

Tea and Cholesterol Lowering

Elevated serum cholesterol is a well established CVD risk factor. Tea consumption has been associated with improved lipid profile.

There are a few studies that suggest that high levels of tea flavonoids may reduce serum cholesterol levels whilst other studies show little or no effect on serum lipid profile. Two well controlled clinical studies have shown some impressive cholesterol lowering benefits of tea and tea flavonoids. Davies and colleagues investigated the effect of black tea consumption on 15 mildly hyperlipidaemic men and women; baseline total and LDL-cholesterol 5.4mmol/L (208.9mg/dL) and 3.49mmol/L (135mg/dL) respectively. The study was randomised, placebo controlled, blinded and cross over. Each subject had a run in period of 2 weeks before being randomised to their first treatment; National Cholesterol Education Program (NCEP) step I diet plus 5 servings of tea a day (approx. 722mg flavonoids and 40mg Caffeine) or NCEP I plus placebo (no caffeine or flavonoids) or NCEP I plus Caffeine Placebo (46mg caffeine). Each treatment was followed by a 4 week wash-out period. All meals and drinks were prepared and supplied by the research institution. Comparing the tea group to the placebo with caffeine group, total and LDL-cholesterol were significantly reduced by 6.5% (p=0.0007) and 11.1% (p=0.0002) respectively.

Maron and colleagues investigated the effect of a theaflavin enriched green tea extract on serum profiles in a randomised, double blinded, placebo controlled parallel study. 220 mildly to moderately hyperlipidaemic men and women (LDL-C 3.4-4.9mmol/L [130mg – 190mg/dL]) were randomised to receive a theaflavin enriched green tea extract capsule or a placebo. Subjects followed a low saturated fat diet and were instructed to consume one capsule per day at breakfast time (each treatment capsule contained 375mg tea flavonoids). Food records were kept throughout the 12 week treatment period. Total and LDL-cholesterol in the treatment group significantly fell in 12 weeks by 11.3% (p<0.01) and 16.4% (p<0.01) respectively. Total to HDL-cholesterol ratio also fell by 12.1% (p<0.001).

Tea and Inhibition of Platelet Aggregation

Another proposed mechanism for tea's heart health benefits is the inhibition of platelet aggregation. However studies are few and more research is needed. One study by Hodgson and colleagues found that consumption of 5 cups of black tea per day (1.25L and 1,463mg flavonoids) for 4-weeks, significantly reduced P-selectin by 15% compared to placebo. P-selectin is a cell adhesion molecule and was correlated with collagen-stimulated platelet aggregation.

The scientific evidence to date, demonstrates an inverse association between tea consumption and CVD. However, the exact mechanism and dosage has yet to be identified. Tea is an exceptional beverage – virtually calorie free, fat free and is a rich source of dietary flavonoids. It is only second to water as the most popular beverage in the world.

References

- 1) Menotti A, Kromhout D, Blackburn H, Fidanza F, Buzina R, Nissinen A. Food intake patterns and 25-year mortality from coronary heart disease: cross-cultural correlations in the Seven Countries Study. The Seven Countries Study Research Group. Eur J Epidemiol 1999;15:507-15.
- 2) Peters U, Poole C, Arab L. Does tea affect cardiovascular disease? A meta-analysis. American Journal Of Epidemiology 2001;154:495-503.
- 3) Huxley RR & Neil HA. The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies. Eur J Clin Nutr 2003;57:904-8.
- 4) Duffy SJ et al. Short- and Long-Term Black Tea Consumption Reverses Endothelial Dysfunction in Patients with Coronary Artery Disease. Circulation 2001;104:151-156.
- 5) Hodgson JM et al. Regular ingestion of black tea improves branchial artery vasodilator function. Clinical Science 2002;102:195-201.
- 6) Hirata K, Shimada K, Watanabe H, Otsuka R, Tokai K, Yoshiyama M, Homma S, Yoshikawa J. Black tea increases coronary flow velocity reserve in healthy male subjects. Am J Cardiol 2004;93:1384-1388.
- 7) Hodgson JM et al. Acute effects of tea on fasting and postprandial vascular function and blood pressure in humans. J Hypertens 2005; 23:47-54.
- 8) Davies MJ, Judd JT, Baer DJ, Clevidence BA, Paul DR, Edwards AJ, Wiseman SA, Muesing RA, Chen SC. Black tea consumption reduces total and LDL cholesterol in mildly hypercholesterolemic adults. J Nutr 2003;133:3298S-3302S.
- 9) Maron DJ, Lu GP, Cai NS, Wu ZG, Li YH, Chen H, Zhu JQ, Jin XJ, Wouters BC, Zhao J. Cholesterol-lowering effect of a theaflavin-enriched green tea extract: a randomized controlled trial. Arch Intern Med 2003;163:1448-1453.
- 10) Hodgson, J.M., Puddey, I.B., Mori, T.A., et al. Effects of regular ingestion of black tea on haemostasis and cell adhesion molecules in humans. Eur J Clin Nutr 2001;55:881-886.

Produced September 2005 by
Beverages Health and Vitality Team, Lipton, Unilever
tea.vitality@unilever.com
Correct at the time of going to press



Tea and Vitality

Facts

Tea and Heart Health

Overall, epidemiological studies support an inverse association between regular consumption of tea and other dietary flavonoids and risk of cardiovascular disease. As tea is the second most widely consumed beverage after water, a positive impact on cardiovascular health will have global significance.

Epidemiological Evidence

Cardiovascular disease is recognised as a multifactorial disease. Established risk factors include high blood pressure, smoking, high blood cholesterol, diabetes, obesity, and family history. The majority of all cardiovascular disease (CVD) deaths are caused by coronary heart disease and cerebrovascular disease. Statistical analyses from The Seven Countries Study¹ revealed non-nutritive antioxidant polyphenols (such as catechins and quercetin) as one of the major determinants of coronary heart disease.

A combination of regular exercising, avoidance of heavy alcohol consumption, cessation of smoking and a healthy low fat diet containing plenty of fresh fruit, vegetables, wholegrains and oily fish is well recognised by health professionals world wide as beneficial to heart health. Recently, the addition of plant sterols and stanols, nuts and soya protein have also been encouraged for better heart health.

Adding tea to the diet (black or green served without sugar and without milk or with low fat milk) may offer further benefits. Two meta-analyses have been undertaken to review the evidence for teas association with heart health^{2,3}.

Peters and colleagues investigated the impact of tea consumption on CVD based on all published epidemiological studies from 1966-2000². As all studies reported different levels of tea consumption in relation to CVD, Peters weighted all studies for the risk of three cups (711ml) of tea per day by using inverse variance-weighted categorical regression. The 10 cohort (follow up periods 4 – 15 years) and 7 case control studies included in the analysis investigated the effect of flavonols, flavones and/or tea consumption on CVD, including strokes (6), CHD (7) and MI (7). The studies were performed in Australia, UK, US, Wales, Italy, Finland and Netherlands. 13 out of the 17 studies demonstrated a 1-75% reduction in CVD for every three cups of tea consumed per day. Four studies demonstrated a positive association. **The overall conclusion was that consumption of three cups of tea per day lead to a significant 11% reduction in Myocardial Infarction risk.** The authors do stress caution in their results as they found evidence for a large publication bias and geographic heterogeneity. Stronger inverse associations between CVD and tea consumption were found in Continental European studies compared to the US studies. Another note of caution is the epidemiological data often used food frequency questionnaires not designed for tea or detailed flavonoid dietary assessment and little account was taken of other lifestyle factors such as exercise.

A more recent meta-analysis investigated the findings of 7 epidemiological studies looking at the correlations between flavonols, flavones and CHD deaths³. Comparisons were made between the top and bottom third intakes of flavonols (2mg vs >34mg flavonols) and risk of CHD deaths. 6 out of the 7 studies demonstrated an association between high flavonol intakes (of which tea was the main source) and a 20% reduced risk of CHD death. 34mg flavonols correlates to approximately 2 cups of tea per day.

The meta-analyses are impressive despite some shortfalls and emphasise the importance for more large well designed studies to specifically investigate tea and CVD outcomes and mechanisms.

Two meta-analyses demonstrate an inverse association between tea and heart health.
Three cups of tea per day may reduce risk of MI by 11%.

Limitations of epidemiological data:

- Tea was not the primary food investigated.
- Food frequency questionnaires are not sensitive or specific enough for tea flavonoid data collection.
- The true quality of the overall diets could not be compared between low and high tea consuming groups.
- Tea consumption habits are often not investigated i.e. the addition of milk and sugar, which may have an impact on overall energy, fat and simple carbohydrate consumption and may explain the different effects seen by the studies.
- Lifestyle and socio-economics may influence outcomes. Tea consumption has been associated with other lifestyle habits such as smoking, exercise and quality of overall diet.
- Flavonoid levels in tea brews will vary significantly depending on brewing time, agitation, size of tea leaf and quality of tea leaf. This makes it difficult to extrapolate exact tea flavonoid intakes.
- Tea is rich in flavanols (catechins, thearubigins), however, many studies collected data for flavonols which are minor components of tea.
- Most studies have investigated black tea and not green tea consumption.
- Different studies used different CVD outcomes.
- Tea flavonoid mechanism for heart health benefits are yet to be determined.

Mechanism of Action

Although the exact mechanism by which tea improves CVD has yet to be identified, a number of avenues have been investigated:

- Improved endothelial function
- Cholesterol Lowering
- Inhibition of platelet aggregation

Improved Endothelial Function

Normal endothelial function regulates vasomotor tone, platelet activity, leukocyte adhesion and vascular smooth muscle cell proliferation via a release of several paracrine factors including nitric oxide. Endothelial dysfunction is associated with the development and progression of atherosclerosis and thrombogenesis and therefore with an increased risk of CVD.

One popular theory for the mechanism by which tea may improve endothelial function relates to the antioxidant capacity of flavonoids and their function in reducing oxidative stress which may improve endothelial function. Experimental studies have demonstrated flavonoids to enhance the synthesis and release of endothelial derived nitric oxide.

Four published clinical trials to date have investigated the effect of tea on endothelial function⁴⁻⁸.

A randomised placebo controlled cross over study, investigated the effect of both long and short term black tea consumption on endothelial dysfunction in 50 patients with coronary artery disease (CAD)⁴. Endothelium-dependent flow mediated dilation (FMD) of the brachial artery measured by high-resolution

vascular ultrasound was used to assess endothelial function. Short term tea effects were studied 2 hours after ingestion of a 450ml black (leaf) tea infusion or 450mL hot water. Long-term effects were measured in a fasting state after a daily consumption of 900mL black tea or 900mL hot water for a four week period. The effect of acute on chronic tea consumption was also investigated by measuring FMD in the long-term group 2 hours after ingesting an additional 450mL of brewed tea. Flavonoid levels for the 450mL infusion were approx. 477mg, whilst for the 900mL powder tea brew, the flavonoid level was 873mg. Patients were allowed to consume the tea in their normal manner i.e. addition of sugar and or milk was permitted. Baseline dietary flavonoid intakes were also assessed using a food frequency questionnaire (FFQ) and patients were asked to abstain from red wine and tea (other than tea provided for the study). Baseline brachial artery FMD was similar in both the water and tea groups. Both short and long term tea consumption improved brachial artery FMD ($p < 0.001$) (figure 1). Compared to the water control group, short-term, long-term and acute on chronic tea consumption increased FMD by 65% (5.7 ± 3.9 vs 9.4 ± 3.9), 56% (6.1 ± 4.3 vs 9.5 ± 3.6) and 77% (6.1 ± 4.3 vs 10.8 ± 4.4) respectively ($p < 0.001$). The additional increase in FMD by an acute consumption of tea following four weeks of chronic consumption was also significant ($p = 0.02$). Caffeine consumption was not associated with a FMD increase, however, plasma catechin levels were.

Table 1. Summary of 4 clinical placebo controlled studies demonstrating a significant improvement in endothelial function after black tea consumption.

Study	n	Subjects	Acute / Chronic Tea Consumption	Tea	Measure for Endothelial Function	Flavonoids mg	% improvement	p value
Duffy, 2001	50	CAD	Acute	450mL BT	FMD	477	65	<0.001*
			Chronic - 4 wks	900mL BT per day		873	56	
			Acute+Chronic	900mL per day + 450mL BT		-	77	
Hodgson, 2002	21	Healthy	Chronic - 4 wks	1.25L BT per day	FMD	1,463	41	=0.01**
Hirata, 2004	10	Healthy	Acute	450mL BT	CVFR	762	16	<0.0001**
Hodgson, 2005	20	CAD	Acute	750mL BT	FMD	756	21	ns*
				750mL BT Plus Meal			37	

* = tea group vs control ** = tea group, baseline vs post treatment

Improved brachial artery FMD after black tea consumption was also demonstrated in 21 healthy men and women with mildly elevated total cholesterol and/or triglycerides⁵. Following a 4 week baseline period of subjects consuming 5 cups of 250mL hot water, individuals were randomised to receive either 5 250mL cups of black tea per day ($n=10$) or 5 250mL cups of hot water ($n=11$). Polyphenol and flavonoid levels of the tea infusion were not provided by the authors, however, based on the USDA flavonoid database, 1.25L of black tea should provide approx. 1,463mg flavonoids per day. Addition of sugar, milk or other additives to the beverage were not permitted. Subjects were asked to abstain from caffeine-containing beverages and not to make any changes to their diet, alcohol consumption or exercise habits. Brachial artery FMD was measured as discussed previously in a fasting state. Regular black tea consumption significantly increased FMD by 41% from baseline (7.2 ± 1.2 vs 5.1 ± 1.0 , $p=0.01$) and was significantly greater than the water control group ($p=0.008$).

Hirata and colleagues investigated the effect of black tea consumption on endothelial function in 10 young healthy males⁶. Endothelial function was measured by Coronary Flow Velocity Reserve (CFVR). CFVR is a useful index for coronary circulation and relates to endothelium-dependent and endothelium-independent vasodilatation. Subjects were randomised to receive 450mL black tea containing 762mg flavonoids and 120mg caffeine or 450mL placebo drink containing 120mg caffeine. After one week, subjects crossed over treatments. CVFR was measured at baseline (fasting) and 2 hours after treatment when plasma flavonoid levels peak. The study found significant group and treatment differences. Caffeine did not affect CVFR. CVFR significantly increased post tea consumption by 15.6% (4.5 ± 0.9 vs 5.2 ± 0.9 , $p < 0.001$). The group assigned to the tea treatment first had a significantly higher improvement in CVFR compared to the group randomised to the water treatment first (1.18 ± 0.07 vs 1.04 ± 0.08 , $p = 0.002$).

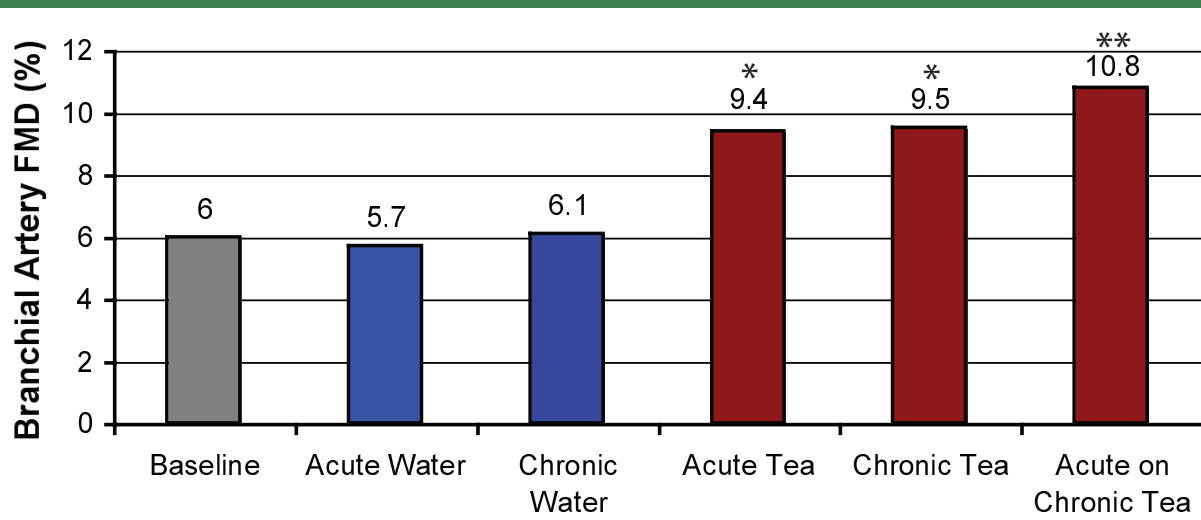
A more recent cross-over study investigated the effect of black tea consumption on fasting and post prandial brachial artery FMD and whether high fat meals attenuate tea benefits⁷. Following a four week run-in period, 20 CAD patients were randomised to receive a total of four treatments: water, tea, water plus meal, tea plus meal. Each treatment was one week apart. Tea consumption comprised of 3 250mL cups of brewed tea providing 900mg of total polyphenols (total flavonoids approx. 756mg). The meals were deliberately high in fat. Brachial artery FMD was measured as explained previously, 3-4 hours post treatment. High fat meals did not blunt acute tea effects on FMD. The only significant improvement was seen between the water only group and the tea plus meal group (4.3 vs 5.9 , $p=0.02$), a 37% improvement. The tea only group showed significant FMD improvements only after values were adjusted for plasma caffeine levels. However the previous three studies found no correlation between caffeine and endothelium-dependent FMD.

Three of four studies show a significant improvement (16% - 77%) in endothelial function after consumption of 2-5 cups of black tea.

The lower (16%) improvement seen by Hirata highlights the fact that FMD and endothelial dysfunction is inversely associated to both age and CVD, therefore, in young healthy males, even a small improvement would be deemed significant.

Excluding Hodgson 2005, the studies showed caffeine consumption from tea to have no effect on endothelial function and therefore, tea flavonoids most likely to be responsible for the improvement. The exact mechanism has not been determined, however, most authors support an antioxidant mechanism by which nitric oxide synthesis is increased and oxidative stress reduced. All the authors concur that the true physiological impact of long-term tea consumption (greater than 4 weeks) has yet to be determined and more long term clinical studies are needed.

Figure 1. Duffy et al 2001. Short and Long Term Black Tea Consumption Reverses Endothelial Dysfunction in Patients with Coronary Artery Disease.



Brachial artery flow-mediated dilation was higher after short and long term tea consumption versus baseline and water (* $p < 0.001$). Short-on-long-term tea ingestion resulted in additional improvement (** $p = 0.02$)

