Plant-Based Diets and Control of Lipids and Coronary Heart Disease Risk

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Coronary heart disease (CHD) is a major cause of death worldwide. Dietary factors have an important role in influencing the outcome of this disease. Dietary guidelines around the world now recommend increased consumption of plant foods for the prevention of CHD. Epidemiologic and human intervention studies have documented an inverse relationship between the consumption of plant-based diets and deaths attributed to heart disease. Plant foods contain many beneficial compounds that, by acting through multiple mechanisms, provide protection against the disease. American and Canadian recommendations for the daily intake of fruits and vegetables provide a sound basis for a healthy diet and the prevention of CHD.

Introduction

Coronary heart disease (CHD) is responsible for many deaths in North America and rest of the world. According to the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC), 16.7 million deaths were reported around the globe due to different types of cardiovascular diseases (CVD). Many factors contribute toward the risk of heart disease. They include nonmodifiable risk factors (advancing age, heredity and family history, gender, and ethnicity), modifiable risk factors (abnormal blood lipids, tobacco use, physical inactivity, obesity, unhealthy diet, and diabetes mellitus), and other risk factors (excess homocysteine, inflammation, and abnormal blood coagulation). Although genetic factors and age are the common risk factors, other factors such as hypertension, hyperlipidemia (including hypercholesterolemia and hypertriglyceridemia), insulin resistance, and lifestyle factors such as diet, cigarette smoking, obesity, lack of physical activity, and other physical and psychological tensions, are also recognized as being equally important risk factors associated with the disease [1]. Among the modifiable risk factors, diet has received a great deal of attention in recent years. Based on epidemiologic and human intervention studies, countries around the world have formulated dietary guidelines for the prevention of CHD. One of the major recommendations is to increase the consumption of plant-based foods. Important sources of plant foods in human diets include fruits, vegetables, cereals, legumes, nuts, and other miscellaneous items such as herbs and medicinal plants. Plant foods contain many components that have been associated with the risk of CHD (Table 1).

Role of Plant Foods in the Progression of CHD

Knowledge of the various steps involved in the progression of CHD would be beneficial in understanding the role of plant foods and their components in its prevention. Figure 1A shows a schematic representation of the multiple-step model for CHD. There is evidence supporting the role of plant foods and their components in the early, middle, and late stages of CHD. Population-based studies have provided observations that consumption of plant foods can reduce rates of mortality associated with CHD [2•,3,4•]. Most of the population-based epidemiologic studies use deaths due to CHD as the end point. However, most of the in vitro investigations study the early events in the progression of the disease. The link between early events of the disease, such as low-density lipoprotein (LDL) oxidation, and the terminal outcome of death is an important area of future research.

Serum lipids, including cholesterol and triglycerides, have been the main focus with respect to the risk of CHD. Serum total, LDL cholesterol, and high-density lipoprotein (HDL) cholesterol and the ratio of LDL/HDL traditionally are used as biomarkers of CHD risk [5]. As a result, most of the dietary strategies for the prevention of CHD have been directed at lowering total and LDL cholesterol while increasing levels of HDL cholesterol. Reducing cholesterol synthesis and increasing its excretion can maintain serum lipids in the recommended range. Dietary fiber, in particular, has provided an effective means of managing serum lipids and reducing the risk of CHD.

Table 1. Components of plant-based foods associated with risk of coronary heart disease

Ingredient	Mode of action
Plant sterols and stanols	Displace cholesterol in the micelles and increase its fecal excretion, leading to decreases in the amounts of cholesterol absorbed by lumen [33].
Types and amounts of fat	Mono- and polyunsaturated fatty acids improve serum lipid profiles [34•]
Dietary fiber	Helps reduce stomach emptying time; improves blood lipid profile and insulin homeostasis [35•]
Antioxidant polyphenols	Inhibit LDL cholesterol oxidation and improve endothelial dysfunction, which are key steps in the development of atherosclerosis; inhibit platelet aggregation [36]
Dietary phytoestrogens (flavonols, flavones)	Prevent oxidation of LDL cholesterol (inhibiting platelet aggregation and improving endothelial dysfunction) and reduce inflammation [37•]
Antioxidant carotenoids	Reduce oxidative damage of lipids, proteins, and DNA by quenching singlet oxygen and trapping peroxyl radicals [38]
Vitamins (B_6, B_9, and B_{12})	Lower homocysteine levels and reduce the risk of CHD [17•,39•]
Antioxidant vitamins (C, E, and A)	Protect cellular components against free radical–induced oxidative damage [34•,40]
Minerals	Act as cofactors for the activity of antioxidant defense enzymes [41]
Plant proteins	Reduce plasma cholesterol and triglyceride levels and raise HDL cholesterol levels [42•]

CHD—coronary heart disease; HDL—high-density lipoprotein; LDL—low-density lipoprotein.

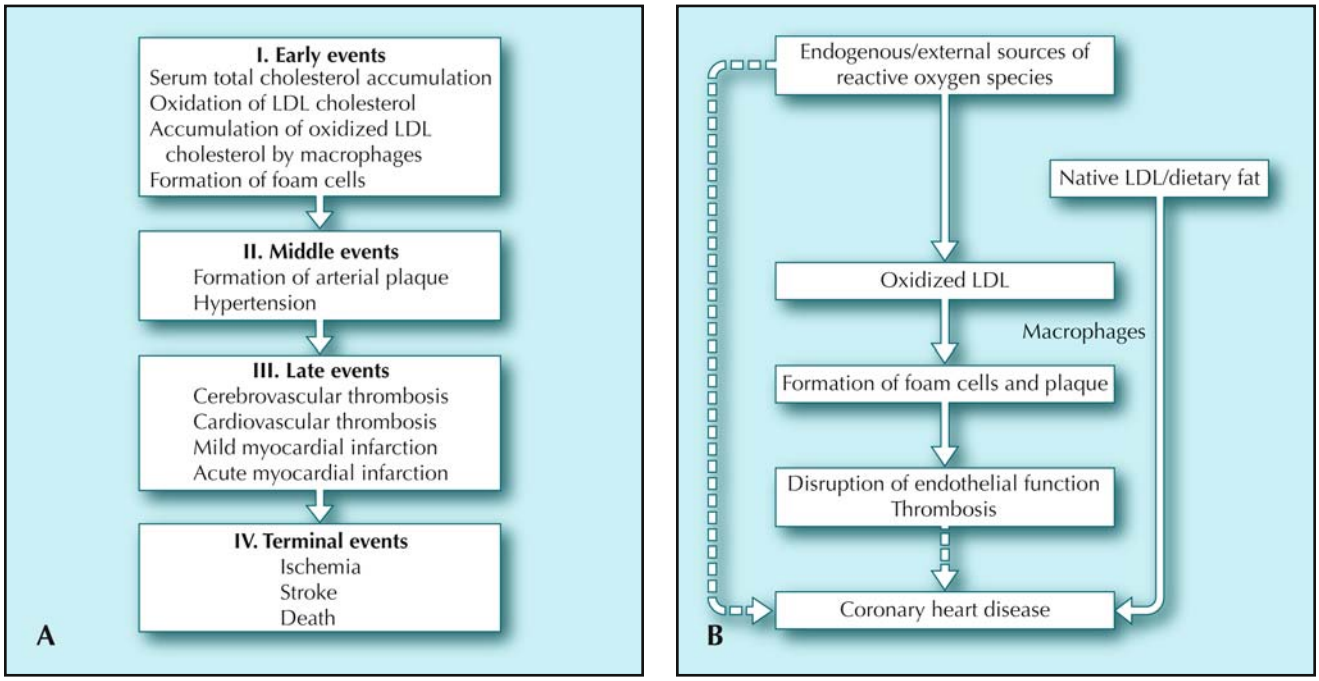

Figure 1. A, Multistep model for the development of coronary heart disease (CHD). **B,** Low-density lipoprotein (LDL) oxidation and CHD.

Oxidative stress induced by reactive oxygen species (ROS) is also considered to play an important part in the etiology of several chronic diseases, including CHD [6•]. Oxidation of the circulating LDL creates oxidized LDL, which is thought to play a key role in the pathogenesis of atherosclerosis, the underlying disorder leading to heart attack and ischemic stroke [5]. Figure 1B shows the LDL oxidation hypothesis in the etiology of CHD. Antioxidant nutrients are believed to slow the progression of atherosclerosis because of their ability to inhibit the damaging oxidative processes [7]. In this respect, plant foods naturally contain several antioxidants, including vitamins, minerals, and phytochemicals. Plant foods are good sources of vitamins A, C, and E, all of which have been documented to have antioxidant properties. Selenium is an important trace mineral that is essential for the activity of the enzyme glutathione-S-peroxidase, an important antioxidant enzyme [8•]. Major antioxidant phytochemicals present in plant foods include carotenoids, such as beta-carotene and lycopene, and polyphenols, such as anthocyanins [9].

Fruits and Vegetables in the Prevention of CHD

Evidence in support of the role of fruits and vegetables in the prevention of CHD comes from epidemiologic, human intervention, and animal studies. Recent epidemiologic studies published in the literature are summarized in Table 2. Based on these observations, dietary recommendations around the world recommend increased consumption of fruits and vegetables. American food guidelines recommend the consumption of 2 to 4 servings of fruits per day and 3 to 5 servings of vegetables per day [10]. Canadian guidelines recommend consumption of 5 to 10 servings of fruits and vegetables per day [11]. Many studies have shown an association between low fruit and vegetable intake and the development of CVD and other degenerative diseases [12•]. Diets rich in fruits and vegetables may help reduce the risk of CHD in a number of ways. They displace from the diet foods that are high in sodium [13], fat [14], and energy. They are also important sources of soluble and insoluble fiber [15•] and sterols, which help reduce serum cholesterol levels [14]. By reducing the intake of sodium, they also help reduce blood pressure and the risk of CHD. As good sources of naturally occurring antioxidants, fruits and vegetables help reduce oxidative stress and improve endothelial function. Together with legumes, they are the main source of folate [16], which is known to protect against CHD by its ability to reduce the level of homocysteine in the blood [17•]. One vegetable that has been studied extensively in recent years for its role in the prevention of CHD is the tomato. Tomatoes and processed tomato products naturally contain lycopene, a carotenoid antioxidant phytochemical. Although several population-based studies showed an inverse relationship between the consumption of tomatoes and the serum levels of lycopene and the incidence of CHD, the strongest evidence comes from a multicenter case-control study that evaluated the relationship between adipose tissue antioxidant status and acute myocardial infarction [18]. Participants (662 cases and 717 controls) from 10 European countries were recruited to maximize the variability in exposure within the study. Needle aspiration biopsy samples of the adipose tissue were taken shortly after the infarction and the level of α-carotene, beta-carotene, lycopene, and α-tocopherol measured. After adjusting for age, body mass index, socioeconomic status, smoking, hypertension, and maternal and paternal history of the disease, lycopene was shown to be protective against the risk of myocardial infarction [19•]. Results from the Nurses' Health Study, Health Professionals Follow-up Study [20], several other long-term studies [21•–23•], and from controlled dietary intervention studies provide compelling evidence supporting the relationship between increased consumption of fruits and vegetables and decreased risk of CHD and stroke.

Cereal Grains, Legumes, Nuts, and Other Plant-Based Foods in the Prevention of CHD

Cereal grains and their products are the major food group for most humans, providing a significant proportion of total energy intake in our diet. Several components of cereals have known potential for reducing risk factors for CHD. They include fiber, linoleic acid, vitamin E, folate, and selenium. Among the phytochemicals present in cereals, phytoestrogens of the lignan family and several phenolic acids with antioxidant properties also have cardioprotective properties. As shown in Table 2, several recent studies support the conclusion that consumption of grains and cereals can help lower plasma lipids, including triglycerides, LDL cholesterol, and total cholesterol. Although the type of cereal grains and the major components that they may contain can have differing effects on plasma lipids, it has been suggested that whole grain cereal foods and oatmeal or bran may reduce the risk of CHD.

Legumes have also been studied for their beneficial effects against heart disease (Table 2). They are a good source of plant protein and complement the high carbohydrate staples such as rice, wheat, maize, and various root and tuber crops. Among the legumes, soybeans have been studied the most. However, other beans classified as legumes also possess beneficial properties. Similar to the cereal grains, they also contain several beneficial compounds associated with lowering the risk of CHD and, in particular, protein, fiber, phytoestrogens, and isoflavones are credited for the cardioprotective properties of legumes.

An extensive body of literature describes the beneficial effects of consuming nuts on serum lipid profiles [24•]. Inclusion of 50 to 100 g (approximately 1.5–3.5 servings) of nuts, five or more times a week, in conjunction with a low-fat diet, can help decrease total and LDL cholesterol and protect against CHD. However, improvement of lipid profiles was also observed with the consumption of 20 g/d of some types of nuts [25•]. Clinically relevant improvement in the reduction of serum LDL cholesterol was also shown with as little as 4 g/d of nuts. Thus, nuts seem to have a broader benefit in dyslipidemia, depending on the level and duration of intake [26•]. The mechanisms whereby the consumption of nuts affords protection against CHD are probably multiple. The fatty acid profile of nuts, in particular the presence of the omega-3 fatty acid α-linoleic acid (ALA), has been suggested as being important with respect to their beneficial cardioprotective properties.

Consumption of certain beverages rich in polyphenols, such as red wine containing resveratrol, green tea containing catechins, and pomegranate juice containing catechins and quercetin, has been shown to protect LDL cholesterol against oxidative damage and to improve endothelial dysfunction, both of which are recognized as early events in atherogenesis [27]. Grape seeds that contain proanthocyanidins can also protect against LDL oxidation [28•]. Several spices, herbs, and condiments used in food preparations have also been shown to inhibit platelet aggregation and

Table 2. Recent studies of plant-based food and risk of coronary heart disease

Plant group	Study	Year	Methods	Major findings
Fruits and vegetables	Radhika et al. [12•]	2008	Analyzed the relation between fruit and vegetable intake and CVD risk factors (blood pressure, obesity, cholesterol) in a cross-sectional sample of inhabitants of southern India	A strong inverse correlation between fruit and vegetable consumption and CVD risk factors
	Nothlings et al. [21•]	2008	Cohort study involved 10,449 European diabetic patients and followed their life pattern for 9 years	A close relationship between intakes of fruits, vegetables, and legumes and physiologic markers of CVD and all-cause mortality
	Takachi et al. [43•]	2008	Food-frequency questionnaire to assess the net impact of fruit and vegetable consumption and ratio of cancer and CVD in the same population in Japan	A significant inverse association between fruit consumption and risk of CVD. This association was more apparent among women and nonsmokers than among men and smokers
	Cai et al. [44•]	2007	Dietary patterns and mortality in 74,942 Chinese women age 40 to 70 years from 1996 to 2000	Inverse relation between fruit consumption and diabetes, CVD, stroke, and mortality incidence
	Shimazu et al. [22•]	2007	Association between dietary patterns and CVD mortality in 40,547 Japanese men and women age 40 to 79 years without a history of diabetes, stroke, myocardial infarction, or cancer at baseline in 1994 and during 7 years of follow-up (based on a validated food-frequency questionnaire)	Japanese dietary pattern high in soybean products, fish, seaweeds, vegetables, fruits, and green tea is associated with a decreased risk of CVD mortality, despite its relation to sodium intake and hypertension
	Bermejo et al. [15•]	2007	The consumption of fruits and vegetables as a specific risk factor for CVD; level of plasma homocysteine in 152 elderly patients	Greater consumption of fruit and vegetables is associated with better food habits, increased vitamin and mineral intakes, and lower homocysteine level
	Hung et al. [45]	2004	Follow-up study included almost 110,000 men and women whose health and dietary habits were followed for 14 years	The higher the average daily intake of fruits and vegetables the lower the chances of developing CVD. Compared with those who consume less than 1.5 servings a day, those who averaged 8 or more servings a day were 30% less likely to have had a heart attack or stroke
Cereal grains, legumes, nuts, other plant-based foods	Griel et al. [42•]	2008	25 moderately hypercholesterolemic participants; 10 men and 15 women aged 25–65 years, representative of the population in the United States that is at high risk for CVD	42.5 g/d of macadamia nuts showed substantial reduction in total and LDL cholesterol
	Goel et al. [30•]	2008	500 mg/d of curcumin for 7 days	Decreased serum lipid peroxidase (33%), increased HDL cholesterol (29%), and decreased total serum cholesterol (12%)

CHD—coronary heart disease; COX—cyclooxygenase; CVD—cardiovascular disease; HDL—high-density lipoprotein; LDL—low-density lipoprotein; oxLDL—oxidized low-density lipoprotein.

Table 2. Recent studies of plant-based food and risk of coronary heart disease *(Continued)*

Plant group	Study	Year	Methods	Major findings
	Lei et al. [29•]	2008	Examined whether diallyl sulfide (DAS), diallyl disulfide (DADS), and diallyl trisulfide (DATS), 3 major organosulfur compounds of garlic oil, reduce adhesion molecule expression induced by oxLDL and, if so, through what mechanism. Human umbilical vein endothelial cells were preincubated with 1 mmol/L of DAS, 200 µmol/L of DADS, or 100 µmol/L of DATS for 16 h and then with 40 mg/L of oxLDL for an additional 24 h. oxLDL induction of cellular and cell surface expression of E-selectin and vascular cell adhesion molecule-1 was suppressed by garlic allyl sulfides in the order DATS > DADS > DAS	The adhesion of HL-60 cells to endothelial cells was inhibited 27% and 33%, and the production of cellular peroxides was inhibited 43% and 50% by DADS and DATS, respectively ($P < 0.05$). oxLDL alone dephosphorylated protein kinase B and cyclic adenosine monophosphate responsive element binding protein; such deactivation was reversed by DADS and DATS.
	Raman et al. [31•]	2008	Echinacea, garlic, ginkgo, ginseng, Siberian ginseng, grape seed extract, kava kava, saw palmetto, and St John's wort were analyzed for their ability to inhibit cyclooxygenase-1 and -2 enzymes and lipid peroxidation in vitro	Varying degrees of COX enzyme inhibition (5%–85% for COX-1 and 13%–28% for COX-2). Interestingly, extracts of garlic, ginkgo, ginseng, Siberian ginseng, kava kava, and St. John's wort selectively inhibited COX-2 enzyme. These supplements also inhibited lipid peroxidation in vitro (5%–99%).
	Lin et al. [37•]	2007	Dietary information from the study's 1990, 1994, and 1998 food-frequency questionnaires and computed cumulative average intakes of flavonols and flavones	938 nonfatal myocardial infarctions and 324 CHD deaths among 66,360 women. They observed no association between flavonol or flavone intake and risk of nonfatal myocardial infarction or fatal CHD. Nevertheless, these prospective data do not support an inverse association between flavonol or flavone intake and CHD risk
	Shanmuganayagam et al. [28•]	2007	Two groups of rabbits (control and treated, $n = 10$ each) were fed a hypercholesterolemic diet for 48 days. Treated group then received supplemental Concord grape juice (225 mL/d), whereas control group received supplemental isocaloric sugar water for 48 days.	Daily consumption of Concord grape juice attenuates hypercholesterolemia-enhanced platelet aggregation, blood pressure, total serum cholesterol, and development of atheroma in rabbits
	Welty et al. [46•]	2007	60 healthy postmenopausal women consumed 25 g/d of soy protein instead of ordinary protein source for 8 wk	Conspicuous improvement in blood pressure and LDL cholesterol levels in hypertensive women and blood pressure in normotensive postmenopausal women
	Erkkila and Lichtenstein [4•]	2006	Postmenopausal women involved for 3 years in long cohort study. The intake was > 3 g/1000 kcal of cereal fiber or > 6 servings of whole grains per week	Progression in percent stenosis tended to be less
	Chen et al. [47•]	2006	Randomized, double-blind clinical trial for 4 weeks testing the ability of 30 g/d of isolated soy protein vs milk protein on 26 patients with hemodyalisis and hypercholesterolemia	Significant changes in total and LDL cholesterol levels

CHD—coronary heart disease; COX—cyclooxygenase; CVD—cardiovascular disease; HDL—high-density lipoprotein; LDL—low-density lipoprotein; oxLDL—oxidized low-density lipoprotein.

Table 2. Recent studies of plant-based food and risk of coronary heart disease *(Continued)*

Plant group	Study	Year	Methods	Major findings
	Griel and Kris-Etherton [24•]	2006	Inclusion of 50–100 g (approximately 1.5–3.5 servings) five or more times a week (in conjunction with a low-fat diet)	Decrease in total and LDL cholesterol and protection against CVD in a dose-dependent manner
	Griel and Kris-Etherton [24•]	2006	Numerous controlled feeding trials	Daily intake of manageable allowances of a variety of nuts for periods of 4–8 weeks has a clear cholesterol-lowering effect
	Ahuja and Ball [48•]	2006	Randomized cross-over study with 27 participants (13 men and 14 women) who ate "freshly chopped chilli" blend (30 g/d, 55% cayenne chilli) or no chilli (bland) diets for 4 weeks each	Regular consumption of chilli for 4 weeks increases the resistance of serum lipoproteins to oxidation
	McKevith [49]	2004	A meta-analysis of 67 controlled studies	Soluble fiber (2–10 g/d) was associated with small but significant reductions in total cholesterol and LDL cholesterol concentrations
	Martinez-Tome et al. [50]	2004	Assessment of antioxidant in cereal bran	The amounts of antioxidants in whole grain are 20-fold higher than in refined grain

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prevent thrombosis [29•–31•]. Extensive work has been carried out on the role of garlic in the prevention of CHD. Both animal and human studies have shown the ability of garlic to protect against cardiovascular disease because of its hypocholesterolemic, hypolipidemic, antihypertensive, antithrombotic, and antihyperhomocysteinemic properties, as well as its ability to inhibit platelet aggregation [32•].

Conclusions

There is compelling evidence to suggest that dietary factors play an important role in influencing CHD. An unhealthy diet that contains high levels of saturated fats and cholesterol, along with obesity, are the major dietary risk factors of the disease. Dietary guidelines around the world now recommend increased consumption of plant foods to lower the risk of CHD. Plant foods inherently contain low levels of total and saturated fat and no cholesterol. In addition, they also contain many compounds that have been shown to be cardioprotective. They include dietary fiber; proteins; antioxidants such as vitamins A, E, and C; selenium; and folate. They help reduce the intake of saturated fats and cholesterol, increase the intake of mono-and polyunsaturated fatty acids, prevent cholesterol synthesis, and protect lipids against oxidative damage. Plants also contain a variety of beneficial phytochemicals that reduce the risk of CHD via multiple mechanisms. Carotenoids and polyphenols present in plant foods have been shown to be potent antioxidants that reduce LDL oxidation and help prevent plaque formation and improve macrophage function. By positively influencing the early events, they can significantly reduce the number of deaths attributed to cardiovascular complications. Future research will continue to identify new components of plant foods beneficial to maintain a healthy heart and the mechanisms of their action. US government food guidelines recommend the consumption of 2 to 4 servings of fruits and 3 to 5 servings of vegetables per day, and Canadian guidelines recommend consumption of 5 to 10 servings of fruits and vegetables per day. On the basis of the mounting scientific evidence in favor of plant foods in preventing CHD, it is prudent to follow these guidelines and the overall recommendation to increase the consumption of plant-based foods.

Disclosures

No potential conflicts of interest relevant to this article were reported.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Mackay J, Mensah G: *The Atlas of Heart Disease and Stroke*. Geneva: World Health Organization; 2004.

2.• Dauchet L, Amouyel P, Hercberg S, Dallongeville J: **Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies.** *J Nutr* 2006, **136:**2588–2593.

This article illustrates the relation between fruit and vegetable consumption and risk of cardiac diseases.

3. Bazzano LA, He J, Ogden LG, et al.: **Dietary fiber intake and reduced risk of coronary heart disease in US men and women: the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study.** *Arch Intern Med* 2003, **163:**1897–1904.

4.• Erkkila AT, Lichtenstein AH: **Fiber and cardiovascular disease risk: how strong is the evidence?** *J Cardiovasc Nursing* 2006, **21:**3–8.

This article discusses dietary fibers and their correlation to CVD.

5. Hayes KC: **Dietary fat and coronary heart disease.** In: *Preventive Nutrition: The Comprehensive Guide for Health Professionals,* edn 2. Edited by Bendich A, Deckelbaum R. Totowa, NJ: Humana Press; 2001:157–173.

6.• Stratil P, Klejdus B, Kubaänÿ V: **Determination of total content of phenolic compounds and their antioxidant activity in vegetables—evaluation of spectrophotometric methods.** *J Agric Food Chem* 2006, **54:**607–616.

A scanning study for some vegetables in regard to their polyphenols and antioxidant potency.

7. Chu YF, Sun J, Wu X, Liu RH: **Antioxidant and antiproliferative activities of common vegetables.** *J Agric Food Chem* 2002, **50:**6910–6916.

8.• Fraga CG: **Relevance, essentiality and toxicity of trace elements in human health.** *Mol Aspects Med* 2005, **26:**235–244.

This article discusses the importance of trace elements to health and their possible adverse effects.

9. Scalbert A, Manach C, Morand C, et al.: **Dietary polyphenols and the prevention of diseases.** *Crit Rev Food Sci Nutr* 2005, **45:**287–306.

10. **American Heart Association Dietary Guidelines.** Available at: http://healthlink.mcw.edu/article/972602194.html. Accessed on July 12, 2008.

11. **Canada's Food Guide.** Available at: http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/choose-choix/fruit/need-besoin-eng.php. Accessed on July 12, 2008.

12.• Radhika G, Sudha V, Mohan Sathya R, et al.: **Association of fruit and vegetable intake with cardiovascular risk factors in urban south Indians.** *Br J Nutr* 2008, **99:**398–405.

A survey in some parts of India that correlates fruit and vegetable consumption to CVD.

13. Miura K, Greenland P, Stamler J, et al.: **Relation of vegetable, fruit, and meat intake to 7-year blood pressure change in middle-aged men: the Chicago Western Electric Study.** *Am J Epidemiol* 2004, **159:**572–580.

14. Djousse L, Arnett D, Coon H, et al.: **Fruit and vegetable consumption and LDL cholesterol: the National Heart, Lung, and Blood Institute Family Heart Study.** *Am J Clin Nutr* 2004, **79:**213–217.

15.• Bermejo LM, Aparicio A, Andrés P, et al.: **The influence of fruit and vegetable intake on the nutritional status and plasma homocysteine levels of institutionalised elderly people.** *Pub Health Nutr* 2007, **10:**266–272.

This article examines the impact of fruits and vegetables on homocysteine levels, which are an independent risk factor for CVD.

16. Rissanen T, Voutilainen S, Virtanen J, et al.: **Low intake of fruits, berries and vegetables is associated with excess mortality in men: the Kuopio Ischaemic Heart Disease Risk Factor (KIHD) Study.** *J Nutr* 2003, **133:**199–204.

17.• Lonn E, Yusuf S, Arnold MJ, et al.: **Homocysteine lowering with folic acid and B vitamins in vascular disease.** *N Engl J Med* 2006, **354:**1567–1577.

A discussion of folate and the vitamin B group and their crucial roles in homocysteine level.

18. Kohlmeier L, Kark JD, Gomez-Garcia E, et al.: **Lycopene and myocardial infarction risk in the EURAMIC study.** *Am J Epidemiol* 1997, **146:**618–626.

19.• Sesso HD, Buring JE, Norkus EP, Gaziano JM: **Plasma lycopene, other carotenoids, and retinol and the risk of cardiovascular disease in men.** *Am J Clin Nutr* 2005, **81:**990–997.
A discussion of the importance of lycopene and other carotenoids in CVD.
20. **Vegetables and Fruits: Get Plenty Every Day.** Available at: http://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/vegetables-full-story/index.html#cvd. Accessed on July 15, 2008.
21.• Nothlings U, Schulze MB, Weikert C, et al.: **Intake of vegetables, legumes, and fruit, and risk for all-cause, cardiovascular, and cancer mortality in a European diabetic population.** *J Nutr* 2008, **138:**775–781.
A systematic review of plant-based diets and all causes of mortality in diabetes.
22.• Shimazu T, Kuriyama S, Hozawa A, et al.: **Dietary patterns and cardiovascular disease mortality in Japan: a prospective cohort study.** *Int J Epidemiol* 2007, **36:**600–609.
A review of lifestyle and CVD in a Japanese population.
23.• Harriss RL, English RD, Powles J, et al.: **Dietary patterns and cardiovascular mortality in the Melbourne Collaborative Cohort Study.** *Am J Clin Nutr* 2007, **86:**221–229.
An Australian survey of dietary pattern and CVD.
24.• Griel AE, Kris-Etherton PM: **Tree nuts and the lipid profile: a review of clinical studies.** *Br J Nutr* 2006, **96(Suppl 2):** S68–S78.
Impact of nuts on lipid profiles in a human clinical study.
25.• Tamizifar B, Rismankarzadeh M, Vosoughi A: **A low-dose almond-based diet decreases LDL-C while preserving HDL-C.** *Arch Iran Med* 2005, **8:**45–51.
Amount of nut consumption and its influence on blood lipid profile.
26.• Zibaeenezhad MJ, Shamsnia SJ, Khorasani M: **Walnut consumption in hyperlipidemic patients.** *Angiology* 2005, **56:**581–583.
Effect of walnut consumption on blood lipid profile in hyperlipidemic patients.
27. Fang JG, Lu M, Chen ZH: **Antioxidant effects of resveratrol and its analogues against the free-radical-induced peroxidation of linoleic acid in micelles.** *Chemistry* 2002, **8:**4191–4198.
28.• Shanmuganayagam D, Warner TF, Krueger CG, et al.: **Concord grape juice attenuates platelet aggregation, serum cholesterol and development of atheroma in hypercholesterolemic rabbits.** *Atherosclerosis* 2007, **190:**135–142.
Relationship between grape juice consumption and the improvement in blood lipids and biomarkers of CVD.
29.• Lei YP, Chen HW, Sheen LY, Lii CK: **Diallyl disulfide and diallyl trisulfide suppress oxidized LDL-induced vascular cell adhesion molecule and E-selectin expression through protein kinase A- and B-dependent signaling pathways.** *J Nutr* 2008, **138:**996–1003.
Effect of garlic oil and its constituents, ex vivo, on biomarkers of cardiovascular risks.
30.• Goel A, Kunnumakkara AB, Aggarwal BB: **Curcumin as "curecuminz": from kitchen to clinic.** *Biochem Pharmacol* 2008, **75:**787–809.
Health benefits of curcumin as a dietary cardioprotective agent.
31.• Raman P, DeWitt DL, Nair MG: **Lipid peroxidation and cyclooxygenase enzyme inhibitory activities of acidic aqueous extracts of some dietary supplements.** *Phytother Res* 2008, **22:**204–212.
Extraction and ex vivo determination of some ingredients in dietary supplements.
32.• Singh DK, Porter TD: **Inhibition of sterol 4 alpha-methyl oxidase is the principal mechanism by which garlic decreases cholesterol synthesis.** *J Nutr* 2006, **136:**759S–764S.
Mechanism of action of garlic and/or its constituents on the production of endogenous cholesterol.
33. Quilez J, Garcila-Lorda P, Salas-Salvado J: **Potential uses and benefits of phytosterols in diet: present situation and future directions.** *Clin Nutr* 2003, **22:**343–351.
34.• Van Horn L, McCoin M, Kris-Etherton PM, et al.: **The evidence for dietary prevention and treatment of cardiovascular disease.** *J Am Diet Assoc* 2008, **108:**287–331.
Cumulative review of many food items in the prevention and treatment of cardiovascular disease.
35.• Lunn J, Buttriss J: **Carbohydrates and dietary fibre.** *Nutr Bull* 2007, **32:**21–64.
Definition, types of carbohydrates, and information on dietary fibers.
36. Russo P, Tedesco I, Russo M, et al.: **Effects of de-alcoholated red wine and its phenolic fractions on platelet aggregation.** *Nutr Metab Cardiovas Dis* 2001, **11:**25–29.
37.• Lin J, Rexrode KM, Hu F, et al.: **Dietary intakes of flavonols and flavones and coronary heart disease in US women.** *Am J Epidemiol* 2007, **165:**1305–1313.
Amount and types of flavones and flavonols and their relationship to heart disease in US patients.
38. Cooper DA: **Carotenoids in health and disease: recent scientific evaluations, research recommendations and the consumer.** *J Nutr* 2004, **134:**221S–224S.
39.• Segura R, Javierre C, Lizarraga MA, Ros E: **Other relevant components of nuts: phytosterols, folate and minerals.** *Br J Nutr* 2006, **96(Suppl 2):**S36–S44.
The importance of regular nut consumption and the nature of the cardioprotective ingredients of nuts.
40. Khaw KT, Bingham S, Welch A, et al.: **Relation between plasma ascorbic acid and mortality in men and women in EPIC-Norfolk prospective study: a prospective population study. European Prospective Investigation into Cancer and Nutrition.** *Lancet* 2001, **357:**657–663.
41. Hercberg S, Preziosi P, Galan P, et al.: "The SU.VI.MAX Study": **a primary prevention trial using nutritional doses of antioxidant vitamins and minerals in cardiovascular diseases and cancers. SUpplementation on VItamines et Mineraux AntioXydants.** *Food Chem Toxicol* 1999, **37:**925–930.
42.• Griel AE, Cao Y, Bagshaw DD, et al.: **A macadamia nut-rich diet reduces total and LDL-cholesterol in mildly hypercholesterolemic men and women.** *J Nutr* 2008, **138:**761–767.
The ability of a diet rich in macadamia nuts to improve lipid blood profiles.
43.• Takachi R, Inoue M, Ishihara J, et al.: **Fruit and vegetable intake and risk of total cancer and cardiovascular disease.** *Am J Epidemiol* 2008, **167:**59–70.
Provides evidence for the protective role of fruits and vegetables against cancer and CVD.
44.• Cai H, Shu XO, Gao Y, et al.: **A prospective study of dietary patterns and mortality in chinese women.** *Epidemiology* 2007, **18:**393–401.
Dietary pattern and amount of cardiovascular disease in China.
45. Hung H, Joshipura K, Jiang R, et al.: **Fruit and vegetable intake and risk of major chronic disease.** *J Natl Cancer Inst* 2004, **96:**1577–1584.
46.• Welty FK, Lee KS, Lew NS, Zhou JR: **Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women.** *Arch Intern Med* 2007, **167:**1060–1067.
Health benefits of soy and its products on cardiovascular disease in postmenopausal women.
47.• Chen S, Chen J, Yang C, et al.: **Effect of soya protein on serum lipid profile and lipoprotein concentrations in patients undergoing hypercholesterolaemic haemodialysis.** *Br J Nutr* 2006, **95:**366–371.
Effects of soy protein on blood lipids in hemodialysis patients.
48.• Ahuja KD, Ball MJ: **Effects of daily ingestion of chilli on serum lipoprotein oxidation in adult men and women.** *Br J Nutr* 2006, **96:**239–242.
The effect of regular consumption of chilli on blood lipids.
49. McKevith B: **Nutritional aspects of cereals.** *Nutr Bull* 2004, **29:**111–142.
50. Martinez-Tome M, Murcia MA, Frega N, et al.: **Evaluation of antioxidant capacity of cereal brans.** *J Agric Food Chem* 2004, **52:**4690–4699.