Molecular Aspects of Medicine xxx (2010) xxx–xxx

Contents lists available at ScienceDirect

Molecular Aspects of Medicine

journal homepage: www.elsevier.com/locate/mam

Review

# Tea flavonoids and cardiovascular health

Jonathan M. Hodgson *, Kevin D. Croft

*School of Medicine and Pharmacology, University of Western Australia, Perth, Western Australia, Australia*

ARTICLE INFO

*Article history:*
Received 9 August 2010
Received in revised form 2 September 2010
Accepted 2 September 2010
Available online xxxx

*Keywords:*
Flavonoids
Tea
Vascular function
Cardiovascular disease

ABSTRACT

The two main types of tea are green and black. Both green and black teas are rich dietary sources of flavonoids. Available evidence suggests that regular tea consumption may reduce the risk of cardiovascular disease. The cardiovascular health benefits of drinking tea are thought to be largely due to flavonoids. Tea intake and intake of flavonoids found in tea have been associated with reduced risk of cardiovascular disease in cross-sectional and prospective population studies. Isolated flavonoids found in tea have also been consistently shown to inhibit the development of atherosclerosis in animal models. A number of possible pathways and mechanisms have been investigated. There is now consistent data indicating that tea and tea flavonoids can enhance nitric oxide status and improve endothelial function, which may be at least partly responsible for benefits on cardiovascular health. There is also evidence, although limited, to suggest benefits of green tea (flavonoids) on body weight and body fatness. Data supporting reduced oxidative damage, inflammation, platelet activation, blood pressure, and risk of type 2 diabetes with tea (flavonoids) remains inadequate to draw any conclusions.



**Contents**

1. Background . . . 00
2. The tea flavonoids . . . 00
3. Tea and cardiovascular disease: results of population studies . . . 00
4. Atherosclerosis: human and animal model studies . . . 00
5. Endothelial function . . . 00
6. Blood pressure . . . 00
7. Oxidative stress . . . 00
8. Cholesterol reduction . . . 00
9. Inflammation . . . 00
10. Platelet function . . . 00
11. Homocysteine . . . 00
12. Body weight, body composition and visceral fatness . . . 00
13. Type 2 diabetes . . . 00
14. Conclusions . . . 00
References . . . 00

* Corresponding author. Address: School of Medicine and Pharmacology, Royal Perth Hospital Unit, GPO Box X2213 Perth, Western Australia 6847, Australia. Tel.: +61 8 9224 0267; fax: +61 8 9224 0246.
*E-mail address:* Jonathan.Hodgson@uwa.edu.au (J.M. Hodgson).

0098-2997/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.mam.2010.09.004

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

## 1. Background

The worldwide consumption of tea is second only to water. Thus any health effects of drinking tea could have a significant impact on public health. Tea has been consumed as a beverage for well over 2000 years, and it is now commonly consumed in most regions of the world. Although tea has historically been thought to promote good health, research into the possible health benefits of tea is more recent.

The term 'tea' refers to the plant *Camellia sinensis*, its leaves, and infusions derived from them. Tea can be classified as green and black. Black teas are produced by promoting the enzymatic oxidation of tea flavonoids leading to formation of condensed flavonoids, such as theaflavins and thearubigins. Enzymes involved in polyphenol oxidation are inactivated to produce green tea. Worldwide most tea consumed is black tea. Green tea is more popular in China, Japan and other Asian countries, but its popularity is increasing in Western populations.

This chapter briefly discusses data from population studies, animal models of atherosclerosis and randomized controlled trials to have investigated effects on cardiovascular health-related endpoints. We must still rely on evidence derived from these studies because to date there have been no randomized controlled trials of primary or secondary prevention of cardiovascular disease (CVD) with tea or tea-derived flavonoids.

## 2. The tea flavonoids

Most phenolic compounds found in tea are polyphenols. Polyphenols are compounds consisting of more than one benzene ring with each containing at least one hydroxyl group (–OH). The main polyphenols present in tea are the flavonoids (Fig. 1). There are six major classes of flavonoids in the diet including flavonols, flavones, flavanols, flavanones, anthocyanins and isoflavones. The most common subclasses of flavonoids in tea are the flavanols (primarily catechins) and flavanols (such as quercetin) (Fig. 1). Also present in tea, but at significantly lower concentrations, are phenolic acids such as gallic acid and cinnamic acid esters of quinic acid.

Research interest in tea has been primarily due to the presence of flavonoids. Health benefits of tea are believed to be largely due to the consumption of these flavonoids. Both green and black teas are rich in flavonoids (Table 1). One cup of

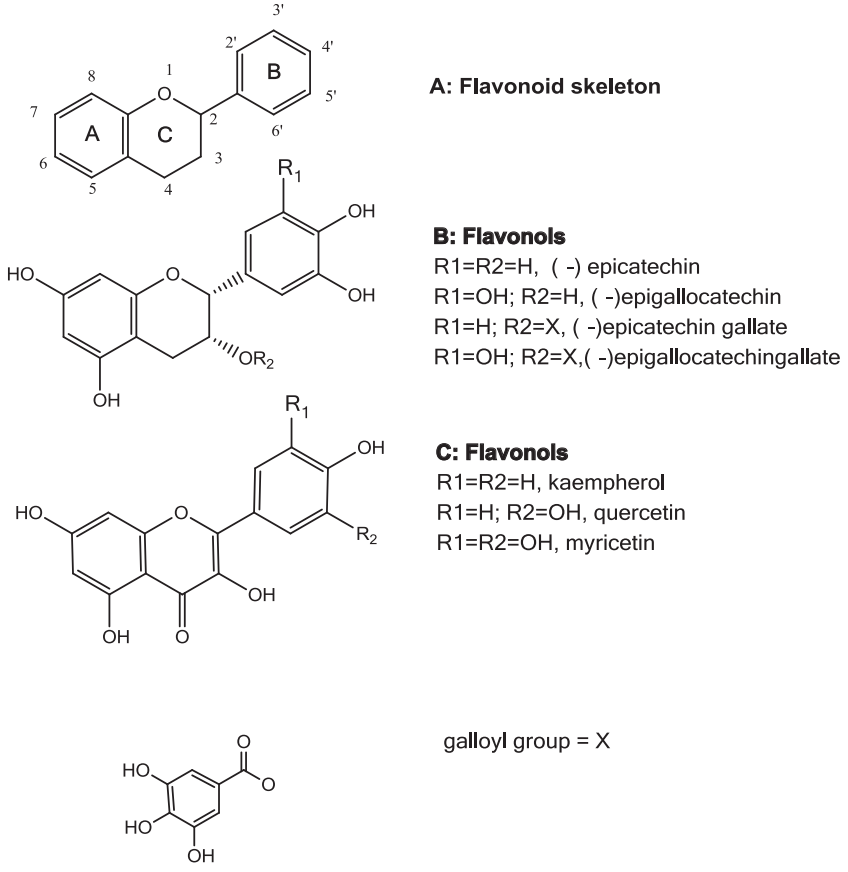


**Fig. 1.** Basic structures of tea flavonoid polyphenols.

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

**Table 1**
Flavonoid composition of tea: percent by dry weight.

| Component | Green tea | Black tea |
|---|---|---|
| Total flavonoids | 15–25 | 15–25 |
| Total catechins | 12–18 | 2–3 |
| (−) Epicatechin | 1–3 | <1 |
| (−) Epicatechingallate | 3–6 | <1 |
| (−) Epigallocatechin | 3–6 | <1 |
| (−) Epigallocatechingallate | 9–13 | 1–2 |
| Flavonols | 2–3 | 1–2 |
| Theaflavins | <1 | 4 |
| Other polyphenols | 2–4 | 7–15 |

tea (2 g of tea leaves infused in hot water for 1–3 min) will provide 150–200 mg of flavonoids. As little as 2–3 cups/day of tea will supply the major contribution to total flavonoid intake in most individuals. Total flavonoid intake from all sources is usually less than 1000 mg/day. Thus in tea-drinking populations tea usually contributes well over half of all flavonoids consumed in the diet.

In green tea, the main flavonoids are the flavanols (catechins). Catechins are a group of flavonoids that include epicatechin (EC), epicatechingallate (ECG), epigallocatechin (EGC) and epigallocatechingallate (EGCG) (Table 1). Catechins are colourless, water-soluble compounds that contribute to the bitterness and astringency of green tea. A typical green tea serving contains approximately 90–100 mg of catechins (Harbowy and Ballentine, 1997). During the production of black tea most of these catechins are oxidized to condensed flavonoids, such as theaflavins and thearubigins.

## 3. Tea and cardiovascular disease: results of population studies

Evidence from population studies suggests that tea consumption and a higher flavonoid intake may reduce the risk for CVD. Peters et al. (2001) performed a meta-analysis of tea consumption in relation to CVD and estimated that the incidence rate of myocardial infarction decreased by 11% with an increase in tea consumption of three cups per day. The analysis included 10 cohort and seven case-control studies. However, some care is needed to interpret these results because of evidence for a publication bias and geographic heterogeneity. Stronger inverse associations between CVD and tea consumption were found in continental European studies compared to US studies. Two UK studies suggested a positive association between tea consumption and risk of CVD. These observations were not specific to green or black tea, but most of the tea consumed in the populations included in this analysis was black tea. Population studies have also investigated the association between green tea consumption specifically and CVD outcomes. Most of these studies have been conducted among Asian populations and suggest a cardioprotective effect of green tea consumption (Iwai et al., 2002; Kuriyama, 2008; Nakachi et al., 2000; Sato et al., 1989). Furthermore, a recent meta-analysis demonstrated that daily consumption of either green or black tea, 3 cups/day, was associated with reduced risk of ischemic stroke (Arab et al., 2009).

Epidemiological studies have also explored the relationships between dietary flavonoids and CVD. The intake of flavonoids has been related to lower risk of heart disease, stroke and total mortality. In another meta-analysis, Huxley and Neil (2003) assessed the association of dietary flavonol intake with the subsequent risk of coronary heart disease (CHD) mortality. This analysis was based on prospective cohort studies published between 1966 and 2001. Flavonols are a subclass of flavonoids present in tea: tea is often the main contributor to flavonol intake in populations. Seven prospective cohorts of men and women ($n$ = 105,000) were identified including a total of 2087 fatal CHD events. Individuals in the top third were compared with those in the bottom third of dietary flavonol intake. Higher flavonoid intake was associated with a 20% reduction in combined risk ratio after adjustment for known CHD risk factors as well as other possible confounders.

Therefore, population studies strongly suggest a decreased risk of CVD with higher tea consumption. The available data also suggest that the magnitude of the benefit of green and black tea is similar.

## 4. Atherosclerosis: human and animal model studies

Few human studies have investigated the relationship between tea or flavonoid intake and atherosclerosis. Debette et al. (2008) showed that carotid plaques were less frequent with increasing tea consumption in women. Mursu et al. (2007) showed that high intake of flavonoids was associated with decreased carotid atherosclerosis in middle-aged Finnish men.

In contrast there is a significant literature describing studies using animal models to investigate the effects of flavonoid-rich foods or extracts on the development of atherosclerosis. The apo E deficient mouse and hamsters have been used as animal models to investigate the effects of flavonoid-rich foods or extracts on the development of atherosclerosis (Hodgson and Croft, 2006). In the apo E deficient mouse inhibition of atherosclerotic lesion development has been demonstrated with tea and tea-derived flavonoids, red wine-derived flavonoids, isolated quercetin or catechin, and a pure phenolic acid derivative from honey. Similar inhibition has been found with red grape extracts in the cholesterol-fed hamster (Auger et al., 2004). More recently Loke et al. (2010) showed that isolated quercetin, found in both green and black tea, as well as theaflavin,

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

an important black tea flavonoid, can inhibit the development of atherosclerosis in the apo E deficient mouse. Overall, the results of studies using animal models clearly show that flavonoids present in tea can inhibit the development of atherosclerosis. Further human studies are needed.

## 5. Endothelial function

The endothelium is the inner lining of all blood vessels. It functions as a selectively permeable barrier between blood and tissues. Normal endothelial function regulates vasomotor tone, platelet activity, leukocyte adhesion and vascular smooth muscle cell proliferation via a release of several factors including nitric oxide (NO). The development of endothelial dysfunction may contribute to the pathogenesis of CVD. It is considered as an early biomarker for the development of CVD (Schroeder et al., 1999) and cardiovascular events (Schächinger et al., 2000). One of the most important molecules released by the endothelium is NO. This molecule is an important regulator of arterial wall tone. Endothelial dysfunction is characterized by the loss of normal endothelium-dependent and NO-mediated vasodilation in the artery.

Endothelial function may be assessed in a number of ways. Isolated vessels from animals can be used to assess the effects of potentially vasoactive substances *in vitro*. The results of several *in vitro* studies indicate that tea and tea flavonoids cause vasorelaxation of rat aortic rings which is NO and endothelium-dependent (Hodgson et al., 2006). In humans, one of the main methods has been to use ultrasonography to measure flow-mediated dilatation of conduit vessels, such as the brachial artery. This is a non-invasive technique that measures NO-dependent vasodilation of the artery in response to shear stress induced by increased blood flow.

A number of studies have now investigated the effects of black or green tea, or tea flavonoids on flow-mediated dilatation of the brachial artery. Most of these studies have shown a significant improvement in flow-mediated dilatation (Hodgson et al., 2006). Green and black teas appear to have similar effects. This has been observed in at least four human trials, in healthy and diabetic subjects, after acute and chronic tea consumption (Alexopoulos et al., 2008; Duffy et al., 2001; Jochmann et al., 2008; Kim et al., 2006; Nagaya et al., 2004). In addition, a dose response of improved endothelial function to black tea polyphenols has recently been demonstrated (Grassi et al., 2009). Similar improvements have been demonstrated using flavonoids derived from chocolate/cocoa, but the results of studies using red wine-derived flavonoids are less consistent (Hodgson and Croft, 2006).

Experimental studies have also demonstrated that isolated flavonoids found in tea can enhance NO status. A recent trial by Loke et al. (2008) showed that dietary flavonoids present in green tea, including quercetin and epicatechin, could augment NO status (plasma S-nitrosothiols and nitrite) and reduce endothelin-1 concentrations – a potent vasoconstrictor. A study by Widlansky et al. (2007) also showed that acute EGCG supplementation can improve endothelial function in humans with coronary artery disease.

Therefore, for endothelial function there is evidence from randomized controlled trials that consumption of black and green tea, and specific flavonoids present in tea, can improve endothelial function. This data is quite consistent.

## 6. Blood pressure

The results of animal models to investigate the effects of tea and flavonoids derived from tea on blood pressure are inconsistent. Results of population studies suggest that long-term regular ingestion of tea may lower blood pressure (Hodgson and Croft, 2006). However, because tea intake is generally associated with a range of lifestyle factors which are related to CVD risk, controlled trials are needed to address the question.

Acutely, tea can increase blood pressure. Both flavonoids and caffeine, present in tea at about 3% of dry weight, cause a transient increase in blood pressure in subjects who avoided caffeine for 12 h or more (Hodgson et al., 2005; Pincomb et al., 1996; Quinlan et al., 1997). The relevance of these acute effects to any longer term effects of regular consumption is uncertain.

In controlled trials, the short-term regular ingestion of tea for up to 8 weeks has not been found to alter blood pressure in largely normotensive individuals (Hodgson, 2006; Hodgson and Croft, 2006). A recent meta-analysis of these trials showed no overall effect on systolic or diastolic blood pressure, whereas analysis of a similar number of trials using flavonoid-rich dark chocolate did show significant blood pressure lowering (Taubert and Roesen, 2007). It is possible that longer-term effects on vasodilator function may be required to alter vascular tone and blood pressure. There have been no controlled trials investigating the longer-term effects of regular ingestion of tea.

Therefore, there is some support for the idea that tea and tea flavonoids can attenuate the development of hypertension. Results of population studies suggest reduced risk of hypertension and lower blood pressure. However, further trials are needed to establish the effect of tea on blood pressure.

## 7. Oxidative stress

The antioxidant flavonoids found in tea are suggested to be responsible for reduced CVD risk. More than 50 studies now convincingly show that flavonoids possess potent antioxidant activity *in vitro*. However, despite the many animal and human studies in this area, there remains limited evidence that flavonoids can actually inhibit oxidative damage *in vivo* (Halliwell

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

et al., 2005; Manach et al., 2005). This is likely to be due partly to poor bioavailability of some flavonoids as well as metabolic transformation that may alter the antioxidant activity of these compounds. Good support for a lack of systemic antioxidant activity of flavonoids *in vivo* comes from studies showing that inhibition of atherosclerosis in animal models is not associated with markers of change in oxidative damage (Waddington et al., 2004; Auger et al., 2004). Thus, it is possible that antioxidant activity is not an important mechanism for benefits of tea flavonoids on endothelial function, atherosclerosis and CVD risk.

## 8. Cholesterol reduction

Results of *in vitro* studies, studies in animal models and population studies suggest that flavonoids could reduce blood cholesterol concentrations (Hodgson, 2008). Most human intervention studies to have investigated the effects of tea on blood cholesterol concentrations have found little or no change with increased flavonoid intake from black tea. For black tea, there have been at least seven randomised controlled trials, with all but one showing no significant effect (Hodgson, 2000, 2008; Manach et al., 2005). Despite the favorable results from animal experiments, results of human studies investigating the effects of green tea (Tsubono and Tsugane, 1997; Unno et al., 2005; Van het hof et al., 1997) are not consistent.

Overall, the lipid lowering effects of tea in humans appear to be for the most part quite small. The discrepancies between experimental and clinical data may be explained by the fact that most animal studies were performed with high doses of tea and tea components.

## 9. Inflammation

Inflammation is thought to play a significant role in the initiation and progression of vascular disease. Inflammatory processes in the vascular wall may be mediated by a range of factors, such as cytokines, eicosanoids and NO, which in turn modulate cellular signaling, cell growth and differentiation and a variety of other cellular processes. Results of *in vitro* studies suggest that flavonoids present in tea and other foods have effects on inflammatory mediators consistent with anti-inflammatory effects (Sies et al., 2005). However, to date there is little support for anti-inflammatory effects in randomized controlled trials. Several studies have shown no effect of regular ingestion of tea for up to 8 weeks on circulating C-reactive protein concentrations, a non specific marker of inflammation (Hodgson, 2008; Lee et al., 2005). Effects of tea on other inflammatory markers remain less clear.

## 10. Platelet function

Too much platelet activation results in an increased susceptibility to aggregation and clotting. This can contribute to thrombosis, myocardial infarction and stroke. I*n vitro* studies have shown that isolated flavonoids at high physiological concentrations can reduce platelet aggregation and markers of platelet activation (Rein et al., 2000). Randomized controlled trials in humans have also investigated the effects of flavonoid-rich foods and beverages on platelet function (Holt et al., 2006). Studies to have investigated the effects of tea on platelet function are not consistent. Four of five trials to assess effects of tea on *ex vivo* platelet aggregation found no effect (Hodgson, 2008 (references therein, Hodgson et al., 2001; Hodgson, 2002). There have however been two trials that have shown that regular ingestion of tea for 4 weeks results in a reduction in circulating p-selectin concentrations (Hodgson et al., 2001; Lee et al., 2005), which is a marker of platelet activation. Additional trials are needed to establish the effects of tea on platelet function.

## 11. Homocysteine

An elevated plasma concentration of total homocysteine (tHcy) is associated with an increased risk for CVD. There remains little evidence that this association is causal. Thus, tHcy concentrations may be a marker of other metabolic changes linked to risk of CVD. Homocysteine is an intermediate in methionine metabolism, and its metabolism can be influenced by several dietary factors including polyphenols and caffeine (Hodgson et al., 2003, Olthof et al., 2001). Results of controlled intervention studies suggest that polyphenols (Olthof et al., 2001) and caffeine (Verhoef et al., 2002) can raise homocysteine. In spite of this, results of cross-sectional population studies generally show that a higher intake of tea is associated with lower tHcy (Hodgson et al., 2006; de Bree et al., 2001, Nygard et al., 1997). A controlled intervention study using high doses of tea solids found that tea solids increased tHcy (Olthof et al., 2001), but a dose more representative of a usual tea intake did not alter tHcy (Hodgson et al., 2003). Thus, any acute effects of tea polyphenols and caffeine to elevate homocysteine acutely do not appear to translate into effects following regular consumption.

## 12. Body weight, body composition and visceral fatness

Green tea is thought to exert a beneficial effect on body weight and composition. There remain almost no data to support an effect of black tea on body weight and composition. Excess visceral fat is specifically associated with metabolic activities linked to poor health, and an increased risk for CVD specifically. Emerging data suggest that regular consumption of green tea may increase energy expenditure and reduce body fatness. Several studies have now shown that green tea, or preparations

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

containing green tea flavonoids and caffeine significantly increase 24 h energy expenditure (Dulloo et al., 1999,Rumpler et al., 2001;Westerterp-Plantenga et al., 2006). In addition, acute and long-term studies have shown that green tea catechin ingestion can increase fat oxidation during exercise (Venables et al., 2008; Takashima et al., 2004). The magnitude of the increase is usually between about 3% and 7%, (about 250–600 kJ/day). The increase in energy expenditure is thought to come about via synergistic effects of tea flavonoids and caffeine, however the relative contributions of these components is not clear (Dulloo et al., 1999; Rumpler et al., 2001). Low doses of caffeine alone, such as those present in tea, appear not to significantly alter energy expenditure (Dulloo et al., 1999; Rumpler et al., 2001). This increase in fat oxidation could contribute to longer-term beneficial effects of high catechin green tea on body weight and composition.

An increase in fat oxidation could contribute to longer-term beneficial effects on body weight and composition. If a small increase in energy expenditure (~5%) is sustained over months a significant reduction in fat mass or body weight could result. Two recent meta-analyses of results from human intervention studies suggest that green tea (flavonoids) with caffeine reduces body weight by approximately 1–1.5 kg over 12 weeks (Hursel et al., 2009; Phung et al., 2010). Almost all studies conducted in Asian populations have shown positive results and results of the few studies in Caucasian populations are mixed. It was concluded by Hursel et al. (2009) that additional studies in Caucasian cohorts are needed. Background caffeine intake may influence the effectiveness of green tea and it is possible that green tea/catechins may be more effective in low to moderate caffeine users.

Therefore, results of randomized controlled trials suggest that green tea can reduce visceral fat during medium-term consumption, but additional studies in Caucasian cohorts are needed. The effects of black tea remain unclear. Benefits of green tea on body weight and body fatness would likely contribute to reduced risk of CVD.

## 13. Type 2 diabetes

The development of type 2 diabetes results in a significant increase in the risk of CVD. Limited data from epidemiological studies suggests that tea consumption is associated with a decreased risk of diabetes (Iso et al., 2006; Song et al., 2005; Panagiotakos et al., 2009) and a reduced level of fasting blood glucose in non-obese people (Polychronopoulos et al., 2008). However, additional prospective population studies are needed to investigate the relationship of tea consumption with risk of type 2 diabetes. Results of studies in animal models (Wu et al., 2004) and human intervention studies (Mackenzie et al., 2007; Fukino et al., 2005; Ryu et al., 2006) do not provide clear support for benefits of tea consumption on glucose and insulin metabolism. Further human studies are needed before drawing any conclusion on the effects of tea on blood glucose control and type 2 diabetes.

## 14. Conclusions

Available data suggests that tea is likely to provide protection against CVD. Results of population studies suggest a decreased risk of CVD with higher green and black tea consumption. Results of studies using animal models of atherosclerosis are consistent with results of population studies. The effects of tea flavonoids to enhance nitric oxide status and to improve endothelial function may be at least partly responsible for benefits on risk of CVD. In addition, there is limited but consistent data to support a benefit of regular consumption of green tea on body fatness and the development of obesity.

## References

Alexopoulos, N., Vlachopoulos, C., Aznaouridis, K., Baou, K., Vasiliadou, C., Pietri, P., Xaplanteris, P., Stefanadi, E., Stefanadis, C., 2008. The acute effect of green tea consumption on endothelial function in healthy individuals. Eur. J. Cardiovasc. Prev. Rehabil. 15, 300–305.
Arab, L., Liu, W., Elashoff, D., 2009. Green and black tea consumption and risk of stroke: a meta-analysis. Stroke 40, 1786–1792.
Auger, C., Gerain, P., Laurent-Bichon, F., Portet, K., Bornet, A., Caporiccio, B., Cros, G., Teissedre, P.L., Rouanet, J.M., 2004. Phenolics from commercialized grape extracts prevent early atherosclerotic lesions in hamsters by mechanisms other than antioxidant effect. J. Agric. Food. Chem. 52, 5297–5302.
de Bree, A., Verschuren, W.M., Blom, H.J., Kromhout, D., 2001. Lifestyle factors and plasma homocysteine concentrations in a general population sample. Am. J. Epidemiol. 154, 150–154.
Debette, S., Courbon, D., Leone, N., Gariepy, J., Tzourio, C., Dartigues, J.F., Barberger-Gateau, P., Ritchie, K., Alperovitch, A., Amouyel, P., Ducimetiere, P., Zureik, M., 2008. Tea consumption is inversely associated with carotid plaques in women. Arterioscler. Thromb. Vasc. Biol. 28, 353–359.
Dulloo, A.G., Duret, C., Rohrer, D., Girardier, L., Mensi, N., Fathi, M., Chantre, P., Vandermander, J., 1999. Efficacy of a green tea extract rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. Am. J. Clin. Nutr. 70, 1040–1045.
Duffy, S.J., Keaney, J.F., Holbrook, M., Gokce, N., Swerdloff, P.L., Frei, B., Vita, J.A., 2001. Short and long term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. Circulation 104, 151–156.
Fukino, Y., Shimbo, M., Aoki, N., Okubo, T., Iso, H., 2005. Randomized controlled trial for an effect of green tea consumption on insulin resistance and inflammation markers. J. Nutr. Sci. Vitaminol. 51, 335–342.
Grassi, D., Mulder, T.P.J., Draijer, R., Desideri, G., Molhuizen, H.O.F., Ferri, C., 2009. Black tea consumption dose-dependently improves flow-mediated dilation in healthy males. J. Hypertens. 27, 774–781.
Halliwell, B., Rafter, J., Jenner, A., 2005. Health promotion by flavonoids, tocopherols, tocotrienols, and other phenols: direct or indirect effects? Antioxidant or not? Am. J. Clin. Nutr. 81, 268S–276S.
Harbowy, M.E., Ballentine, D.A., 1997. Tea Chemistry. Crit. Rev. Plant Sci. 16, 415–480.
Hodgson, J.M., Burke, V., Beilin, L.J., Croft, K.D., Puddey, I.B., 2003. Can black tea influence plasma total homocysteine concentrations? Am. J. Clin. Nutr. 77, 907–911.
Hodgson, J.M., Burke, V., Puddey, I.B., 2005. Acute effects of tea on fasting and postprandial vascular function and blood pressure in humans. J. Hypertens. 23, 47–54.
Hodgson, J.M., Croft, K.D., 2006. Dietary flavonoids: effects on endothelial function and blood pressure. J. Sci. Food Agric. 86, 2492–2498.

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

Hodgson, J.M., Devine, A., Puddey, I.B., Beilby, J., Prince, R.L., 2006. Drinking tea is associated with lower plasma total homocysteine in older women. Asia Pacific J. Clin. Nutr. 15, 253–258.
Hodgson, J.M., Puddey, I.B., Burke, V., Beilin, L.J., Mori, T.A., Chan, S.Y., 2002. Acute effects of ingestion of black tea on postprandial platelet aggregation in humans. Br. J. Nutr. 87, 141–145.
Hodgson, J.M., Puddey, I.B., Mori, T.A., Burke, V., Baker, R., Beilin, L.J., 2001. Effects of regular ingestion of black tea on haemostasis and cell adhesion molecules in humans. Eur. J. Clin. Nutr. 55, 881–886.
Hodgson, J.M., 2006. Effects of tea and tea flavonoids on endothelial function and blood pressure: a brief review. Clin. Exp. Pharmacol. Physiol. 33, 838–841.
Hodgson, J.M., 2000. Tea and cardiovascular disease: a review. Proc. Nutr. Soc. Austr. 24, 241–249.
Hodgson, J.M., 2008. Tea flavonoids and cardiovascular disease. Asia Pacific J. Clin. Nutr. 17, S288–S290.
Holt, R.R., Actis-Goretta, L., Momma, T.Y., Keen, C.L., 2006. Dietary flavanols and platelet reactivity. J. Cardiovasc. Pharmacol. 47, S187–S196.
Hursel, R., Viechtbauer, W., Westerterp-Plantenga, M.S., 2009. The effects of green tea on weight loss and weight maintenance: a meta-analysis. J. Obes. 33, 956–961.
Huxley, R.R., Neil, H.A., 2003. The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies. Eur. J. Clin. Nutr. 57, 904–908.
Iso, H., Date, C., Wakai, K., Fukui, M., Tamakoshi, A., 2006. JACC Study Group. The relationship between green tea and total caffeine intake and risk for self-reported type 2 diabetes among Japanese adults. Ann. Intern. Med. 144, 554–562.
Iwai, N., Ohshiro, H., Kurozawa, Y., Hosoda, T., Morita, H., Funakawa, K., Okamoto, M., Nose, T., 2002. Relationship between coffee and green tea consumption and all-cause mortality in a cohort of a rural Japanese population. J. Epidemiol. 12, 191–198.
Jochmann, N., Lorenz, M., von Krosigk, A., Martus, P., Böhm, V., G, Baumann, Stangl, K., Stangl, V., 2008. The efficacy of black tea in ameliorating endothelial function is equivalent to that of green tea. Br. J. Nutr. 99, 863–868.
Kim, W., Jeong, M.H., Cho, S.H., Yun, J.H., Chae, H.J., Ahn, Y.K., Lee, M.C., Cheng, X., Kondo, T., Murohara, T., Kang, J.C., 2006. Effect of green tea consumption on endothelial function and circulating endothelial progenitor cells in chronic smokers. Circ. J. 70, 1052–1057.
Kuriyama, S., 2008. The relation between green tea consumption and cardiovascular disease as evidenced by epidemiological studies. J. Nutr. 138, 1548S–1553S.
Lee, W., Min, W.K., Chun, S., Lee, Y.W., Park, H., Lee, D.H., Lee, Y.K., Son, J.E., 2005. Long-term effects of green tea ingestion on atherosclerotic biological markers in smokers. Clin. Biochem. 38, 84–87.
Loke, W.M., Hodgson, J.M., Proudfoot, J.M., McKinley, A.J., Puddey, I.B., Croft, K.D., 2008. Pure dietary flavonoids, quercetin and (−)-epicatechin augment nitric oxide products and reduce endothelin-1 acutely in healthy human volunteers. Am. J. Clin. Nutr. 88, 1018–1025.
Loke, W.M., Proudfoot, J.M., McKinley, A.J., Hodgson, J.M., Croft, K.D., 2010. Pure dietary polyphenols attenuate atherosclerosis in apo E knockout mice via alleviating oxidative stress, inflammation and endothelial dysfunction. Arterioscl. Thrombos. Vasc. Biol. 30, 749–757.
Mackenzie, T., Leary, L., Brooks, W.B., 2007. The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metabolism 56, 1340–1344.
Manach, C., Mazur, A., Scalbert, A., 2005. Polyphenols and prevention of cardiovascular disease. Curr. Opin. Lipidol. 16, 77–84.
Mursu, J., Nurmi, T., Tuomainen, T.P., Ruusunen, A., Salonen, J.T., Voutilainen, S., 2007. The intake of flavonoids and carotid atherosclerosis: the Kuopio ischaemic heart disease risk factor study. Br. J. Nutr. 98, 814–818.
Nagaya, N., Yamamoto, H., Uematsu, M., Itoh, T., Nakagawa, K., Miyazawa, T., Kangawa, K., Miyatake, K., 2004. Green tea reverses endothelial dysfunction in healthy smokers. Heart 90, 1485–1486.
Nakachi, K., Matsuyama, S., Miyake, S., Suganuma, M., Imai, K., 2000. Preventive effects of drinking green tea on cancer and cardiovascular disease: epidemiological evidence for multiple targeting prevention. Biofactors 13, 49–54.
Nygard, O., Refsum, H., Ueland, P.M., et al, 1997. Coffee consumption and plasma total homocysteine: the Hordal and homocysteine study. Am. J. Clin. Nutr. 65, 136–143.
Olthof, M.R., Hollman, P.C., Zock, P.L., Katan, M.B., 2001. Consumption of high doses of chlorogenic acid, present in coffee, or of black tea increases plasma total homocysteine concentrations in humans. Am. J. Clin. Nutr. 73, 532–538.
Panagiotakos, D.B., Lionis, C., Zeimbekis, A., Gelastopoulou, K., Papairakleous, N., Das, U.N., Polychronopoulos, E., 2009. Long-term tea intake is associated with reduced prevalence of (type 2) diabetes mellitus among elderly people from Mediterranean islands: MEDIS epidemiological study. Yonsei Med. J. 50, 31–38.
Peters, U., Poole, C., Arab, L., 2001. Does tea affect cardiovascular disease? A meta-analysis. Am. J. Epidemiol. 154, 495–503.
Phung, O.J., Baker, W.L., Matthews, L.J., Lanosa, M., Thorne, A., Coleman, C.I., 2010. Effect of green tea catechins with or without caffeine on anthropometric measures: a systematic review and meta-analysis. Am. J. Clin. Nutr. 91, 73–81.
Pincomb, G.A., Lovallo, W.R., McKey, B.S., Sung, B.H., Passey, R.B., 1996. Everson SA and Wilson MF: acute blood pressure elevations with caffeine in men with borderline systemic hypertension. Am. J. Cardiol. 77, 270–274.
Polychronopoulos, E., Zeimbekis, A., Kastorini, C.M., Papairakleous, N., Vlachou, I., Bountziouka, V., Panagiotakos, D.B., 2008. Effects of black and green tea consumption on blood glucose levels in non-obese elderly men and women from Mediterranean islands (MEDIS epidemiological study). Eur. J. Nutr. 47, 10–16.
Quinlan, P., Lane, J., Aspinall, L., 1997. Effects of hot tea, coffee and water ingestion on physiological responses and mood: the role of caffeine, water and beverage type. Psychopharmacology 134, 164–173.
Rein, D., Paglieroni, T.G., Pearson, D.A., Wun, T., Schmitz, H.H., Gosselin, R., Keen, C.L., 2000. Cocoa and wine polyphenols modulate platelet activation and function. J. Nutr. 130, 2120S–2126S.
Rumpler, W., Seale, J., Clevidence, B., Judd, J., Wiley, E., Yamamoto, S., Komatsu, T., Sawaki, T., Ishikura, Y., Hosoda, K., 2001. Oolong tea increases metabolic rate and fat oxidation in men. J. Nutr. 131, 2848–2858.
Ryu, O.H., Lee, J., Lee, K.W., Kim, H.Y., Seo, J.A., Kim, S.G., Kim, N.H., Baik, S.H., Choi, D.S., Choi, K.M., 2006. Effects of green tea consumption on inflammation, insulin resistance and pulse wave velocity in type 2 diabetes patients. Diabetes Res. Clin. Pract. 71, 356–358.
Sato, Y., Nakatsuka, H., Watanabe, T., Hisamichi, S., Shimizu, H., Fujisaku, S., Ichinowatari, Y., Ida, Y., Suda, S., et al, 1989. Possible contribution of green tea drinking habits to the prevention of stroke. Tohoku J. Exp. Med. 157, 337–343.
Schächinger, V., Britten, M.B., Zeiher, A.M., 2000. Prognostic impact of coronary vasodilator dysfunction on adverse long-term outcome of coronary heart disease. Circulation 101, 1899–1906.
Schroeder, S., Enderle, M.D., Ossen, R., et al, 1999. Noninvasive determination of endothelium-mediated vasodilation as a screening test for coronary artery disease: pilot study to assess the predictive value in comparison with angina pectoris, exercise electrocardiography, and myocardial perfusion imaging. Am. Heart J. 138, 731–739.
Sies, H., Schewe, T., Heiss, C., Kelm, M., 2005. Cocoa polyphenols and inflammatory mediators. Am. J. Clin. Nutr. 81, 304S–312S.
Song, Y., Manson, J.E., Buring, J.E., Sesso, H.D., Liu, S., 2005. Associations of dietary flavonoids with risk of type 2 diabetes, and markers of insulin resistance and systemic inflammation in women: a prospective study and cross-sectional analysis. J. Am. Coll. Nutr. 24, 376–384.
Takashima, S., Kataoka, K., Shibata, E., Hoshino, E., 2004. The long term intake of catechins improves lipid catabolism during exercise. Prog. Med. 24, 3371–3379.
Taubert, D., Roesen, R., Schomig, E., 2007. Effect of cocoa and tea intake on blood pressure: a meta-analysis. Arch. Intern. Med. 167, 626–634.
Tsubono, Y., Tsugane, S., 1997. Green tea intake in relation to serum lipid levels in middle-aged Japanese men and women. Ann. Epidemiol. 7, 280–284.
Unno, T., Tago, M., Suzuki, Y., Nozawa, A., Sagesaka, Y.M., Kakuda, T., Egawa, K., Kondo, K., 2005. Effect of tea catechins on postprandial plasma lipid responses in human subjects. Br. J. Nutr. 93, 543–547.

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004

Van het Hof, K.H., deBoer, H.S.M., Wiseman, S.A., Lien, N., Weststrate, J.A., Tijburg, L.B.M., 1997. Consumption of green or black tea does not increase resistance of low-density lipoprotein to oxidation in humans. Am. J. Clin. Nutr. 66, 1125–1132.

Venables, M.C., Hulston, C.J., Cox, H.R., Jeukendrup, A.E., 2008. Green tea extract ingestion, fat oxidation, and glucose tolerance in healthy humans. Am. J. Clin. Nutr. 87 (3), 778–784.

Verhoef, P., Pasman, W.J., van Vliet, T., Urgert, R., Katan, M.B., 2002. Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. Am. J. Clin. Nutr. 76, 1244–1248.

Waddington, E., Puddey, I.B., Croft, K.D., 2004. Red wine polyphenolic compounds inhibit atherosclerosis in apolipoprotein E-deficient mice independently of effects on lipid peroxidation. Am. J. Clin. Nutr. 79, 54–61.

Westerterp-Plantenga, M. et al, 2006. Metabolic effects of spices, teas, and caffeine. Physiol. Behav. 89, 85–91.

Widlansky, M.E., Hamburg, N.M., Anter, E., Holbrook, M., Kahn, D.F., Elliott, J.G., Keaney, J.F., Vita, J.A., 2007. Acute EGCG supplementation reverses endothelial dysfunction in patients with coronary artery disease. J. Am. Coll. Nutr. 26, 95–102.

Wu, L.Y., Juan, C.C., Ho, L.T., Hsu, Y.P., Hwang, L.S., 2004. Effect of green tea supplementation on insulin sensitivity in Sprague–Dawley rats. J. Agric. Food Chem. 52, 643–648.

Please cite this article in press as: Hodgson, J.M., Croft, K.D. Tea flavonoids and cardiovascular health. Molecular Aspects of Medicine (2010), doi:10.1016/j.mam.2010.09.004