pressure medications (n=7), a small mean reduction was seen in body weight 0.770.3 kg (P=0.036). The corresponding reductions from baseline in systolic and diastolic blood pressure at 1 year (n=66 subjects) were -4.271.3mm Hg (P=0.002) and -2.370.7mm Hg (P=0.001), respectively. Blood pressure reductions occurred within the first 2 weeks, with stable blood pressures 6 weeks before and 4 weeks after starting the diet. Diastolic blood pressure reduction was significantly related to weight change (r=0.30, n=50, P=0.036). Only compliance with almond intake advice related to blood pressure reduction (systolic: r=-0.34, n=50, P=0.017; diastolic: r=-0.29, n=50, P=0.041). A dietary portfolio of plant-based cholesterol-lowering foods reduced blood pressure significantly, related to almond intake. The dietary portfolio approach of combining a range of cholesterol lowering plant foods may benefit cardiovascular disease risk both by reducing serum lipids and also blood pressure.

Jenkins, D.J.A, C.W.C. Kendall, D.A. Faulkner, T. Nguyen, T. Kemp, A. Marchie, J. M. W. Wong, R. de Souza, A. Emam, E. Vidgen, E. A. Trautwein, K. G. Lapsley, C. Holmes, R. G. Josse, L. A. Leiter, P. W. Connelly, and W. Singer, 2006. **Assessment of the longer-term effects of a portfolio of cholesterol-lowering foods in hypercholesterolemia.** *Am J Clin Nutr.* 83:582-91.

The goal of this research phase was to determine the effectiveness of consuming a combination of cholesterol-lowering foods (dietary portfolio) under real-world conditions and to compare these results with published data from the same participants who had undergone four week metabolic studies to compare the same dietary portfolio with the effects of a statin. Fifty-five middle-aged men and women were followed for 12 months. Patients were prescribed diets high in plan sterols (1 g/1,000 calories), soy protein (22.5 g/1,000 calories), viscous fibers (10 g/1,000 calories) and almonds (23 g/1,000 calories) and then were released to choose, purchase, and prepare foods on their own. One-third of patients lowered their LDL cholesterol levels by 20 percent. Two-thirds of this group was eating a mixed diet, showing that the diet does not need to be vegan or even vegetarian to achieve these results.

Jenkins, D.J.A., C.W.C. Kendall, D. Faulkner, E. Vidgen, E.A. Trautwein, T.L. Parker, A. Marchie, G. Koumbridis, K.G. Lapsley, R.G. Josse, L.A. Leiter, P.W. Connelly, 2005. **A dietary portfolio approach to cholesterol reduction: combined effects of plant sterols, vegetable proteins and viscous fibers in hypercholesterolemia.** *Metabolism.* 51:1596-1604.

This seven-week pilot study with 13 men and women was the first of its kind to examine the combined effect of a “portfolio” of foods with heart-health related claims—almonds as well as foods high in soy protein, viscous fiber and plant sterols. The plan, whose hypothesis is that combining foods with cholesterol-lowering properties into one diet will work in synergy resulting in greater reductions in “bad” cholesterol, reduced LDL cholesterol by 29% and the ratio of LDL cholesterol to HDL cholesterol by 26%. Results were so encouraging that the researchers developed a multi-phase research plan.

Jenkins J. D. A., C. W. C. Kendall, A. R. Josse, S. Salvatore, F. Brighenti, L. S. A. Augustin, P. R. Ellis, E. Vidgen, and A. V. Rao. 2006. **Almonds decrease postprandial glycemia, insulinemia, and oxidative damage in healthy individuals.** *J Nutr.* 136:1-6.

The effect of decreasing postprandial glucose excursions on measures of oxidative damage was assessed. Fifteen healthy subjects ate 2 bread control meals and 3 test meals: almonds and bread; parboiled rice; and instant mashed potatoes, balanced in carbohydrate, fat, and protein, using butter and cheese. Blood samples were obtained at baseline and for 4 h postprandially. Glycemic indices for the rice and almond meals were less than for the potato meal, as were the postprandial areas under the insulin concentration time curve. No postmeal treatment differences were seen in total antioxidant capacity. However, the serum protein thiol concentration increased following the almond meal, indicating less oxidative protein damage, and decreased after the control bread, rice, and potato meals, when data from these 3 meals were pooled. The change in protein thiols was also negatively related to the postprandial incremental peak glucose and peak insulin responses observations. Therefore, lowering postprandial glucose excursions may decrease the risk of oxidative damage to proteins. Almonds are likely to lower this risk by decreasing the glycemic excursion and by providing antioxidants. These actions may relate to mechanisms by which nuts are associated with a decreased risk of coronary heart disease.

Jenkins, D.J.A., C.W.C. Kendall, A. Marchie, D.A. Faulkner, A.R. Josse, J.M.W. Wong, R. de Souza, A. Emam, T.L. Parker, T.J. Li, R.G. Josse, L.A. Leiter, W. Singer and P.W. Connelly. 2005. **Direct comparison of dietary portfolio vs statin on C-reactive protein.** *Eur. J. Clin. Nutr.* 59:851-860.

This study compared the efficacy of a dietary combination (portfolio) of cholesterol-lowering foods vs a statin in reducing C-reactive protein (CRP) as a biomarker of inflammation linked to increased cardiovascular disease risk. 34 hyperlipidemic subjects completed 3 1-month treatments as outpatients in random order: a very low-protein (21.4g/1000 kcal), viscous fibers (9.8 g/1000 kcal), and almonds (14 g/1000 kcal) (portfolio). Fasting blood samples were obtained at weeks 0, 2, and 4. Using the complete data, no treatment reduced serum CRP. However, when subjects with CRP levels above the 75th percentile for previously reported studies (>3.5 mg/l) were excluded, CRP was reduced similarly on both statin, -16.3 +/- 6.7% and dietary portfolio, 23.8 +/- 6.9%. Both statin and portfolio treatments were similar in reducing CRP and numerically more effective than control. A combination of cholesterol-lowering foods reduced C-reactive protein to a similar extent as the starting dose of a first-generation statin.

Jenkins, D.J.A., C.W.C Kendall, A. Marchie, D. Faulkner, E. Vidgen, K.G. Lapsley, E.A. Trautwein, T.L. Parker, R.G. Josse, L.A. Leiter, P.W. Connelly, 2003. **The effect of combining**

plant sterols, soy protein, viscous fibers, and almonds in treating hypercholesterolemia. *Metabolism.* 52:11:1478-83.

In this second phase of the portfolio approach to lowering cholesterol a control arm was added, which was the National Cholesterol Education Program's Step 2 diet. There were 23 subjects tested for a one-month, randomized controlled parallel study. The LDL and the LDL:HDL-cholesterol ratio were both significantly lower on the portfolio diet than on the control diet. Mean weight loss was similar on the test and control diets, and no difference was seen in blood pressure, HDL-C, serum triglycerides, lipoprotein, or homocysteine concentrations between diets.

Jenkins, D.J.A., C.W.C. Kendall, A. Marchie, D. Faulkner, J.M.W. Wong, R. de Souza, A. Emam, T.L. Parker, E. Vidgen, K.G. Lapsley, E.A. Trautwein, R.G. Josse, L.A. Leiter, P.W. Connelly, 2003. **Effects of a dietary portfolio of cholesterol-lowering foods vs. lovastatin on serum lipids and c-reactive protein.** *JAMA.* 290:502-10.

The study directly compared three randomized groups of patients with high cholesterol. One group of 16 people ate the National Cholesterol Education Program's Step 2 diet, which is a very low-saturated fat diet based on whole-wheat cereals and low-fat dairy foods. Another group of 14 people ate this same diet in addition to taking a 20-milligram lovastatin, a cholesterol-lowering drug, each day. A third group of 16 ate the portfolio diet high in almonds and other foods high in plant sterols and vegetable protein as well as viscous fiber. The control, statin and dietary portfolio had mean decreases in low-density lipoprotein cholesterol of 8.0%, 30.9% and 28.6%, respectively. Respective reductions in c-reactive protein were 10.0%, 33.3% and 28.2%. This study found that patients on the portfolio diet were the first documented to lower their c-reactive protein levels through dietary intervention. C-reactive protein is an indication of inflamed arteries and a risk factor for heart disease.

Jenkins, D.J.A., C.W.C. Kendall, A. Marchie, D. Faulkner, J.M.W. Wong, R. de Souza, A. Emam, T.L. Parker, E. Vidgen, E.A. Trautwein, K.G. Lapsley, R.G. Josse, L.A. Leiter, W. Singer, P.W. Connelly, 2005. **Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants.** *Am J Clin Nutr.* 81:380-387.

In phase 3, 34 men and women underwent all 3 (1-month) treatments in random order as outpatients: a very low-saturated fat diet (control diet); the same diet with 20 mg lovastatin (statin diet); and a diet high in plant sterols (1.0 g/1000 kcal), soy protein foods (including soy milks and soy burgers, 21.4 g/1000 kcal), almonds (14 g/1000 kcal), and viscous fibers from oats, barley, psyllium, and the vegetables okra and eggplant (10 g/1000 kcal) (portfolio diet). Fasting blood samples were obtained at weeks 0, 2 and 4. LDL-cholesterol concentrations decreased by $8.5 \pm 1.9\%$, $33.3 \pm 1.9\%$, and $29.6 \pm 1.3\%$ after 4 weeks of the control, statin and portfolio diets, respectively. Although the absolute difference between the statin and the portfolio treatments was significant at 4 weeks ($P = 0.013$), 9 participants (26%) achieved their lowest LDL-cholesterol concentrations with the portfolio diet. Moreover, the statin ($n = 27$) and the portfolio ($n = 24$) diets did not differ significantly ($P = 0.288$) in their ability to reduce LDL cholesterol below the 3.4-mmol/L primary prevention cutoff.

Jenkins, D.J.A., C.W.C. Kendall, A. Marchie, A.R. Josse, T.H. Nguyen, D.A. Faulkner, K.G. Lapsley, J. Blumberg, 2008. **Almonds Reduce Biomarkers of Lipid Peroxidation in Older Hyperlipidemic Subjects.** *J. Nutr.* 138:908-913.

Nut consumption reduces coronary heart disease (CHD) risk. However, apart from cholesterol-lowering, mechanisms for beneficial effects are not clear, although nut antioxidants may limit oxidative damage to lipids and lipoproteins. Almonds were therefore tested for antioxidant effects in a randomized dose-response crossover study with 27 hyperlipidemic subjects consuming each for one month; control, half- and full- dose almonds (73+/- g/d). Antioxidant effects of almonds were demonstrated as lower concentrations of serum malondialdehyde (MDA) and urinary isoprostane output on the full dose at 4 wks. Antioxidant activity may be added to the lipid-lowering property to explain the CHD protective effect of nuts.

Jenkins, D.J., C.W. Kendall, A. Marchie, T.L. Parker, P.W. Connelly, W. Qian, J.S. Haight, D. Faulkner, E. Vidgen, K.G. Lapsley, G.A. Spiller. 2002. **Dose response of almonds on coronary heart disease risk factors: blood lipids, oxidized low-density lipoproteins, lipoprotein (a), homocysteine, and pulmonary nitric oxide: a randomized, controlled, crossover trial.** *Circulation* 106(11):1327-32.

Researchers found that patients with high cholesterol who ate about one ounce of almonds each day lowered their LDL (low density lipoprotein) cholesterol at least 3%. There was an even greater decrease for those who ate about two handfuls of almonds per day, indicating that there is a dose response effect. According to the authors, almonds reduced coronary heart disease risk factors in a dose-dependent manner and may be used as healthy snacks without weight gain.

Jenkins, D.J.A., C.W.C. Kendall, T.H. Nguyen, J. Teitel, A. Marchie, M. Chius, A.Y. Taha, D.A. Faulkner, T. Kemp, J.M.W. Wong, R. de Souza, A. Emam, E.A. Trautwein, K.G. Lapsley, C. Holmes, R.G. Josse, L. A. Leiter, W. Singer, 2007. **Effect on hematologic risk factors for coronary heart disease of a cholesterol reducing diet.** *Eur. J. Clin. Nutr.* 61:483-492.

A dietary portfolio of cholesterol-lowering ingredients has proved effective in reducing serum cholesterol. However, it is not known whether this dietary combination will also affect hematologic risk factors for coronary heart disease (CHD). Reductions in hematocrit and polymorphonuclear leukocytes have been reported to improve cardiovascular risk. We, therefore, report changes in hematological indices, which have been linked to cardiovascular health, in a 1-year assessment of subjects taking an effective dietary combination (portfolio) of cholesterol-lowering foods.

Jia, X., N. Li, W. Zhang, X. Zhang, K. Lapsley, G. Huang, J. Blumberg, G. Ma, J. Chen, 2006. **A pilot study on the effects of almond consumption on DNA damage and oxidative stress in smokers.** *Nutrition and Cancer.* 54(2), 179-183.

The effects of almond consumption on DNA damage and oxidative stress among cigarette smokers were studied. Results from this pilot study indicate that almond consumption has preventive effects on oxidative stress and DNA damage caused by smoking.

Joice, C, 2004. **A practical approach to the portfolio diet.** *On the Cutting Edge of Diabetes. American Dietetics Association Newsletter.* Volume 25 Number (5):1-8.

Current dietary recommendations for the treatment of coronary heart disease have been expanded beyond the restriction of fat and cholesterol to include viscous fibres, plant sterols,

vegetable protein foods (soy) and nuts (almonds). Research at the University of Toronto has shown that combining these dietary components in a single dietary strategy, known as the Portfolio Diet, results in cholesterol reduction proven to be equivalent to therapeutic doses of first generation Statins. This article presents an overview of the clinical research studies demonstrating the effectiveness of the Portfolio Diet and focuses on the necessary dietary modifications to realize the goals of the Portfolio Diet. Future consideration is directed towards the potential benefits of the Portfolio Dietary regime to the diabetic population.

Joice, C., 2007. **A practical approach to the Portfolio Eating Plan; a dietary regime to prevent cardiovascular disease.** *Cah Nutr Diét.* 42(1):42-45.

(As translated from French) Current dietary strategies for the treatment of coronary heart disease have expanded beyond the restriction of saturated and trans-fat and cholesterol to include viscous fibers, plant sterols, vegetable protein foods (soy) and nuts (almonds). Research at the University of Toronto, Canada, has shown that combining these dietary components in a single dietary strategy, known as the Portfolio eating plan, results in cholesterol reduction proven to be equivalent to a starting therapeutic dose of first generation statins. This overview of the clinical research studies demonstrates the effectiveness of the Portfolio eating plan and focuses on the necessary dietary modifications to realize the goals of this cardio-protective dietary strategy. In addition, a perspective is directed towards the Mediterranean diet, a regime well recognized in France for its cardiovascular benefits.

Joice, C. K. Lapsley, J.B. Blumberg, 2008. **Almonds as a value added ingredient: Benefits of a nutrient rich, high fiber nut.** *AgroFood.* 19(3):16-18.

Increased consumption of plant foods high in dietary fiber and phytochemicals is associated with a reduced risk of obesity, heart disease, diabetes, and some forms of cancer. As part of a healthful diet and lifestyle, almond consumption promotes satiety, serum cholesterol reduction, and blood sugar control by serving as a good source of monounsaturated fat, dietary fiber, phytochemicals, and vitamin E. Awareness of the health benefits of whole almonds and their components could provide additional appeal for consumers and add value to food manufacturers reformulating products to provide higher levels of fiber and other important nutrients.

Josse, A.R., C.W.C. Kendall, L.S.A. Augustin, P.R. Ellis, D.J.A. Jenkins, 2007. **Almonds and postprandial glycemia – a dose-response study.** *Metabolism.* 56(3):400-404.

The effects of varying amounts of almonds on the postprandial blood glucose response to a carbohydrate meal were assessed. The aim was to assess the effect of adding almonds to a bread meal. Nine healthy volunteers (2 women, 7 men, mean age 27.8 years; mean body mass index 22.9 kg/m²) were randomly fed with 3 test meals and 2 white bread control meals on separate days. Subjects were fed the meals after a 10- to 12-hour overnight fast. Each meal contained 50 g of available carbohydrate from white bread eaten alone or with 30, 60 or 90 g (1, 2, or 3 oz) of almonds. Capillary fingerprint blood samples for glucose analysis were obtained at 0, 15, 30, 45, 60, 90 and 120 minutes. Glycemic responses were assessed by calculating the incremental area under the 2-hour blood glucose curve. The addition of almonds to white bread resulted in a progressive reduction in the glycemic index of the composite mean in a dose-dependent manner for the 30-g (105.8 +/- 23.3), 60-g (63. +/- 9.0), and 90-g (45.2 +/- 5.8) doses of almonds ($r = -$

0.524, n = 36, P = .001) The conclusion is that, in addition to lowering serum cholesterol levels, almonds may also reduce the glycemic impact of carbohydrate foods with which they are eaten.

Kendall, C.W.C., D.J.A. Jenkins, A. Marchie, Y. Ren, P.R. Ellis, K.G. Lapsley, 2003. **Energy availability from almonds: implications for weight loss and cardiovascular health. A randomized controlled dose-response trial.** *FASEB Journal*. 17(4):A339.

Twenty-seven hyperlipidemic men and women consumed three iso-energetic (mean 423 kcal/day) supplements consisting of full-dose almonds (50-100g/d), half-dose almonds with half-dose muffins, and full-dose muffins, each for one month in a randomized controlled crossover study. The results showed that almond consumption improved blood lipid risk factors for CHD in a dose-dependent manner without weight gain. It appears that a portion of energy from almonds is unavailable because the cell walls act as a physical barrier to gastrointestinal digestion of nutrients.

Kurlandsky, S.B., K.S. Stote, 2006. **Cardioprotective effects of chocolate and almond consumption in healthy women.** *Nutr. Res.* 26:509-516.

The aim of this 4-armed parallel design study was to assess the synergistic or additive effect of a dietary intervention combining dark chocolate with almonds, in the framework of a low fat National Cholesterol Education Program Adult Treatment panel (NCEP III) diet, on circulating levels of serum lipids and inflammatory markers: intercellular adhesion molecule (ICAM), vascular adhesion molecule, and high-sensitivity C-reactive protein. Over a six week intervention 49 healthy normocholesterolemic participants were randomized to 1 of 3 treatments: chocolate (41 g/d), almonds (60 g/d), chocolate and almonds, or control (no chocolate or almonds). At the end of the intervention no participants reported a weight change and comparison to national guidelines demonstrated improvement in the dietary intake for all participants. No changes were noted in serum cholesterol concentration but triacylglycerol levels were reduced by approximately 21%, 13%, 19%, and 11% (P < .05), in the chocolate, almond, chocolate and almond, and control groups, respectively. The chocolate only treatment (P = .027) reported a significant 10 % decrease in circulating ICAM levels. No significant changes were observed for vascular adhesion molecule and high-sensitivity C-reactive protein levels in any treatment arm. The chocolate and almond combination did not result in any synergistic or additive effect. In conclusion, all treatment arms demonstrated improvement in serum triacylglycerol levels while the chocolate only treatment reduced levels of circulating ICAM. A combined consumption of chocolate and almonds over a six week period as part of the NCEP III diet did not show any harmful effects in healthy women.

Lamarche, B., S. Desroches, D.J.A. Jenkins, C.W.C. Kendall, A. Marchie, D. Faulker, E. Vidgen, K.G. Lapsley, E. Trautwein, T. Parker, R. Josse, L. A. Leiter, P. W. Connelly, 2004. **Combined effects of a dietary portfolio of plant sterols, vegetable protein, viscous fibre and almonds on LDL particle size.** *Brit J Nutr.* 92:657-63.

Small dense LDL particles have been associated with an increase for CVD. In this study 12 patients with mildly elevated plasma LDL-cholesterol levels were placed on the portfolio eating plan for one month. Fasting blood lipids were obtained at the start and at 2-week intervals. The diet induced reductions on plasma LDL cholesterol of 30% was attributed to the concurrent reductions in large (30%), medium (29%) and small (21%) LDL particles. These results indicate

that the combination of these foods and dietary components are effective in reducing CVD risk and serum concentrations of all LDL fractions, including small dense LDL.

Lapsley, K.G., G. Huang, 2004. **Health Benefits of Almonds.** *Cereal Foods World.* 49:1: 6-10.

This overview focuses first on the nutrition research linking almonds and heart health whether as a single food within a dose-response study (with a cholesterol lowering effect of approximately 5%) or in a dietary portfolio of other foods with proven heart health benefits (where there are combined cholesterol lowering effects of up to 30%). The emerging research that almonds as a nutrient-rich, satiating food may have a role to play in weight control and maintenance is reviewed next, followed by the latest information on almond phytochemicals and their potential role in cancer prevention. The article ends with a description of the California almond industry and the almond varieties grown and their uses.

Li, N., X. Jia, C.-Y.O. Chen, J.B. Blumberg, Y. Song, W. Zhang, X. Zhang, G. Ma, J. Chen, 2007. **Almond consumption reduces oxidative DNA damage and lipid peroxidation in male smokers.** *J. Nutr.* 137:2717 -2722.

Smoking increases the risk of several chronic diseases associated with elevated oxidative stress status. Almonds are a good source of antioxidant nutrients and may diminish smoking-related biomarkers of oxidative stress. This study investigated whether almond consumption decreases biomarkers of oxidative stress in young male Chinese smokers. The Chinese CDC researchers conducted a randomized, crossover clinical trial with 60 healthy male soldiers (18–25 y) who were habitual smokers (5–20 cigarettes/d) and supplemented their diet with 84 g almonds or 120 g pork (to control for calories) daily for 4 wk with a 4-wk washout period between treatment periods. In addition, 30 healthy nonsmoking men were provided the same daily serving of pork as reference comparison. Blood and urine were collected and assessed for biomarkers of oxidative stress. Baseline values of urinary 8-hydroxy-deoxyguanosine (8-OHdG) and malondialdehyde (MDA) and peripheral lymphocyte DNA strand breaks were significantly higher by 185, 64, and 97% in smokers than nonsmokers, whereas activities of plasma superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase were significantly lower by 15, 10, and 9%, respectively. After the almond intervention, serum α -tocopherol, SOD, and GPX increased significantly in smokers by 10, 35, and 16%, respectively and 8-OHdG, MDA, and DNA strand breaks decreased significantly by 28, 34, and 23%. No significant changes were found in smokers or nonsmokers after pork treatment. In smokers, after almond supplementation, the concentration of 8-OHdG remained significantly greater than in nonsmokers by 98%. These results suggest almond intake can enhance antioxidant defenses and diminish biomarkers of oxidative stress in smokers.

Lovejoy, J. C., M.M. Most, M. Lefevre, F.L. Greenway, J.C. Reed, 2002. **Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes.** *J Nutr.* 76(5):1000-6.

Results from this study suggest that almonds have no effect on insulin sensitivity in healthy adults nor do they affect glycemia in Type 2 diabetics. The researchers did find that almonds had beneficial effects on serum lipids in these patients.

Mandalari, G., R.M. Faulks, G.T. Rich, V.L. Turcos, D.R. Picout, R.B.L. Curto, G. Bisignano, G. Dugo, K. W. Waldron, P.R. Ellis, M.S.J. Wickham, 2008. **Release of protein, lipid, and vitamin E from almond seeds during digestion.** *J. Agric. Food Chem.* 56:3409-3416.

Though incomplete, the current status of knowledge on the evaluation of the bioaccessibility of almond macro, micro and phytonutrients may have important implications for the prevention and management of obesity and cardiovascular disease. This study quantified the release of lipid, protein and vitamin E from almonds during digestion and determined the role played by cell walls in the bioaccessibility of intracellular nutrients. Four different almond meals were digested in vitro under simulated gastric and gastric followed by duodenal conditions. Finely ground almonds were the most digestible with 39, 45 and 44% of lipid, vitamin E and protein released after duodenal digestion, respectively. Consistent with longer residence time in the gut, preliminary in vivo studies showed higher percentages of nutrient release and microscopic examination of digested almond tissue demonstrated cell wall swelling. Bioaccessibility is improved by increased residence time in the gut and is regulated by almond cell walls.

Mandalari, G., C. Nueno-Palop, G. Bisignano, M.S.J. Wickham, A. Narbad, 2008. **Potential prebiotic properties of almond (*Amygdalus communis* L.) seeds.** *Applied and Environmental Microbiology.* 74 (14):4264-4270.

Almonds are known to have a number of nutritional benefits, including cholesterol lowering effects and protection against diabetes. They are also a good source of minerals and vitamin E, which are associated with promoting health and reducing the risk for chronic disease. This study investigated the potential prebiotic effect of almonds in vitro using mixed faecal bacterial cultures. Two almond products, finely ground almonds (FG), and defatted finely ground almonds, (DG), were subjected to a combined model of the gastrointestinal tract which includes in vitro gastric and duodenal digestion, and the resulting fractions were subsequently used as substrates for the colonic model to assess their influence on the composition of gut bacteria and their metabolic activity. FG significantly increased the population of bifidobacteria and Eubacteria rectale, resulting in a higher prebiotic index (4.43) compared with the commercial prebiotic fructo-oligosaccharides (4.08) at 24 h incubation. No significant differences in the proportions of gut bacteria groups were detected in response to DG. The increase in Eubacteria rectale numbers during fermentation of finely ground almonds correlated with increased butyrate production. In conclusion, we have shown that FG has beneficial effect on the human microflora and the presence of almond lipid influenced the growth of gut bacteria.

Milbury, P. E., C.-Y. Chen, G. G. Dolnikowski, J. B. Blumberg, 2006. **Determination of flavonoids and phenolics and their distribution in almonds.** *J. Agr. Food Chem.* 54(14):5027-5033.

Limited information is available concerning the qualitative and quantitative composition of polyphenolic compounds, especially flavonoids, in almonds. The total phenols, flavonoids and phenolic acids in California almond (*Prunus dulcis*) skins and kernels among the principal almond varieties (Butte, Carmel, Fritz, Mission, Monterey, Nonpareil, Padre and Price) with high-performance liquid chromatography (HPLD)/electrochemical detection and UV detection were determined. Liquid chromatography/tandem mass spectrometry under identical HPLC conditions was utilized to verify identities of the predominant flavonoids and phenolic acids. Total phenols ranged from 127 (Fritz) to 241 (Padre) mg gallic acid equivalents/100g of fresh weight. The analyses were compiled to produce a data set of 18 flavonoids and three phenolic

acids. Using the existing approach of calculating only the aglycone form of flavonoids for use in the U.S. Department of Agriculture nutrient database, whole almonds would provide the most prevalent aglycones of isorhamnetin at 17.31 (4.91), kaempferol at 12.21 (0.35), catechin at 1.93 (0.55), quercetin at 0.04 (0.27), and epicatechin at 0.85 (0.24) mg/100g of fresh weight (mg/oz serving), respectively. These data can lead to a better understanding of the mechanisms of action underlying the relationship between almond consumption and health-related outcomes and provide values for whole and balanced almonds suitable for inclusion in nutrient databases. This approach allows for comparisons of flavonoid intake from different foods, e.g., on a weight basis, showing that almonds provide similar amount of flavonols as red onions, but 9-fold more isorhamnetin than white onions. The kaempferol and quercetin contents of almonds are comparable to that of broccoli and its concentrations of catechin is between that of brewed black and green tea.

Milbury, P., C.-Y. Chen, K., H.-K. Kwak, J. Blumberg, 2002. **Almond skins polyphenolics act synergistically with α -tocopherol to increase the resistance of low-density lipoproteins to oxidation.** *Free Radical Research*. 36:1 Supp.: 78-80.

Researchers found in this study that the nutrients in almonds work together in synergy to produce a greater health-promoting effect than from individual nutrients consumed alone. Their emerging evidence indicates that the unique combination of almond skins keep LDL cholesterol from oxidizing, a mechanism associated with the formation of plaque in arteries of the heart. Even at very low levels, when the almond skins compounds combine with the vitamin E in the almonds and vitamin C from other foods, they act in synergy and play a co-defensive role against atherosclerosis--in a fashion where the sum of their actions is much greater than each part.

Monagas, M., I. Garrido, R. Lebron-Aguilar, B. Bartolome, C. Gomez-Cordoves, 2007. **Almond (*Prunus dulcis* (Mill.) D.A. Webb) skins as a potential source of bioactive polyphenols.** *J. Agric. Food Chem.* 55:8498-8507.

The phenolic composition of almond skins was examined in order to evaluate their potential application as a functional food ingredient. Using the HPLC-DAD/ESI-MS technique, a total of 33 compounds corresponding to flavanols, flavonols, dihydroflavonols and flavanones, and other nonflavonoid compounds were identified. Peaks corresponding to another 23 structure-related compounds were also detected. MALDI-TOF MS was applied to characterize almond skin proanthocyanidins, revealing the existence of a series of A- and B-type procyanidins and propelargonidins up to heptamers, and A- and B-type prodelphinidins up to hexamers. Flavanols and flavonol glycosides were the most abundant phenolic compounds in almond skins, representing up to 38–57% and 14–35% of the total quantified phenolics, respectively. Due to their antioxidant properties, measured as oxygen-radical absorbance capacity (ORAC) at 0.398–0.500 mmol Trolox/g, almond skins can be considered as a value-added byproduct for elaborating dietary antioxidant ingredients.

Ren, Y, K.W. Waldron, J.F. Pacy, P.R. Ellis, 2001. **Chemical and histochemical characterization of cell wall polysaccharides in almond seeds in relation to lipid bioavailability.** *Biologically-active phytochemicals in food*, (ed.) W. Pfannhauser, G.R. Fenwick & S. Khokhar, Royal Soc. of Chem., Cambridge, U.K. 448-452.

The research team reported that almond cell walls may prevent the body's absorption of all the fat present in almonds. Normal chewing of almonds breaks down only some of the cell walls, leaving others intact. Thus, not all the fat was available for digestion.

Roux, K.H., S.S. Teuber, J.M. Robotham, S.K. Sathe, 2001. **Detection and stability of the major almond allergen in foods.** *J Agric Food Chem.* 49:2131-6.

Almond major protein (AMP or amandin), the primary storage protein in almonds is the major allergen recognized by almond-allergic patients. This study showed that AMP is also an excellent marker protein for detecting trace amounts of almond in food.

Sabaté, J., E. Haddad, 2001. **Almond-rich diets simultaneously improve plasma lipoproteins and alpha-tocopherol levels in men and women.** *Ann Nutr Metab.* 45(1):596.

Researchers examined the effect of eating almonds on blood lipids, particularly on the levels of the powerful antioxidant vitamin E in the blood. According to the authors, this study shows that a natural source of vitamin E, almonds, is efficiently utilized by the body. Moreover, surveys show that on average men need 5 mg of alpha-tocopherol, and women need 8 mg of alpha-tocopherol a day to meet their vitamin E needs. Just an ounce of almonds a day can effectively close the gap on vitamin E consumption.

Sabaté, J., E. Haddad, J.S. Tanzman, P. Jambazian, S. Rajaram, 2003. **Serum lipid response to the graduated enrichment of a step 1 diet with almonds: a randomized feeding trial.** *Am J Clin Nut.* 77(6):1379-84.

Researchers compared the dose response effects for 25 healthy individuals who consumed low or high almond doses with those following the National Cholesterol Education Program's Step 1 Diet. In a randomized crossover design, subjects were fed three isoenergetic diets for four weeks each after being fed a two-week run-in diet (containing 34% of energy from fat). All meals were prepared, weighed, and consumed at the test facility. The experimental diets included a Step 1 diet, a low-almond diet, and a high-almond diet, in which almonds contributed 0%, 10% and 20% of total energy, respectively, or about one to two handfuls of almonds. The results showed a decrease in total cholesterol, as well as LDL or "bad" cholesterol levels across all diets--with a 4.4% reduction in total cholesterol compared to the Step 1 Diet. However, the most significant changes were seen among individuals consuming the diet with the most almonds. Individuals with normal cholesterol levels also benefited from this eating plan by maintaining healthy cholesterol levels.

Sang, S., H. Kikuzaki, K. Lapsley, R.T. Rosen, N. Nakatani, C.-T. Ho, 2002. **Sphingolipid and other constituents from almond nuts (*Prunus amygdalus* Batsch).** *J Agric Food Chem.* 50:4709-12.

A sphingolipid compound was isolated from almonds for the first time. Four other compounds: B-sitosterol, dancosterol, uridine, and adenosine were also isolated.

Sang, S., K. Lapsley, X. Cheng, H.-Y. Fu, D.-E. Shieh, N. Bai, R.T. Rosen, R.E. Stark, C.-T. Ho, 2002. **New type sesquiterpene lactone from almond hulls (*Prunus amygdalus* Batsch).** *Tetrahedron Letters*. 43:2547-9.

An unusual sesquiterpene lactone, named amygdalactone, was isolated from almond hulls for the first time. This class of compounds is comprised of natural products with known anti-carcinogenic properties.

Sang, S., K. Lapsley, W.S. Jeong, P.A. Lachance, R.T. Rosen, C.T. Ho, 2002. **Antioxidative phenolic compounds isolated from almond skin (*Prunus amygdalus* Batsch).** *J Agric Food Chem*. 50:2459-63.

Nine phenolic compounds were isolated from the ethyl acetate and n-butanol fractions of almond skins for the first time on the basis of NMR and MS data. Several showed strong radical scavenging activity.

Sang, S., K. Lapsley, R.T. Rosen, C.T. Ho, 2002. **New prenylated benzoic acid and other constituents from almond hulls (*Prunus amygdalus* Batsch).** *J Agric Food Chem*. 50:607-9.

One new prenylated benzoic acid derivative and three known constituents (catechin, protocatechuic acid and ursolic acid) have been isolated from almond hulls for the first time. Each of these compounds have known antioxidant activity, which might be beneficial since the current major use of almond hulls is as cattle feed.

Sang, S., G. Li, S. Tian, K. Lapsley, R.E. Stark, R.K. Pandey, R.T. Rosen, C.T. Ho, 2002. **An unusual diterpene glycoside from the nuts of almond (*Prunus amygdalus* Batsch).** *Tetrahedron Letters*. 44:1199-1202.

A new unusual diterpene glycoside, named amygdaloside, was isolated from almonds. Since this family of compounds is known to have anti-tumor and anti-inflammatory effects, further research is needed in this area.

Sathe, S.K., 1993. **Solubilization, electrophoretic characterization and in vitro digestibility of almond (*Prunus amygdalus*) proteins.** *J Food Biochem*. 16:249-64.

The six major varieties of California almonds were fully characterized for moisture, protein, fat and ash. Two fatty acids, oleic and linoleic, accounted for up to 90% of the total fat. Over 95% of almond proteins were water soluble with a minimum solubility at pH less than 4.

Sathe, S.K., S.S. Teuber, T.M. Gradziel, K.H. Roux, 2001. **Electrophoretic and immunological analyses of almond (*Prunus dulcis* L.) genotypes and hybrids.** *J Agric and Food Chem*. 49(4): 2043-52.

Aqueous extracts from 60 almond samples were analyzed for protein and peptide content. A single major storage protein (almond major protein--AMP or amandin) dominated the total soluble protein composition. In addition to AMP, several minor polypeptides were present in all genotypes and variability was evident. AMP was recognized by human IgE and rabbit polyclonal antibodies in all genotypes tested, indicating AMP is an excellent allergy relevant target molecule for the purpose of detecting the presence of almonds.

Sathe, S.K., W.J. Wolf, K.H. Roux, S.S. Teuber, M. Venkatachalam, K.W.C. Sze-Tao, 2002. **Biochemical characterization of amandin, the major storage protein in almond (*Prunus dulcis* L.).** *J of Agric Food Chem.* 50(15):4333-41.

The major almond storage protein, amandin, was characterized by several methods for molecular weight distribution. Regardless of preparation method, all amandins are antigenically related and suitable for purposes of detecting almonds using ELISA procedures.

Spiller, G.A., D.A.J. Jenkins, O. Bosello, J.E. Gates, L.N. Cragen, B. Bruce, 1998. **Nuts and plasma lipids: an almond-based diet lowers LDL-C while preserving HDL-C.** *J Am Coll Nutr.* 17(3):285-90.

This study involved 45 hypercholesterolemic adults in a randomized, controlled, parallel study that lasted four weeks (following one week on a baseline diet). The control group consumed a diet of whole and unrefined foods plus 85g/day of cheddar cheese, 28g/day of butter, and 21g/day of rye crackers. The olive oil group consumed a base diet of whole and unrefined foods plus 48g/day of olive oil, 113g/day of cottage cheese and 21g/day of rye crackers. The almond group consumed the same base diet of whole and unrefined foods plus 100g/day of raw, unblanched almonds (both whole and ground). The almond diet lowered total cholesterol by 12% and LDL by 15% compared to baseline values, while the olive oil diet had no significant effects.

Spiller, G.A., D.J. Jenkins, L.N. Cragen, J.E. Gates, O. Bosella, K. Berra, C. Rudd, M. Stevenson, R. Superko, 1992. **Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins.** *J Am Coll Nutr* 11(2):126-30.

This study was a consecutive, supplemental field study involving 26 hypercholesterolemic adults that examined the effect of almonds on serum lipids as part of a low saturated fatty acid (SFA), low cholesterol, high-fiber diet. The study consisted of a two-week baseline period followed by a nine-week intervention period. The baseline diet was comprised mainly of grains, beans, vegetables, fruit and low-fat milk products. Meat, fatty fish, high-fat milk products, eggs and SFA were limited. The almond diet consisted of the baseline diet with the addition of 100g/d of raw almonds that supplied 34g/d of monounsaturated fatty acids (MUFA), 12g/d of (polyunsaturated fatty acids (PUFA), and 6g/d of SFA. Almond oil was the only oil allowed for food preparation. There was a rapid and sustained reduction in LDL without changes in HDL. Total cholesterol was decreased by 9% and LDL was decreased by 12% compared to baseline values. There were no significant changes in HDL or triglycerides.

Spiller, G.A., A. Miller, K. Olivera, J. Reynolds, B. Miller, S.J. Morse, A. Dewell, J.W. Farquhar, 2003. **Effects of plant-based diets high in raw or roasted almonds, or roasted almond butter**

on serum lipoproteins in humans. *J Am Coll Nutr*, 22(3):195-200.

This study compared the lipid-altering effect of roasted salted almonds and roasted almond butter with that of raw almonds, as part of a plant-based diet in 38 free-living, hypercholesterolemic men and women (n = 26) with a mean total serum cholesterol (TC) of 245 + 29 mg/dL (mean + SD). All three forms of almonds in the context of a heart-healthy diet significantly lowered low-density lipoprotein-cholesterol (LDL) from baseline to the completion of the study. Both raw and roasted almonds significantly lowered TC, whereas the decrease by almond butter (in a smaller cohort) did not reach statistical significance. High-density lipoprotein-cholesterol (HDL) did not significantly change with raw or roasted almonds but slightly increased with almond butter. At the end of the study, blood pressure did not change significantly from baseline values for any of the groups. These results suggest that unblanched almonds—whether raw, dry roasted, or in roasted butter form—can play an effective role in cholesterol-lowering, plant-based diets.

Sriwardahana, S.S.K.W., F. Shahidi, 2002. **Antiradical activity of extracts of almond and its by-products.** *J Am Oil Chem Soc*. 79(9):903-8.

Antioxidant activities of ethanolic extracts of whole almonds, almond skins and hulls were evaluated using different free radical trapping assays. Total antioxidant capacities of skins and hulls were over ten times greater than almonds.

Sze-Tao, K.W.C., S.K. Sathe, 2000. **Functional properties and in vitro digestibility of almond (*Prunus dulcis* L.) protein isolate.** *Food Chem*. 69:153-60.

Almond protein isolates (API) solutions were less viscous than those of soy protein isolates. Foaming and oil absorption capacities were comparable. Emulsion activity index was significantly higher. API was easily hydrolyzed by pepsin in vitro.

Venkarachalam, M., S.S. Teuber, K.H. Roux, S.K. Sathe, 2002. **Effects of roasting, blanching, autoclaving, and microwave heating on antigenicity of almonds.** *J Agric Food Chem*. 50(12):35448.

These researchers have characterized the major storage proteins of almonds, which cause allergic reactions in approximately one percent of the U.S. population. Their most recent research focused on the effects of processing on various forms of almonds and how to reduce almond allergenicity.

Wien, M.A., J.M. Sabaté, D.N. Ikle, S.E. Cole, and F.R. Kandeel, 2003. **Almonds vs. complex carbohydrates in a weight reduction program.** *Intl J Obesity*. 27:1365-72.

A moderate-fat diet with almonds resulted in more weight loss than a low-fat diet in a six-month study, even though the total number of calories was the same for both groups. Researchers concluded that there may be qualities in almonds which helped the first group lose more weight. According to the authors, since a side effect of some diabetes medication is increased hunger, the faster one can get off of medications during weight loss, the better, because

when you take away something creating hunger behind the scenes, it can lead to greater success in the weight-loss effort.

Wijeratne, S. S. K., M. M. Abou-Zaid, and F. Shahidi. 2006. **Antioxidant polyphenols in almond and its coproducts.** *J. Agric. Food Chem.* 54:312-318.

Antioxidant efficacy of whole defatted almond brown skin, and green hull extracts were evaluated by monitoring inhibition of human of low-density lipoprotein (LDL) oxidation. Brown skin extract at 50 ppm effectively inhibited copper-induced oxidation of human LDL cholesterol compared to whole seed and green hull extracts, which reached the same level of efficacy at 200 ppm. All three almond extracts exhibited excellent metal ion chelation efficacies. High-performance liquid chromatographic (HPLC) analysis revealed the presence of quercetin, isorhamnetin, quercetin, kaempferol 3-*O*-glucoside, and morin as the major flavonoids in all extracts. The total phenolic contents of ethanolic extracts of brown skin and green hull of almond were 10 and 9 times higher than that of the whole seed, respectively.

Wijeratne, S.S.K.; R.. Amarowicz, F. Shahidi, 2006. **Antioxidant activity of almonds and their by-products in food model systems.** *JAACS.* 83(3):223-230.

This study examined the antioxidant activities of almond whole seed, brown skin, and green shell cover extracts, at 100 and 200 ppm quercetin equivalents using a cooked comminuted port mode, a β -carotene-linoleate model, and a bulk stripped corn oil system. Retention of β -carotene in a β -carotene-linoleate model system by almond whole seed, brown skin, and green shell cover extracts was 84-96, 74-83, and 71-93% respectively. In a bulk stripped corn oil system, green shell cover extract performed better than brown skin and whole seed extracts in inhibiting the formation of both primary and secondary oxidation products, while in a cooked comminuted port model system, green shell cover and brown skin extracts inhibited the formation of TBARS, total volatiles and hexanal more effectively than did the whole seed extract. HPLC analysis revealed the presence of caffeic, ferulic, p-coumaric and sinapic acids as the major phenolic acids in all three almond extracts examined.

Wolf, W.J., S.K. Sathe, 1998. **Ultracentrifugal and polyacrylamide gel electrophoretic studies of extractability and stability of almond meal proteins.** *J Sci Food Agric.* 78:511-21.

Solubility and stability properties of almond proteins were determined to gain a better insight into the complexity of these proteins. The 14S amandin fraction constitutes 65-70% of the extractable proteins.

Xiao, Y., J.B. Wang, S.F. Yan, X.J. Lian, Y. Tang, Y. Liu, 2002. **Effect of nut rich in monounsaturated fatty acid on serum lipids in hyperlipidemia patients.** *J of China Pub Health.* 18(8):931-2.

Researchers at Peking Medical University studied 85 Chinese hyperlipemic patients. After a four-week experimental phase, with patients eating 75g (over 2 oz.) of almonds daily, total cholesterol and apolipoprotein B decreased significantly.

Young, C. T., W. E. Schadel, H. E. Pattee, T. H. Sanders, 2004. **The microstructure of almond (*Prunus dulcis* (Mill.) D. A. Webb cv. 'Nonpareil') cotyledon.** *Lebensm.-Wiss. u.-Technol.* 37:317-322.

Microstructure of almond cotyledon was observed with light, scanning and transmission electron microscopy. The objective of this study was to characterize almond cotyledon surfaces as well as to describe internal and sub cellular organization. This study will serve as a reference for future evaluation of the Microstructural changes, which occur as almonds are cooked or processed into other forms such as paste or butter. The testa has an outer epidermis, which consists of relatively large thin-walled cells, which range from 100 to 300 µm in width. The major portion of the testa consists of approximately 14-20 layers of flattened parenchymal vascular tissue. The embryo consisted primarily of parenchymal tissue with relatively thin cell walls (1-3 µm in thickness) and a small amount of provascular tissue. Protein bodies up to 12 µm in width and spaces once occupied by lipid bodies up to 3µm in width were present in all cells of the embryo.

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HAZELNUT REFERENCES

Alphan, E., M. Pala, F. Ackurt, T. Yilmaz, 1997. **Nutritional composition of hazelnuts and its effects on glucose and lipid metabolism.** In: Kosal AI, Oky Y, Gunes NT, eds. Proceedings of the Fourth International Symposium on Hazelnut. *Acta Hort.* 445:305-10.

Amaral, J.S., S. Casal, R.M. Seabra, B.P.P. Oliveira, 2006. **Effects of roasting on hazelnut lipids.** *J. Agric. Food Chem.* 54:1315-21.

In this study, hazelnuts were submitted to several different thermal treatments, comprising different temperatures and times of exposure and analyzed for their moisture and crude fat. Raw and roasted hazelnuts were also analyzed for their compositions in phytosterols and fatty acids (including trans isomers), triacylglycerols, and tocopherols and tocotrienols. Minor changes occurred in the fatty acid and triacylglycerol compositions. As temperatures and roasting periods increased, generally, a modest increase of oleic and saturated fatty acids and a decrease of linoleic acid, expressed as relative percentages, occurred. Similarly, an increase of triacylglycerols containing oleic acid moieties and a decrease of those containing linoleic acid moieties were found in the roasted samples. Roasting caused a modest decrease of the beneficial phytosterols (maximum 14.4%) and vitamin E homologues (maximum 10.0%) and a negligible increase of the trans fatty acids.

Durak, I., I. Koksall, M. Kacmaz, S. Buyukkocak, B.M. Cimen, H.S. Ozturk, 1999. **Hazelnut supplementation enhances plasma antioxidant potential and lowers plasma cholesterol levels.** [Letter to the Editor]. *Clin Chim Acta.* 284(1):113-5.

In this study, 30 healthy medical students added 1 gram of hazelnuts per kilogram of body weight per day to their normal daily diet for 30 days. Total cholesterol was lowered by 6%, LDL by 19%, while HDL increased 7% and triglycerides 25% compared to baseline values. Plasma antioxidant potential (AOP) also increased by 20%.

Mercanlıgil, S.M., P. Arslan, C. Alasalvar, E. Okut, E. Akgül, A. Pınar, P.Ö. Geyik, L. Tokgözoğlu and F. Shahidi, 2007. **Effects of hazelnut-enriched diet on plasma cholesterol and lipoprotein profiles in hypercholesterolemic adult men.** *European Journal of Clinical Nutrition*, 61, 212–220.

This study was conducted to investigate the effects of hazelnut-enriched diet on plasma cholesterol and lipoprotein profiles in hypercholesterolemic adult men compared with baseline and control diet, and also to measure the anthropometric parameters, habitual physical activities, nutrient intake and endothelial function. Fifteen hypercholesterolemic men aged 48 ± 8 years were recruited voluntarily. A well-controlled, 2-period (P1 and P2) study design with a total of 8-week was implemented. In the P1, subjects consumed a control diet (low-fat, low-cholesterol and high-carbohydrate). During the P2, the control diet was supplemented with MUFA-rich hazelnut (40 g/day), which provided 11.6% of total energy content. Anthropometric parameters and habitual physical activities were recorded. Plasma total and HDL cholesterol, TAG, ApoA-1, Apo B, total homocysteine and glucose concentrations were measured. All parameters and measurements were obtained at baseline and end of each 4-week diet period. Body weights of subjects remained stable throughout the study. Compared with baseline, the hazelnut-enriched diet decreased ($P < 0.05$) the concentrations of VLDL cholesterol, triacylglycerol, apolipoprotein B by 29.5, 31.8, and 9.2%, respectively, while increasing HDL cholesterol concentrations by 12.6%. Total/HDL cholesterol and LDL/HDL cholesterol ratios favorably decreased ($P < 0.05$). Although insignificant there was a decreasing trend for the rest of parameters, particularly in total (5.2%) and LDL cholesterol (3.3%) in subjects consuming a hazelnut-enriched diet compared to that of the baseline. No changes were found in fasting levels of glucose, Apo A-1 and homocysteine between the control and hazelnut-enriched diets. This study demonstrated that a high-fat and high-MUFA-rich hazelnut diet was superior to a low-fat control diet because of favorable changes in plasma lipid profiles of hypercholesterolemic adult men and, thereby positively affecting the CHD risk profile.

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MACADAMIA REFERENCES

Colquhoun, D.M., J.A. Humphries, D. Moores, S.M. Somerset, 1996. **Effects of a macadamia nut enriched diet on serum lipids and lipoproteins compared to a low fat diet.** *Food Australia*. 48(5):216-22.

Curb, J.D., G. Wergowske, J.C. Dobbs, R.D. Abbott, B. Huang, 2000. **Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts.** *Arch Intern Med*. 160(8):1154-8.

This study involved 30 subjects who consumed three different diets each for 30 days. The first diet was a typical American diet (AM), high in saturated fat, the second diet was the American Heart Association (AHA) Step 1 diet and the third diet was a macadamia based diet (MAC) high in monounsaturated fatty acids. Compared to the AM diet, the MAC diet lowered

total cholesterol, LDL and HDL each by 5% and triglycerides by 10%. The AHA diet had similar results except for an 8% increase in triglycerides.

Garg, M. L., P. Rudra, R. Blake, R. Wills, 2003. **Macadamia nut consumption lowers plasma cholesterol levels in hypercholesterolemic men.** *J Nutr.* 133:1060-3.

This study assessed the cholesterol-lowering potential of macadamia nuts in 17 hypercholesterolemic men. The subjects were given 40-90g/d macadamia nuts—the equivalent to 15% energy intake for 4 weeks. At the end of the study, total cholesterol and LDL-cholesterol levels decreased by 3.0 and 5.3% respectively, and HDL-cholesterol levels increased by 7.9%. According to the authors, “This study demonstrates that macadamia nut consumption as part of a healthy diet favorably modifies the plasma lipid profile in hypercholesterolemic men despite their being high in fat.

Griel, A.E., Y. Cao, D.D. Bagshaw, A.M. Cifelli, B. Holub, P.M. Kris-Etherton, 2008. **A Macadamia nut-rich diet reduces total and LDL-cholesterol in mildly hypercholesterolemic men and women.** *J. Nutr.* 138:761-767.

Epidemiologic studies and clinical trials have demonstrated that the unique fatty acid profile of nuts beneficially affects serum lipids/lipoproteins, reducing cardiovascular disease (CVD) risk. Nuts are low in SFA and high in PUFA and monounsaturated fatty acids (MUFA). Macadamia nuts are a rich source of MUFA. A randomized, crossover, controlled feeding study (5-wk diet periods) compared a Macadamia nut-rich diet [42.5g (1.5 ounces)/8.79 MJ (2100 kcal)] [MAC; 33% total fat (7% SFA, 18% MUFA, 5% PUFA)] vs. an average American diet [AAD; 33% total fat (13% SFA, 11% MUFA, 5% PUFA)] on the lipid/lipoprotein profile of mildly hypercholesterolemic (n = 25; 15 female, 10 male) subjects. Serum concentrations of total cholesterol (TC) and LDL cholesterol (LDL-C) following the MAC (4.94 ± 0.17 mmol/L, 3.14 ± 0.14 mmol/L) were lower than the AAD (5.45 ± 0.17 mmol/L, 3.44 ± 0.14 mmol/L; $P < 0.05$). The serum non-HDL cholesterol (HDL-C) concentration and the ratios of TC:HDL-C and LDL-C:HDL-C were reduced following consumption of the MAC diet (3.83 ± 0.17 , 4.60 ± 0.24 , and 2.91 ± 0.17 , respectively) compared with the AAD (4.26 ± 0.17 , 4.89 ± 0.24 , and 3.09 ± 0.18 , respectively; $P < 0.05$). There was no change in serum triglyceride concentration. Thus, macadamia nuts can be included in a heart-healthy dietary pattern that reduces lipid/lipoprotein CVD risk factors. Nuts as an isocaloric substitute for high SFA foods increase the proportion of unsaturated fatty acids and decrease SFA, thereby lowering CVD risk.

Hiraoka-Yamamoto, J., K. Ikeda, H. Negishi, M. Mori, A. Hirose, S. Sawada, Y. Onobayashi, K. Kitamori, S. Kitano, M. Tashiro, T. Miki, Y. Yamori, 2004. **Serum lipid effects of a monounsaturated (palmitoleic) fatty acid-rich diet based on macadamia nuts in healthy, young Japanese women.** *Clin Exp Pharmacol Physiol.* 31(suppl 2):S37-8.

Macadamia nuts contain 75% fat by weight, 80% of which is monounsaturated (palmitoleic) fatty acid (MUFA). This study looked at the variations in serum lipid levels in response to a high-MUFA diet based on macadamia nuts. Three week interventions of macadamia nuts, coconuts and butter were given to young, healthy Japanese female students.

After 3 weeks intervention, serum levels of total cholesterol and low-density cholesterol were significantly decreased in the macadamia nut and coconut diets and bodyweight and body mass index were decreased in the group fed macadamia nuts. There were no statistically significant changes in the group fed butter.

Kaijser, A., P. Dutta, G. Savage, 2000. **Oxidative stability and lipid composition of macadamia nuts grown in New Zealand.** *Food Chemistry.* 71:67-70.

This study looked at the parameters which might influence the stability and storage characteristics of some selected cultivars of macadamia nuts grown in New Zealand. Four cultivars of macadamia nuts (*Macadamia tetraphylla*) were harvested from the North Island of New Zealand during 1997. Total lipids, composition of fatty acids, tocopherols, sterols and stability of oils, were determined on the oil extracted from the fresh nuts. The total lipid content of the nuts ranged from 69 to 78%, while the stability of the oil measured by Rancimat test ranged from 3.6 to 19.8 h. Peroxide values of the fresh oil ranged from 0.56 to 3.61 meq O₂/kg oil. The major fatty acids were oleic acid, palmitoleic acid and palmitic acid; oleic acid accounted for 40.6 to 59% of the total fatty acids. The polyunsaturated fatty acid content was low, ranging from 3.0 to 4.7%. α -Tocopherol and d-tocopherol were the only two tocopherols identified in the extracted oil. The major sterols identified were sitosterol, Δ 5-avenasterol, campesterol and stigmasterol.

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PECAN REFERENCES

Haddad, E., P. Jambazian, M. Karunia, J. Tanzman, J. Sabaté, 2006. **A pecan-enriched diet increases γ -tocopherol/cholesterol and decreases thiobarbituric acid reactive substances in plasma of adults.** *Nutrition Research.* 26:397-402.

This randomized, controlled, cross-over feeding study looked at the effect of a pecan-rich diet on plasma α - and γ -tocopherol concentrations on measures of antioxidant capacity and lipid peroxidation in 24 healthy persons. The subjects were assigned to 2 diets, each for 4 weeks: a control diet and a pecan-enriched (20% of calories) diet. Cholesterol-adjusted plasma γ -tocopherol increased by 10.1%, α -tocopherol decreased by 4.6%, and malondialdehyde concentrations measured as thiobarbituric acid reactive substances decreased by 7.4% on the pecan diet. These data provide some evidence for potential protective effects of pecan consumption in healthy individuals.

Morgan, W.A., B.J. Clayshulte, 2000. **Pecans lower low-density lipoprotein cholesterol in people with normal lipid levels.** *J Am Diet Assoc.* 100(3):312-8.

A randomized, controlled, parallel study involved 19 healthy adults who followed either a control diet (no nuts) or a pecan diet which included 68 grams of pecans per day (with no additional nuts). After eight weeks, those following the pecan diet had a 6% decrease in LDL compared to the baseline value. Effects on total cholesterol, HDL and triglycerides were not significant.

Rajaram, S., K. Burke, B. Connell, T. Myint, J. Sabaté, 2001. **A monounsaturated fatty acid-rich pecan enriched diet favorably alters the serum lipid profile of healthy men and women.** *J Nutr.* 131:2275.

This study looked at the effect of pecans rich in monounsaturated fat as an alternative to the Step 1 diet in modifying serum lipids and lipoproteins in men and women with normal to moderately high serum cholesterol. In a single-blind, randomized, controlled, crossover feeding study, researchers assigned 23 subjects (mean age: 38 y; 9 women, 14 men) to follow two diets, each for 4 wk: a Step I diet and a pecan-enriched diet (accomplished by proportionately reducing all food items in a Step I diet by one fifth for a 20% isoenergetic replacement with pecans). The percentage of energy from fat in the two diets was 28.3 and 39.6%, respectively. Both diets improved the lipid profile; however, the pecan-enriched diet decreased both serum total and LDL cholesterol by 0.32 mmol/L (6.7 and 10.4%, respectively) and triglyceride by 0.14 mmol/L (11.1%) beyond the Step I diet, while increasing HDL cholesterol by 0.06 mmol/L (2.5 mg/dL). Serum apolipoprotein B and lipoprotein(a) decreased by 11.6 and 11.1%, respectively, and apolipoprotein A1 increased by 2.2% when subjects consumed the pecan compared with the Step I diet. These differences were all significant ($P < 0.05$). A 20% isoenergetic replacement of a Step I diet with pecans favorably altered the serum lipid profile beyond the Step I diet, without increasing body weight. Nuts such as pecans that are rich in monounsaturated fat may therefore be recommended as part of prescribed cholesterol-lowering diet of patients or habitual diet of healthy individuals.

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PISTACHIO REFERENCES

Edwards, K., I. Kwaw, J. Matud, I. Kurtz, 1999. **Effect of pistachio nuts on serum lipid levels in patients with moderate hypercholesterolemia.** *J Am Coll Nutr.* 18(3):229-32.

Ten patients with moderate hypercholesterolemia were enrolled in a controlled, randomized, crossover study for two 3-week periods. A reference diet of 37% total fat was compared to a pistachio diet of 39% total fat (66g/day of pistachios) in which 20% of the daily caloric intake was substituted with pistachios. Compared to initial values, the pistachio diet decreased total cholesterol by 2%, and increased HDL by 12%, while there was no significant effect on LDL or triglycerides.

Gebauer S.K., S.G. West, C.D. Kay, P. Alaupovic, D. Bagshaw, P.M. Kris-Etherton, 2008. **Effects of pistachios on cardiovascular risk factors and potential mechanisms of action: a dose-response study.** *Am J Clin Nutr.* 88:651-9.

This randomized crossover controlled-feeding study looked at the effects of 2 doses of pistachios, added to a lower-fat diet, on lipids and lipoproteins, apolipoprotein (apo)-defined lipoprotein subclasses, and plasma fatty acids. To investigate the mechanisms of action, cholesteryl ester transfer protein and indexes of plasma stearoyl-CoA desaturase activity (SCD) were measured. Twenty-eight individuals with LDL cholesterol ≥ 2.86 mmol/L consumed 3 isoenergetic diets for 4 weeks each. Baseline measures were assessed after 2 weeks of a typical Western diet. The experimental diets included a lower-fat control diet with no pistachios [25% total fat; 8% saturated fatty acids (SFAs), 9% monounsaturated fatty acids (MUFAs), and 5%

polyunsaturated fatty acids (PUFAs)], 1 serving/d of a pistachio diet (1 PD; 10% of energy from pistachios; 30% total fat; 8% SFAs, 12% MUFAs, and 6% PUFAs), and 2 servings/d of a pistachio diet (2 PD; 20% of energy from pistachios; 34% total fat; 8% SFAs, 15% MUFAs, and 8% PUFAs). The results showed that the 2 PD decreased ($P < 0.05$ compared with the control diet) total cholesterol (-8%), LDL cholesterol (-11.6%), non-HDL cholesterol (-11%), apo B (-4%), apo B/apo A-I (-4%), and plasma SCD activity (-1%). The 1 PD and 2 PD, respectively, elicited a dose-dependent lowering ($P < 0.05$) of total cholesterol/HDL cholesterol (-1% and -8%), LDL cholesterol/HDL cholesterol (-3% and -11%), and non-HDL cholesterol/HDL cholesterol (-2% and -10%). Inclusion of pistachios in a healthy diet beneficially affects CVD risk factors in a dose-dependent manner, which may reflect effects on SCD.

Kocyigit, A., A.A. Koylu, H. Keles, 2006. **Effects of pistachio nuts consumption on plasma lipid profile and oxidative status in healthy volunteers.** *Nutrition, Metabolism & Cardiovascular Diseases*. 16:202-9.

This study looked at the effects of pistachio nuts consumption on plasma lipid profile and oxidative status in 24 healthy men and 20 healthy women with normal lipid levels. All subjects consumed their regular diets during a 1-week period. After this period, half of the subjects were randomized to a regular diet group and the other half were randomized to a pistachio group which involved substituting pistachio nuts for 20% of their daily caloric intake for 3 weeks. After 3 weeks, with the pistachio diet, the mean plasma total cholesterol, malondialdehyde (MDA) levels and, total cholesterol/HDL and LDL/HDL ratios were found to be significantly decreased; on the contrary, HDL and antioxidant potential (AOP) levels, and AOP/MDA ratios were significantly increased. Triglyceride and LDL levels also decreased but this was not statistically significant. These results indicate that consumption of pistachio nuts decreased oxidative stress, and improved total cholesterol and HDL levels in healthy volunteers.

Sheridan, M.J., J.N. Cooper, M. Erario, 2003. **Pistachio nuts and serum lipid levels in patients with moderate hypercholesterolemia.** (Submitted to *AJCN*)

In an 8-week cross-over trial, 15 subjects with moderate hypercholesterolemia were randomized to one of two diets after a lead-in period of one week: 20% of calories as pistachio nuts for 4 weeks followed by regular diet for 4 weeks or the reverse. On the pistachio nut diet, total fat was 48% of calories and monounsaturated fat intake was 20% of total calories in comparison to the regular diet where calories were 31% total fat and 11% monounsaturated fat. Significant reductions were seen in total/HDL cholesterol ratios (-8%, $p=0.001$) and LDL/HDL cholesterol ratios (-13%, $p=0.004$), and a significant increase was seen in HDL (6%, $p=0.02$). Although statistically marginal, trends in the optimal direction also were seen for total cholesterol (-4%, $p=0.11$), LDL-C (-9%, $p=0.06$) and apolipoprotein B-100 (-6%, $p=0.08$). No changes were seen in triglycerides or apolipoprotein A-1. No differences were seen in BMI or blood pressure.

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WALNUT REFERENCES

Almario, R.U., V. Vonghavaravat, R. Wong, S.E. Kasim-Karakas, 2001. **Effects of walnut consumption on plasma fatty acids and lipoproteins in combined hyperlipidemia.** *Am J Clin Nutr*. 74:72-9

In this study with 7 men and 16 postmenopausal women, participants sequentially adhered to the following diets in free-living conditions: (1) habitual diet, (2) habitual diet plus walnuts, (3) low-fat diet and (4) low-fat diet plus walnuts. Compared to the diets without walnuts, the proportion of small particle LDL decreased by 27% with the habitual diet plus walnuts and 7% with the low-fat diet plus walnuts. Small particle LDL is considered to be a promoter of cardiovascular disease.

Anderson et al, 2001. **Walnut polyphenolics inhibit in vitro human plasma and LDL oxidation.** *J Nutr.* 0022-3166

Polyphenol-rich extracts from walnuts were studied in vitro and compared with ellagic acid for their ability to inhibit in vitro plasma and LDL oxidation, as well as their effects on LDL during oxidative stress.

Results: Walnut polyphenolics are effective inhibitors of in vitro plasma and LDL oxidation.

Chisolm, A., J. Mann, M. Skeaff, C. Franpton, W. Sutherland, A. Duncan, S. Tiszavari, 1998. **A diet rich in walnuts favorably influences plasma fatty acid profile in moderately hyperlipidemic subjects.** *Eur J Clin Nutr.* 52:12-6.

In this randomized, crossover study with 21 male subjects, researchers found that despite an unintended increase in the total fat intake on the walnut diet, fatty acid profile of the major lipid fractions showed changes, which might be expected to reduce risk of cardiovascular disease.

Comstock, S.S., G. McGranahan, W.R. Peterson, S.S. Teuber, 2004. **Extensive in vitro cross-reactivity to seed storage proteins is present among walnut (*Juglans*) cultivars and species.** *Clin Exp Allergy.* 34:1583-90.

This study looked at the possibility of developing a hypoallergenic walnut using English walnut cultivars or other *Juglans* species that showed decreased IgE binding to major seed storage proteins or an inability to cross-react with Jug r 1 or Jug r 2 (important English walnut allergens). However, based on their findings, the researchers concluded that it is unlikely that a composite hypoallergenic walnut could be bred from available germplasm. Patients with severe allergy to English walnuts are likely to be clinically allergic to all commercial English walnut cultivars and other closely related *Juglans* species.

Cortés, B., I. Núñez, M. Cofán, R. Gilabert, A. Pérez-Heras, E. Casals, R. Deulofeu, E. Ros, 2006. **Acute effects of high-fat meals enriched with walnuts or olive oil on postprandial endothelial function.** *J Am Coll Cardiol.* 48:1666–71.

This study looked at 12 healthy adult subjects and 12 with hypercholesterolemia were randomized in a cross-over design to consume high-fat meals to which 25 grams of olive oil or 40 grams of walnuts were added. Brachial artery function was evaluated while subjects were fasting and 4 hours after test meals. The results showed that flow mediated dilation was better after the walnut meal in both groups. E-selection, an inflammatory marker, was significantly lower after the walnut meal. Researchers noted in their conclusion that, “Adding walnuts to a high-fat meal acutely improves FMD independently of changes in oxidation, inflammation or ADMA.”

Davis, P., G. Valacchi, E. Pagnin, Q. Shao, H.B. Gross, L. Calo, W. Yokoyamaz, 2006. **Walnuts reduce aortic ET-1 mRNA levels in hamsters fed a high-fat, atherogenic diet.** *J of Nu.* 136(2):428-32

This study was designed to determine the mechanisms behind walnuts' ability to reduce coronary vascular disease risk. Male Golden Syrian hamsters fed high-fat, hyperlipidemic diets supplemented with either walnuts; alpha-tocopherol, a form of vitamin E; walnut oil; or gamma-tocopherol, the form of vitamin E found in walnuts. Hamsters fed the walnut supplemented diet had the greatest reduction in aortic endothelin, an endothelial cell regulator, and the lowest concentration of aortic cholesterol ester, a measure of arterial plaque development.

Esposito, K., R. Marfella, M. Ciotola, C. Di Palo, F. Giugliano, G. Giugliano, M. D'Armiento, F. D'Andrea, D. Giugliano, 2004. **Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome.** *JAMA.* 292:1440-6.

This study looked at the effect of a Mediterranean-style diet on both endothelial function and vascular inflammatory markers in patients with metabolic syndrome. The latter has been associated with an increased risk of cardiovascular disease, yet the role of diet in metabolic syndrome is poorly understood. In a randomized, single-blind 2-year trial, 180 men and women with metabolic syndrome were assigned to two different diets. The intervention group was instructed to follow a Mediterranean-style diet that included walnuts, and the control group followed a prudent diet (50-60% carbohydrate; 15-20% protein; and total fat less than 30%). After 2 years, the intervention group consumed more foods rich in mono- and polyunsaturated fats, fiber and had a lower ratio of omega-6 to omega-3 fatty acids. The level of physical activity increased in both groups by 60%. Mean body weight decreased more in the intervention group. High-sensitivity C-reactive protein was significantly reduced and insulin resistance was decreased compared to the control group. After 2 years of follow-up, 40 patients in the intervention group still had features of the metabolic syndrome compared to 78 patients in the control group.

Feldman, E.B., 2002. **LSRO Report: The scientific evidence for a beneficial health relationship between walnuts and coronary heart disease.** *J Nutr.* 132:1062S-101S.

Gillen, L.J., L.C. Tapsell, C.S. Patch, A. Owen, M. Batterham, 2005. **Structured dietary advice incorporating walnuts achieves optimal fat and energy balance in patients with type 2 diabetes mellitus.** *J Am Diet Assoc.* 105:1087-96.

A parallel-design, controlled trial was completed by 55 free-living men and women with established type 2 diabetes mellitus. Participants were randomly assigned to three different diet groups: low-fat, modified low-fat and walnut-specific (modified low-fat including 30g of walnuts per day). Dietary intakes and clinical outcomes were measured at baseline, 3 months and 6 months. The results showed that at baseline dietary intakes were not significantly different between the groups. At 3 and 6 months calories and macronutrient intakes were similar among the groups. However, the walnut group was the only group to achieve all fatty acid targets and had the greatest proportion of subjects achieving targets. Walnuts were the main source of dietary fat (31%) and omega-3 fatty acids (50%), while 350 grams of oily fish per day provided an additional 17% of omega-3 fatty acids consumed by this group. The authors concluded that

recommending patients with type 2 diabetes include walnuts regularly in their diet can help them achieve optimal fat intake without adverse effects on total fat or calorie intakes.

Griel A.E., P.M. Kris-Etherton, K.F. Hilpert, G. Zhao, S.G. West, R.L. Corwin, 2007. **An increase in dietary n-3 fatty acids improves bone health in humans.** *Nutrition Journal.* 6:2.

Human, animal, and in vitro research indicates a beneficial effect of appropriate amounts of omega-3 (n-3) polyunsaturated fatty acids (PUFA) on bone health. This is the first controlled feeding study in humans to evaluate the effect of dietary plant-derived n-3 PUFA on bone turnover, assessed by serum concentrations of N-telopeptides (NTx) and bone-specific alkaline phosphatase (BSAP). Twenty-three subjects consumed each diet for 6 weeks in a randomized, 3-period crossover design: 1) Average American Diet (AAD; [34% total fat, 13% saturated fatty acids (SFA), 13% monounsaturated fatty acids (MUFA), 9% PUFA (7.7% LA, 0.8% ALA)]), 2) Linoleic Acid Diet (LA; [37% total fat, 9% SFA, 12% MUFA, 16% PUFA (12.6% LA, 3.6% ALA)]), and 3) α -Linolenic Acid Diet (ALA; [38% total fat, 8% SFA, 12% MUFA, 17% PUFA (10.5% LA, 6.5% ALA)]). Walnuts and flaxseed oil were the predominant sources of ALA. NTx levels were significantly lower following the ALA diet (13.20 ± 1.21 nM BCE), relative to the AAD (15.59 ± 1.21 nM BCE) ($p < 0.05$). Mean NTx level following the LA diet was 13.80 ± 1.21 nM BCE. There was no change in levels of BSAP across the three diets. Concentrations of NTx were positively correlated with the proinflammatory cytokine TNF α for all three diets. The results indicate that plant sources of dietary n-3 PUFA may have a protective effect on bone metabolism via a decrease in bone resorption in the presence of consistent levels of bone formation.

Iwamoto M., K. Imaizumi, M. Sato, Y. Hirooka, K. Sakai, A. Takeshita, M. Kono. 2002. **Serum lipid profiles in Japanese women and men during consumption of walnuts.** *Eur J Clin Nutr.* 56(7):629-37.

In this 4-week controlled, single-blind crossover designed study with 40 healthy men and women, subjects were randomly assigned to two mixed natural diets. After four weeks, the groups switched diets. Researchers found that LDL cholesterol was lowered by 8.9% in men and 10.6% in women. Total cholesterol was lowered by 3.8% in men and 4.9% in women. There was no significant change in HDL cholesterol.

Lavedrine, F., D. Zmirou, A. Ravel, F. Balducci, J. Alary, 1999. **Blood cholesterol and walnut consumption: a cross-sectional survey in France.** *Prev Med.* 28(4):333-9.

In this cross-sectional study with 793 men and women, ages 18-65, researchers observed a positive effect of walnut consumption on blood HDL cholesterol and apo A1. This is of special interest since these lipid parameters have been shown to be negatively correlated with cardiovascular morbidity.

Munoz, S., M. Merlos, D. Zambon, C. Rodriguez, J. Sabaté, E. Ros, J.C. Laguna, 2001. **Walnut-enriched diet increases the association of LDL from hypercholesterolemic men with human HepG2 cells.** *J Lipid Res.* 42(12):2069-76.

In this randomized, crossover feeding trial, 10 hypercholesterolemic men followed a control, Mediterranean-type cholesterol-lowering diet, and a diet of similar composition in which walnuts replaced 35% of energy from unsaturated fat. Each diet was followed for six weeks. The walnut diet reduced serum total and LDL cholesterol by 4.2% and 6.0% respectively.

Reiter, R.J., L.C. Manchester, D. Tan, 2005. **Melatonin in walnuts: influence on levels of melatonin and total antioxidant capacity of blood.** *Nutrition.* 21:920-24.

This study looked at whether or not walnuts contain melatonin, a molecule found in plants that has beneficial effects on the cardiovascular system, and if so, whether eating walnuts influences melatonin levels and the total antioxidant status of the blood in rats. The results showed that walnuts do contain melatonin, which was easily absorbed in the rats and increased blood levels of melatonin roughly three-fold. The study also showed that the increase in blood levels of melatonin after walnut consumption correlated with an increase in total antioxidant capacity of the blood.

Ros, E., I. Núñez, A. Pérez-Heras, M. Serra, R. Gilabert, E. Casals, R. Deulofeu, 2004. **A walnut diet improves endothelial function in hypercholesterolemic subjects.** *Circulation.* 109:1609-14.

To determine whether or not walnut intake would reverse endothelial dysfunction, researchers randomized 21 hypercholesterolemic men and women (ages 25-75) to a cholesterol-lowering Mediterranean diet, and a diet of similar energy and fat content in which approximately 1.4-2.3 ounces of walnuts daily replaced roughly 32 percent of the energy from monounsaturated fat. Participants followed each diet for four weeks. At the end of the study researchers observed that substituting walnuts for monounsaturated fat in a Mediterranean diet improved endothelium-dependent vasodilatation in individuals with high cholesterol levels.

Sabate, J., Z. Cordero-MacIntyre, G. Siapco, S. Torabian, E. Haddad, 2005. **Does regular walnut consumption lead to weight gain?** *Brit J Nutr.* 94(5):859-64.

This 12-month randomized cross-over trial with 90 free-living subjects looked at the effect of daily walnut consumption (~12% energy intake) on body weight. Subjects consumed a walnut-supplemented diet (1-2 ounces of walnuts/day) for 6 months and a control diet with no supplemented walnuts for the other 6 months. The walnut-supplemented diet resulted in an increase in weight, BMI, fat mass and lean mass, but after adjusting for energy differences between the control and walnut supplemented diets, no significant differences were seen. The weight gain from adding walnuts to the diet (control→walnut diet) was less than the weight loss from withdrawing walnuts from the diet (walnut diet→control). The results show that regular walnut intake resulted in weight gain much lower than expected and which became non-significant after controlling for differences in energy intake.

Sabaté, J., G.E. Fraser, K. Burke, S.F. Knutsen, H. Bennett, K.D. Lindsted, 1993. **Effects of walnuts on serum lipid levels and blood pressure in normal men.** *NEJM.* 328(9):603-7.

In this 8-week randomized crossover feeding study, researchers compared the Step 1 Diet of the National Cholesterol Education Program, recommended by the American Heart

Association, and a walnut diet (walnuts substituted for some of the saturated fat in the diet). In the walnut diet, LDL cholesterol dropped 16% and total cholesterol dropped 12%, out-performing the Step 1 control diet.

Simon J., J. Sabaté, J. Tanzman, 2007. **Lack of effect of walnut on serum levels of prostate specific antigen: A brief report.** *AJCN.* 26; 4; 317-320.

This study examined whether the short-term consumption of walnuts, a food rich in α -linolenic acid, affects levels of serum prostate-specific antigen (PSA), a marker of prostate enlargement, inflammation, and cancer. Using data from a 12-month randomized crossover study examining the effect of walnut consumption on body composition, the researchers examined whether increased walnut consumption (mean 35 grams daily, 12% total energy) affected serum PSA levels among 40 middle-aged men. The results showed that there was no significant difference between mean PSA level at the conclusion of the 6-month walnut-supplemented diet (1.05 $\mu\text{g/L}$, 95% CI [0.81, 1.37]) and the conclusion of the 6-month control diet (1.06 $\mu\text{g/L}$, 95% CI [0.81, 1.38]) ($P = 0.86$) (or a mean proportional decrease in PSA of -1%). The researchers concluded that their results suggest that short-term consumption of walnuts is unlikely to affect PSA levels adversely among otherwise normal men.

Spaccarotella, K.J., Kris-Etherton P.M., Stone, W.L., Bagshaw, D.M., Fishell V.K., West S.G., Lawrence F.R., and Hartman T.J., 2008. **The Effect of Walnut Intake on Factors Related to Prostate and Vascular Health in Older Men.** *Nutrition Journal.* 7:13.

This 8-week walnut supplement study looked at the effect of walnuts, which are rich in tocopherols, on markers of prostate and vascular health in men at risk for prostate cancer. Subjects ($n = 21$) consumed (in random order) their usual diet +/- a walnut supplement (75 g/d) that was isocalorically incorporated in their habitual diets. Prior to the supplement study, 5 fasted subjects participated in an acute timecourse experiment and had blood taken at baseline and 1, 2, 4, and 8 h after consuming walnuts (75 g). The results showed that during the timecourse experiment, triglycerides peaked at 4 h, and gamma-tocopherol (γ -T) increased from 4 to 8 h. Triglyceride – normalized γ -T was two-fold higher ($P = 0.01$) after 8 versus 4 h. In the supplement study, change from baseline was $+0.83 \pm 0.52 \mu\text{mol/L}$ for γ -T, $-2.65 \pm 1.30 \mu\text{mol/L}$ for alpha-tocopherol (α -T) and -3.49 ± 1.99 for the tocopherol ratio (α -T: γ -T). A linear mixed model showed that, although PSA did not change, the ratio of free PSA:total PSA increased and approached significance ($P = 0.07$). The α -T: γ -T ratio decreased significantly ($P = 0.01$), partly reflecting an increase in serum γ -T, which approached significance ($P = 0.08$). The significant decrease in the α -T: γ -T ratio with an increase in serum γ -T and a trend towards an increase in the ratio of free PSA:total PSA following the 8-week supplement study suggest that walnuts may improve biomarkers of prostate and vascular status.

Tapsell, L.C., L.J. Gillen, C.S. Patch, M. Batterham, A. Owen, M. Baré, M. Kennedy, 2004. **Including walnuts in a low-fat/modified-fat diet improves HDL cholesterol-to-total cholesterol ratios in patients with Type 2 diabetes.** *Diabetes Care.* 27:2777-83.

This parallel randomized controlled trial compared three different diets, each containing 30% calories from fat: low fat, modified low fat and modified low fat inclusive of 30g of walnuts per day. The walnut group achieved a significantly greater increase in HDL cholesterol-to-total cholesterol ratio and HDL than the other two treatment groups. A 10% reduction in LDL cholesterol was also achieved in the walnut group. There were no significant differences between groups for changes in body weight, percent body fat, total antioxidant capacity, or HbA_{1c} levels.

Zambón, D., J. Sabaté, S. Munoz, B. Campero, E. Casals, M. Merlos, J.C. Laguna, E. Ros, 2000. **Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women. A randomized crossover trial.** *Ann Intern Med.* 4:132(7):538-46.

In a 12-week randomized crossover feeding trial, 49 men and women with high cholesterol levels followed a cholesterol-lowering Mediterranean diet, or a walnut diet in which walnuts were substituted for some of the monounsaturated fat in the diet. Researchers found that LDL cholesterol lowered by 5.9% and total cholesterol lowered by 4.1%, out-performing a cholesterol-lowering Mediterranean diet.

Zhao, G., T.D. Etherton, K.R. Martin, P.J. Gillies, S.G. West, P.M. Kris-Etherton, 2007. **Dietary alpha-linolenic acid inhibits proinflammatory cytokine production by peripheral blood mononuclear cells in hypercholesterolemic subjects.** *Am J Clin Nutr.* 85:385-91.

Zhao, G., T.D. Etherton, K.R. Martin, J.P. Vanden Heuvel, P.J. Gillies, S.G. West, P.M. Kris-Etherton, 2005. **Anti-inflammatory effects of polyunsaturated fatty acids in THP-1 cells.** *Biochemical and Biophysical Research Communications.* 336:909-17.

The effects of three polyunsaturated fatty acids (linoleic acid (LA), alpha-linolenic acid (ALA), and docosahexaenoic acid (DHA)) were compared to that of a saturated fatty acid, palmitic acid (PA), on inflammatory responses in human monocytic THP-1 cells. This study examined the gene signaling the leads to reduced inflammation and showed PUFAs activate PPAR γ . Researchers conclude, "Importantly, the plant-derived omega-3 fatty acid (i.e., ALA) resulted in a comparable anti-inflammatory effect compared to the marine-derived omega-3 fatty acid, DHA. Thus, a diet that provides food sources of ALA and DHA (including walnuts, walnut oil, and fish, respectively) should be encouraged as a means for reducing inflammation and, in turn, CVD risk."

Zhao, G., T.D. Etherton, K.R. Martin, S.G. West, P.J. Gillies, P.M. Kris-Etherton, 2004. **Dietary α -linolenic acid reduced inflammatory and lipid cardiovascular risk factors in hypercholesterolemic men and women.** *J. Nutr.* 134:2991-97.

This study showed that diets high in polyunsaturated fats (PUFA), especially α -linolenic acid (ALA), elicit cardioprotective effects by decreasing lipid and lipoprotein levels and by eliciting vascular anti-inflammatory effects. The fact that ALA has marked, beneficial effects on multiple cardiovascular disease (CVD) risk factors further underscores its potentially important role in CVD risk reduction.

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GENERAL NUTRITION REFERENCES RELEVANT TO TREE NUTS

Alper, C.M., R.D. Mattes, 2002. **Effects of chronic peanut consumption on energy balance and hedonics.** *Int J of Obesity.* 26:1129-37.

In this 30-week, cross-over, intervention study, 15 healthy, normal weight adults, aged 33±9 years were placed on three different diets. In one diet, subjects were provided with 505±118 kcal/day as peanuts for 8 weeks with no dietary guidance (free feeding—FF); in another, subjects were given 3 weeks of instructions to add peanuts to their customary diet (addition—ADD); and in the third, peanuts replaced an equal amount of other fats in the diet for 8 weeks (substitution—SUB). Subjects were unaware that body weight was a research focus. During FF, peanut consumption resulted in a strong compensatory response (subjects compensated for 66% of the energy provided by the nuts) and body weight gain (1.0 kg) was significantly lower than expected. In the SUB phase both caloric intake and body weight were maintained precisely. Resting energy expenditure was increased by 11% after regular peanut consumption for 19 weeks. Chronic peanut consumption did not lead to a decline in pleasantness or hunger ratings for peanuts, nor did it lead to a hedonic shift for selected snack foods during any of the treatments. Conclusion: Peanuts have a high satiety value and chronic ingestion elicits strong dietary compensation and little change in energy balance.

Ginter, E., 1998. **Cardiovascular disease prevention in Eastern Europe.** *Nutrition.* 14(5):452-7.

Over the last three decades the region of highest premature cardiovascular mortality has shifted from the US and Finland to Central and Eastern Europe. Previous studies have shown that the high mortality from CVD in Eastern Europe was not caused by traditional factors alone. Other factors including psychosocial stress and antioxidant deficiencies, alcoholism and smoking are more important than cholesterol or saturated fat intakes in some regions. The intake of antioxidants from domestic and imported vegetables, vegetable oils and nuts in most East European countries has been substantially lower than in the West. More prospective research is needed in the region.

Gregory, J., K. Foster, H. Tyler, M. Wiseman, 1990. **The dietary and nutritional survey of British adults.** London: HMSO.

Grundy, S.M., N. Abate, M. Chandalia, 2002. **Diet composition and the metabolic syndrome: what is the optimal fat intake?** *Am J Med.* 113(9B):25S-29S.

The researchers concluded the studies with the Mediterranean population reveal that in healthier populations, diets relatively high in unsaturated fatty acids are well tolerated and are associated with a low prevalence of both coronary heart disease and type 2 diabetes.

Hodson, L., C.M. Skeaff, W.-A.H., Chisolm, 2001. **The effect of replacing dietary saturated fat with polyunsaturated or monounsaturated fat on plasma lipids in free-living young adults.** *Eur J of Clin Nutr.* 55:908-15.

In two randomized cross-over trials, researchers tried to determine the effects of substituting saturated fat rich foods with either n-6 polyunsaturated fat (PUFA) rich foods or monounsaturated fat (MUFA) rich foods on plasma cholesterol, while still adhering to a total fat intake of 30-33% of total calories. In trials I (n=29) and II (n=42), free-living college students eating self-selected diets were asked to follow a diet high in saturated fat for 2½ weeks. During

the 2½ week comparison diet, saturated fat foods were replaced with foods rich in n-6 PUFAs (trial I) and in trial II the replacement foods were high in MUFAs.

The results showed that when replacing saturated fats with MUFAs or PUFAs, total fat intakes decreased by 2.9% of calories and 5.1% of calories respectively. Replacing saturated fats with PUFAs decreased total cholesterol by 19%, LDL by 22% and HDL by 14%. Replacing saturated fats with MUFAs decreased total cholesterol by 12%, LDL by 15% and HDL by 4%. The change in the total cholesterol to HDL ratio was similar during trial I and II. The researchers concluded that replacing saturated fats with PUFAs or MUFAs is equally effective in decreasing the total to HDL cholesterol ratio.

Johnston, C.S., A.J. Buller, 2005. **Vinegar and peanut products as complementary foods to reduce postprandial glycemia.** *J Am Diet Assoc.* 105:1939-42.

This study examined whether complementary foods (vinegar and peanut products) could lower postprandial glycemia without altering mealtime glycemic load. Eleven healthy subjects consumed two test meals (bagel and juice, glycemic load=81; or chicken and rice, glycemic load=48) under three conditions (control, vinegar, or peanut) using a randomized, crossover design. Vinegar or peanut ingestion reduced the 60-minute glucose response to both test meals by ~55%, but these reductions were significant only for the high-glycemic load meal. After consumption of the high-glycemic load meal, energy consumption for the remainder of the day was weakly affected by the vinegar and peanut treatments, a reduction of ~200 to 275 calories. Regression analyses indicated that 60-minute glucose response later energy consumption. In conclusion, the addition of vinegar or peanut products to a high-glycemic load meal significantly reduced postprandial glycemia.

Kafatos, A.G., 1999. **Diet, antioxidants, and health - case study: the Cretan experience.** In: **Mediterranean Diets** (World Review of Nutrition and Dietetics. Vol. 87). A.P. Simopoulos (ed.) CRC Press LLC. 119-29.

Kouris-Blazos, A., C. Gnardellis, M.L. Wahlqvist, D. Trichopoulos, W. Lukito, A. Trichopoulos, 1999. **Are the advantages of the Mediterranean diet transferable to other populations? A cohort study in Melbourne, Australia.** *Br J Nutr.* 82:57-61.

Krawczyk, T., 2001. **Fat in dietary guidelines around the world.** *Inform.* 12:126-40.

Kris-Etherton, P.M., T.A. Pearson, Y. Wan, R.L. Hargrove, K. Moriarty, V. Fishell, T. D. Etherton. 1999. **High-monounsaturated fatty acid diets lower both plasma cholesterol and triacylglycerol concentrations.** *Am J Clin Nutr.* 70(6):1009-15.

In this randomized, double-blind, 5-period crossover study with 22 subjects, researchers compared the CVD risk profile of an Average American (AA) diet with those of four cholesterol-lowering diets: American Heart Association Step II diet and three high-monounsaturated fatty acid (MUFA) diets [olive oil (OO), peanuts and peanut butter (PPB) and peanut oil (PO)]. The results showed that the MUFA diets lowered total cholesterol by 10% and LDL by 14%--a response comparable to the Step II diet. The OO, PO and PPB diets reduced CVD risk by an

estimated 25%, 16% and 21% respectively, whereas the Step II diet lowered CVD risk by only 12%. The high-MUFA diet may be preferable to a low-fat diet in lowering cholesterol because of more favorable effects on the CVD risk profile.

Langseth, L., 1995. **Oxidants, antioxidants, and disease prevention.** ILSI Europe Concise Monograph Series, Brussels, Belgium: ILSI Europe.

Liu, S., W. Willett, M. Stampfer, et al., 2000. **A prospective study of dietary glyceemic load, carbohydrate intake and risk of coronary heart disease in US women.** *Am J Clin Nutr.* 71:1455-61.

Researchers prospectively evaluated the relations of the amount and type of carbohydrates with risk of CHD in a cohort of women, aged 38-63 years, from the Nurses' Health Study. The data suggest that a high dietary glyceemic load from refined carbohydrates increases the risk of CHD, independent of known coronary disease risk factors.

Nanos, G.D., D.G. Gerasopoulos, 2001. **Fruits, vegetables, legumes and grains. In: The Mediterranean diet: Constituents and health promotion.** A.L. Matalas, A. Zampelas, V. Stavrinou, I. Wolinsky (eds) CRC Press, London. 97-125.

N.A.S., 2000. **Dietary reference intakes for vitamin C, vitamin E, selenium, and carotenoids.** Food and Nutrition Board, Inst. of Med., National Academy Press, Washington, D.C.

N.I.H. **Expert Panel on Detection, Evaluation and Treatment of High Cholesterol in Adults, 2001. Executive summary of the third report of the National Cholesterol Education Program expert panel on detection, evaluation & treatment of high blood cholesterol in adults (adult treatment panel III).** *J Am Med Assn.* 285:2486-97.

O'Byrne, D.J., Knauff, D.A., R.B. Shireman, 1997. **Low fat-monounsaturated rich diets containing high-oleic peanuts improve serum lipoprotein profiles.** *Lipids.* 32:687-95.

Twelve postmenopausal hypercholesterolemic women, who previously consumed high-fat diets (34% calories from fat), were put on a low fat (26% calories from fat)-monounsaturated rich diet (LFMR: 14% of calories from monounsaturated fat) for 6 months. Thirteen women already eating low fat (LF) diets (24% calories from fat) were also followed to monitor variations in blood lipids. At the end of the study, blood cholesterol decreased 10% and low density lipoprotein decreased 12% in the LFMR group, but did not change in the LF group. Only the LFMR group showed a trend toward beneficial changes in LDL/HDL and apo A-1/apo B ratios. Conclusion: the LFMR diet was well-tolerated and resulted in an improved serum lipid and apolipoprotein profile. [Subjects consumed 35-68 g of high-oleic peanuts/day in the LFMR group.]

Panico, S., I.R. Dello, E. Celentano, R. Galasso, P. Muti, M. Salvatore, M.P. Mancini, 1992. **ATENA, a study on the etiology of major chronic diseases in women: design, rationale and objectives.** *Eur J Epidemiol.* 8:601-8.

Pelkman, C.L., V.K. Fishell, D.H. Maddox, T.A. Pearson, D.T. Mauger, P.M. Kris-Etherton, 2004. **Effects of moderate-fat (from monounsaturated fat) and low-fat weight-loss diets on serum lipid profile in overweight and obese men and women.** *Am J Clin Nutr.* 79:204-12.

This study evaluated the effects of calorie-controlled, low-fat and moderate-fat diets on changes in lipids and lipoproteins during weight loss and subsequent weight maintenance. In a parallel-arm study design, 53 overweight and obese healthy men and women were assigned to a low-fat diet (18% of calories) or moderate-fat diet (33% of calories and included peanuts and peanut butter) for 6 weeks to achieve weight loss, which was followed by 4 weeks of weight maintenance. All foods were provided and body weight was monitored to ensure equal weight loss between groups. The results showed that the moderate-fat diet produced favorable changes in the lipoprotein profile. Compared with baseline, HDL was unchanged, triacylglycerol and the ratios of total and non-HDL cholesterol to HDL cholesterol were lower at the end of the weight-maintenance period in the moderate-fat diet group. Despite similar weight loss, triacylglycerol rebounded, HDL decreased, and the ratios of total and non-HDL cholesterol to HDL cholesterol did not change during the 10-week interval in the low-fat group. The researchers concluded that a moderate-fat weight-loss and weight-maintenance diet improves the cardiovascular disease risk profile via favorable changes in lipids and lipoproteins.

Rajaram, S., M. Wien, 2001. **Vegetarian diets in the prevention of osteoporosis, diabetes, and neurological disorders.** In: Sabaté, J., (ed.) *Vegetarian Nutrition*, CRC Press, Boca Raton, 109-34.

Rimm, E.B., M.J. Stampfer, 2004. **Diet, lifestyle, and longevity—the next steps?** *JAMA.* 292(12):1490-92.

In this editorial, the authors comment that although the relation of lifestyle and health outcomes will continue to be refined, there is enough evidence now to take action. The US spends billions of dollars on chronic disease treatments and intervention for risk factors, and if we spent only a fraction of that on promoting healthful lifestyles and primary prevention we'd probably be much healthier.

Serra Majem, L., N. Armas, B.L. Ribas, 2000. **Food consumption and food sources of energy and nutrients in Canary Islands (1997-1998)** [in Spanish]. *Arch Latinoam Nutr.* 50(suppl 1): 23-33.

Serra-Majem L, R. García-Closas, L. Ribas, C. Pérez-Rodrigo, J. Aranceta, 2001. **Food patterns of Spanish schoolchildren and adolescents: The enKid Study.** *Public Health Nutrition.* 4(6A): 1433-8.

Serra-Majem L. B. Roman, R. Estruch, 2006. Scientific evidence of interventions using the Mediterranean diet: A systematic review. *Nutrition Reviews*. 64(2):S27-47.

A recent systematic review using the Mediterranean diet showed favorable results on lipoprotein levels, insulin resistance, metabolic syndrome, endothelium vasodilatation, antioxidant capacity, myocardial and cardiovascular mortality, and cancer incidence in patients with previous myocardial infarction and in obese patients.

Slimani, N., P. Ferrari, M. Ocke, et al., 2000. **Standardization of the 24-hour diet recall calibration method used in the European prospective investigation into cancer and nutrition (EPIC): general concepts and preliminary results. *Eur J Clin Nutr*. 54(12):900-17.**

Trichopoulou, A., T. Costacou, C. Bamia, D. Trichopoulou, 2003. **Adherence to a Mediterranean diet and survival in a Greek population. *NEJM*. 348:2599-2608.**

In this population-based, prospective investigation involving 22,043 adults in Greece, researchers studied the effects of a Mediterranean diet on mortality. Greater adherence to the traditional Mediterranean diet was associated with a significant reduction in total mortality. According to the authors, “After adjusting for age, sex, education, smoking status, BMI, waist-to-hip ratio, energy expenditure score and total energy intake, the only individual measures that were predictive of total mortality were the intake of fruits and nuts and the ratio of monounsaturated fats to saturated fats.”

Trichopoulou, A., E. Vasilopoulou, 2000. **Mediterranean diet and longevity. *Br J Nutr*. 84(suppl 2):S205-9.**

Trichopoulou, A., P. Lagiou, 1997. **Healthy traditional Mediterranean diet: an expression of culture, history, and lifestyle. *Nutrition Reviews* 55(11):383-9.**

USDA Dietary Guidelines for Americans 2000, 5th Edition, Center for Nutrition Policy and Promotion.

Willett, W.C., 2003. **Eat, drink, and be healthy. The Harvard Medical School Guide to Healthy Eating.** Simon & Schuster Source, NY.

According to the author, contrary to popular opinion, nuts aren't junk food. They're actually a great source of protein and other nutritional goodies. An ounce of almonds, walnuts, peanuts, or pistachios provides about 8 grams of protein, the same as a glass of milk. While nuts have quite a bit of fat, it is mostly unsaturated fats that reduce LDL cholesterol and keep HDL cholesterol high.

However it happens, the message is the same—nuts are good for you, if eaten the right way. Eat nuts instead of chips or chocolate as a snack. They'll take the edge off hunger every bit as well as true junk food, they taste as good as or better than junk food, and they provide healthy nutrients to boot.

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