

## Cardiovascular Friendly Natural Foods and Supplements - A Brief Review: Part I

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### ABSTRACT

Cardiovascular disease is the leading cause of death globally. Epidemiological studies demonstrate that populations consuming a large proportion of plant-based foods, especially fruits and vegetables, are known to have a lower incidence of cardiovascular diseases. These cardio-protective effects result primarily from the lipid lowering effects, antioxidant actions, and decreased homocysteine levels of these foods. Many of these naturally occurring functional foods also exhibit beneficial anti-inflammatory effect. These healthy diets are usually associated with lower intakes of saturated fats and calories, contributing to the heart healthy low body weights, low blood pressure, and low blood cholesterol concentrations seen in these populations. This brief review looks at heart healthy foods with evidence based data supporting their functional significance.

### 1. INTRODUCTION

Cardiovascular diseases are the main cause of death worldwide. Data from experimental, epidemiological and clinical studies provide compelling evidence that several natural products have protective and therapeutic activity against cardiovascular diseases. These cardio-friendly effects are exerted through intriguing complex substances, which include flavonoids, resveratrol, lycopene, omega 3 fatty acids, procyanidins and many others. The mechanisms include anti-inflammatory, anti-oxidative, vaso-protective (decreased TNF $\alpha$  production), reduced platelet reactivity and reducing thrombosis, promoting normal endothelial function, blocking expression of cellular adhesion molecules and reduction in blood pressure and lipids. Many of these natural substances however do not provide the same cardio-protective effect when taken as a single purified compound. On the contrary, several large and well structured evidence based studies have shown that some supplementation may even be harmful. Healthy food choices therefore play an important role in ingesting these agents in their cardio-protective form. Nutritional lifestyle changes

incorporating heart healthy natural foods can greatly help stem the scourge of cardiovascular morbidity and mortality sweeping throughout the world. Studies also show that prudent dietary ingestion of these products help promote general health, and delay or attenuate several other disease processes. This brief review looks at sixteen heart healthy foods with scientifically documented beneficial effects. The first part looks at eight of these natural foods.

## 2. METHODS

A review of all citations on PubMed regarding each food item and cardiovascular disease was done. The results were as follows: cocoa - 107 entries dating back to 1986, coffee -951 entries dating back to 1949, fish oil - 3729 citations dating back to 1946. Flaxseed - 20 entries dating back to 1993, fruits and vegetables - 3395 entries dating back to 1947, garlic - 413 entries dating back to 1955, ginger - 51 entries dating back to 1991 and grapes - 253 listings dating back to 1966. Other pertinent scientific articles and studies with evidence based data were also reviewed.

## 3. DISCUSSION

Natural foods are derived from nature. They are minimally processed and do not contain manufactured ingredients. Evidence based medicine has confirmed the health benefits of the following products, in the prevention, management and treatment of cardiovascular diseases.

### 3.1. Cocoa

#### 3.1.1. Clinical Studies

A growing number of epidemiologic studies have shown a link between the ingestion of cocoa and chocolate and cardiovascular health benefits. Cocoa consumption was associated with a decrease in blood pressure and overall cardiovascular mortality in the Zutphen Elderly Study (Buijsse et al. 2006). 100 grams of Dark Chocolate intake daily: 5.1 mm Hg reduction of systolic pressure, 1.8 mm Hg reduction of diastolic pressure = 21% reduction in the risk of heart disease (Oscar et al. 2004). A major reduction in myocardial infarction was seen in people who ate more than three portions of chocolate per day when compared with the population that consumed less than one (Gallus et al. 2009). Patients with class II heart failure, primarily with ejection fractions less than 50%, show forearm vasodilatation after eating chocolate – a therapeutically benefit effect in these patients (Flammer et al. 2012).

#### 3.1.2. Mechanisms of action

Cocoa related cardio-protective effects include: Improved vasodilatation, decrease in LDL, increase bioavailability of nitric oxide, anti-oxidant effects, anti-inflammatory actions, decreased platelet reactivity, decrease in insulin resistance, reduced CRP levels and release of endogenous endorphins (Mehrinfar et al. 2008, Keen et al. 2005).

#### 3.1.3. Clinical Implications

Evidence based data provides compelling evidence that cocoa supplementation is associated with cardiovascular protection. Consumption of about 100 grams of dark chocolate a day should be part of a healthy diet.

### 3.2. Coffee

#### 3.2.1. Clinical Studies

The results of several epidemiological studies are suggestive for the existence of a U-shaped relationship between coffee consumption and both cardiovascular events and mortality (Montagnana et al. 2012). In a large sample of Swedish women followed for almost 10 years, there was a 22% to 25% risk reduction in stroke (Larsson et al. 2011). Moderate coffee intake was associated with a lower risk for coronary heart disease in a population followed for 10 years (Wu et al. 2009). There are also protective actions of imbibing an average of 2 cups of filtered coffee a day against heart failure (Mostofsky et al. 2012). In the Iowa Women's Health Study there was a 24% reduction in cardiovascular disease (3-4 cups/day) (Andersen et al. 2006). Health Professionals Follow-up Study and Nurses' Health Study revealed a decrease in diabetes mellitus by 30% (4-6 cups/day) (ADA, 2003).

#### 3.2.2. Mechanism of actions

Epidemiological studies suggest that consumption of boiled coffee has two diterpenes namely cafestol and kahweol which may be associated with an elevated risk for cardiovascular disease. However, filtered coffee removes these harmful compounds and is rich in chlorogenic acids and polyphenols. Chlorogenic acids are effective in decreasing blood pressure, systemic inflammation, risk of type 2 diabetes mellitus, and platelet aggregation. Phytochemicals such as flavan-3-ols (monomers and procyanidins), hydroxycinnamic acids, flavonols and anthocyanidins in the filtered coffee are associated with an increased flow mediated vascular dilatation through positive effects on the endothelial function, an improvement in glucose metabolism, an increased reverse cholesterol transport and

inhibition of foam cell formation, an inhibition of oxidative stress, immune-modulation and beneficial cardiovascular effects on platelet function.

### 3.2.3. Clinical Implications

Evidence based data provides compelling evidence that ingestion of 2-4 cups of filtered coffee daily is associated with cardiovascular protection. A growing body of research also shows that coffee drinkers, compared to nondrinkers, may be less likely to develop obesity, depression, death from any cause, and neuro-degenerative diseases, such as Parkinson's and Alzheimer's diseases. It also appears to be beneficial in patients with liver diseases.

## 3.3. Fish Oil

### 3.3.1. Clinical Evidence

Epidemiological studies have shown that men who eat fish have a lower coronary artery mortality rate compared to those who eat none. The 36 country ecological study by Zhang and associates in 1999 showed that fish consumption was associated with a reduced risk from all-cause, ischemic heart disease and stroke mortality (Zhang et al. 1999). The Nurses' Health Study reported in JAMA in 2002 established an inverse association between fish intake and omega-3 fatty acids and CHD death (Hu et al. 2002). Rizos and colleagues showed a 4% reduction in all cause mortality, a 9% reduction in cardiac death, a 13% reduction in sudden death and an 11% reduction in myocardial infarction with fish derived omega 3 supplementation (Rizos et al. 2012). Increases in cardiac ejection fraction have been observed in heart failure patients taking omega-3 PUFAs (Penny et al. 2002).

### 3.3.2. Mechanism of actions

Omega-3 polyunsaturated fatty acids (PUFAs) are primarily found in sea food. They have a number of beneficial cardiovascular actions. Mozaffarian and Wu (Mozaffarian et al. 2011) reported several positive cardiovascular actions of fish oil consumption, including lowering of blood pressure, serum triglycerides, inflammatory markers and coagulability. There is also a reduction of heart rate, an increase in heart rate variability, an enhancement of insulin sensitivity, an improvement of endothelial function, an anti-arrhythmic effect and plaque-stabilizing effects. These actions improve cardiovascular health and reduce the risk of clinical events.

### 3.3.3. Clinical Implications

Evidence based data provides compelling evidence that consuming two or more servings of fatty fish per week or fish oil supplements (patients with known CHD should consume about 800–1000 mg/d of combined EPA/DHA, and individuals with no known disease should consume at least 500 mg/d.) significantly reduces cardiac and all-cause mortality.

## 3.4. Flaxseed

### 3.4.1. Clinical Data

In vitro studies show a slowing of the progression of atherosclerosis and an associated lowering of serum triglycerides (Rodriguez-Leyva et al. 2010; Bloedon et al. 2010). Flaxseed oil ingestion in animals suppresses oxygen radical production by white blood cells, prolongs bleeding time and reduces inflammation. Human studies have shown that flaxseed can modestly lower serum total cholesterol, reduce low-density lipoprotein cholesterol levels, improve postprandial dysglycemia and decrease some mediators of inflammation (Bloedon et al. 2008; Prasad et al. 2009; Pan et al. 2007). Other potential benefits include improvement the symptoms of dry eye in people with Sjogren's syndrome and help prevent the growth of breast tumors.

### 3.4.2. Mechanism of action

Flax seed is a rich source of plant-based omega-3 fatty acid, alpha-linolenic acid (ALA). Flaxseed contains 35% of its mass as oil, of which 55% is alpha-linolenic acid. Flaxseed is also rich in phytoestrogens as well as soluble fiber. The major component, a lignan called secoisolariciresinol diglucoside (SDG), is the main precursor of enterodiols and enterolactone, the active phyto-estrogens in humans. Both fiber and ligands help reduce cholesterol and help glycemic control. Ligands may also have anti-oxidant effects. These actions are overall cardio-protective. However, the antiplatelet, antioxidant, and hypotensive effects noted with fish oils which are rich in EPA and DHA are not seen with flax seed consumption. Conversion of ALA into EPA and DHA is minimal in the human body. Clinical studies have also failed to attribute reduction of cardiovascular morbidity and mortality to flax seed consumption. Flaxseeds are also a good source of manganese, folate, vitamin B6, as well as the minerals magnesium, phosphorus, and copper.

### 3.4.3. Clinical Implications

Flaxseed and its components should improve cardiovascular health because of their numerous cardiovascular beneficial attributes. Flaxseed oil can be taken as 1 - 2 tablespoonfuls daily or 1 - 2 capsules daily. However, published human data provides little evidence that flax seed supplementation as a food choice is associated with clinically relevant cardiovascular protection. More human studies are needed to objectively validate the cardiovascular benefits of flax seeds.

## 3.5. Fruits and Vegetables

### 3.5.1. Clinical Studies

Epidemiological and scientific evidence suggests a higher consumption of vegetables confers a protective effect against the risk of cardiovascular disease (Yusuf et al. 2004). In the Dietary Approaches to Stop Hypertension (DASH) study, researchers found that people with high blood pressure who followed this diet that was rich in fruits, vegetables, and low-fat dairy products and that restricted the amount of saturated and total fat reduced their systolic blood pressure by about 11 mm Hg and their diastolic blood by almost 6 mm Hg (Appel et al. 1997). A recent meta-analysis report of the results of 61 prospective studies conducted on more than 1 million hypertensive subjects demonstrated that throughout middle and old age, even small reductions in BP were clinically significant. A reduction of 10 mm Hg in SBP resulted in a 40% reduction in overall and vascular mortality. A 2 mm Hg reduction in SBP resulted in a 10% reduction in 5-year stroke and cardiovascular mortality (Lewington et al. 2002). In the National Heart, Lung, and Blood Institute's Family Heart Study: 4466 subjects consumed on average a shade over 3 servings of fruits and vegetables a day. Men and women with the highest daily consumption (more than 4 servings a day) had significantly lower levels of LDL cholesterol than those with lower consumption (Djousse, 2004). The Nurses' Health Study and Health Professionals 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 cardiovascular disease was noted in these patients. Compared with those in the lowest category of fruit and vegetable intake (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 (Hung et al. 2004). A meta-analysis of 9 studies showed a 26% reduction in cardiovascular mortality in people with the highest vegetable consumption. Another meta-analysis of several studies revealed a 26% reduction in stroke in a population consuming more than 5 servings of fruits and vegetables per day compared to those consuming less than 3 servings per day (Dauchet et al. 2006; Vasanthi et al. 2012). A recent study further established the role of certain berries in cardioprotection. A diet rich in anthocyanins, abundant in blueberries and strawberries, is associated with a 32% drop in the risk of incident MI in a cohort of >93 000 women from the Nurses' Health Study 2 (Cassidy et al. 2013). The anthocyanins are a class of flavonoids with evidence based heart-friendly antioxidant and anti-inflammatory effects.

### 3.5.2. Mechanisms

The beneficial effects are due to a diverse range of phyto-chemicals present in vegetables (8) and fruits such as polyphenols, flavonoids, steroidal saponins, organosulphur compounds, vitamins and fiber. These phyto-chemicals exert the following cardio-protective effects – anti-oxidative, hypo-lipidemic, anti-angiogenic, anti-ischemic, inhibition of platelet aggregation and anti inflammatory actions.

### 3.5.3. Clinical Implications

Only 6% of US Adults eat enough vegetables and just 8% eat enough fruit every day. Epidemiological and experimental data provides compelling evidence that incorporating 5 or more servings of fruits and vegetables in our daily diet is cardio-protective.

## 3.6. Garlic

### 3.6.1. Clinical Data

Garlic (*Allium sativum*) has multiple cardiovascular protective properties and several studies have suggested that it may combat some of the factors responsible for atherosclerosis (Rahman et al. 2001). In vitro studies have shown that cardio-protective effects of garlic ingestion include cholesterol and lipid-lowering effects, antithrombotic and anti-platelet aggregatory effects, blood coagulation, fibrinolysis and circulatory effects, blood pressure and vascular tone effects and positive modulation of endogenous antioxidant defenses (Rahman et al. 2006). In vivo studies in humans have shown that cardio-protection by garlic ingestion is related to cholesterol-lowering effects, inhibition of platelet aggregation and lowering of blood pressure (Banerjee et al. 2002). Other cardio-protective effects include a decrease in unstable angina, an improvement in arterial vasodilatation, and a decrease in peripheral vascular disease (Li et al. 2000). There is also an inhibition of the progression of coronary calcification in some patients receiving associated statin therapy.

### 3.6.2. Mechanism of actions

Animal and human studies with garlic have demonstrated multiple beneficial cardiovascular effects by the following mechanisms an inhibition of platelet aggregation, enhancement of fibrinolytic activity, reduction in cholesterol and triglyceride synthesis, protection of the elastic properties of the aorta.(Lawson, 1996) It exerts antiplatelet activity by reducing thromboxane production, oxidative stress reduction, prevention of lipid peroxidation of LDL and inhibition of the angiotension-converting enzyme (Dhawan et al. 2004).

### 3.6.3. Clinical Implications

Evidence based data provides suggestive evidence that increased use of garlic in diet and enteric coated dried garlic supplementation is associated with cardiovascular protection. Larger clinical studies with standardized preparations are needed to conclusively demonstrate a reduction in cardiovascular morbidity and mortality with this natural bulb belonging to the Alliaceae family. Garlic may be taken as follows: 2 to 5 g of fresh raw garlic; 0.4 to 1.2 g of dried garlic powder; 2 to 5 mg garlic oil; or 300 to 1,000 mg of garlic extract daily.

## 3.7. Ginger

### 3.7.1. Clinical Studies

Thompson and associated reported in the Prostaglandins Leukot Essent Fatty Acids that ginger could be used as a cholesterol-lowering, antithrombotic and anti-inflammatory agent (Thomson et al. 2002). (1) Fugh-Berman in the Preventive Cardiology presented data confirming the in vitro blood pressure lowering effects of ginger. They attributed this to ginger related blockade of voltage-dependent calcium channels; (2) The antioxidant properties of gingerol related compounds from ginger were reported by Masuda Y, Kikuzaki and associates in Biofactors; (3) The antiplatelet activity of ginger was documented by Nicoll and Henein in the International Journal of Cardiology; (4) However, clinical studies documenting similar results in humans and a resultant decrease in cardiovascular morbidity and mortality are lacking.

### 3.7.2. Mechanism of actions

Ginger is the underground stem, or rhizome, of the plant *Zingiber officinale* Roscoe. It has been used as a herbal medicine in Asian, Indian, Chinese and Arabic traditions since ancient times. Several in vitro studies have documented many cardio-protective benefits of ginger use. These include its actions as hypo-lipidemic, anti-thrombotic, anti-inflammatory, hypotensive, anti-oxidative and exhibiting anti-platelet effects. These are all potentially cardio-protective in humans and suggest an anti-atherogenic effect which should reduce coronary artery disease and strokes.

### 3.7.3. Clinical Implications

Evidence based in vitro data is suggestive of a cardiovascular protective role of ginger. However this data is essentially scant with most studies done in animals and with small doses of the root. Standardized human trials with larger doses of ginger are needed. The effective dose may be 5 gm or more daily. At this time, there is inconclusive evidence that ginger supplementation in humans is associated with cardiovascular protection.

## 3.8. Grapes

### 3.8.1. Clinical Studies

Epidemiological studies suggest that consumption of wine, grapes and grape products, and other foods containing polyphenols is associated with decreased risk for cardiovascular disease (Dohadwala et al. 2009). In animal and human studies, grape products have been shown to produce a reduction in cardiovascular risk factors (Perez-Jimenez et al. 2008). In a study of 34,489 postmenopausal American women, foods containing flavanones and anthocyanidins, lowered cardiovascular and all-cause mortality (Pamela et al. 2007). A meta-analysis revealed that grape seed extract significantly lowered systolic blood pressure and heart rate in humans (Feringa et al. 2011). Average intake of antioxidant flavanoids was inversely associated with mortality from coronary heart disease (Hertog et al. 1995). Consumption of grape and grape extracts and/or grape products such as red wine are beneficial in preventing the development of cardiovascular disease (Leifert et al. 2008).

### 3.8.2. Mechanisms

The cardio-protective actions of grapes and grape products are primarily based on their rich content of polyphenols which include resveratrol, phenolic acids, anthocyanins, and flavonoids. These polyphenols possess potent antioxidant properties and provide clinically significant anti-atherosclerotic, anti-arrhythmic, and vaso-relaxation actions. They also exhibit anti-inflammatory effects. In animals, grape polyphenols also have an anti-hyperglycemic effect and improve insulin sensitivity. They induce a reduction in systolic blood pressure and heart rate. They also

prevent oxidation of low density lipoprotein, decrease platelet aggregation and reduce inflammation. The highest concentrations of grape polyphenols are found in the skin, stems, and seeds and may be 10 fold higher in red grapes when compared to green grapes.

### 3.8.3. Clinical Implications

Evidence based data provides compelling evidence that grape and grape product supplementation as a food choice is associated with cardiovascular protection. This can also be achieved by drinking 4 oz to 8 oz in men and 4 oz of red wine per day in women.

## 4. CONCLUSION

The 5000 year old Indian science of Ayurveda, stresses the preventive and therapeutic benefits of natural foods, herbs and spices. The medicinal use of natural foods has also been explored by the Chinese, Egyptians and the Sumerians. Hippocrates the father of Western medicine said, “*Let food be thy medicine*”. Modern medicine is recognizing that several natural foods and supplements have biologically active compounds that confer additional health benefits, besides having a nutritional value. Incorporation of these natural products in our daily diet can significantly help prevent, manage and treat cardiovascular diseases.

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