SUMMARY

1. The consumption of tea worldwide is second only to water. Thus, any physiological effects of tea could have a significant impact on population health.

2. Tea is the major contributor to total flavonoid intake in many populations. Flavonoids in tea have been shown to have a range of activities and effects that could contribute to improved health. Tea intake and the intake of flavonoids found in tea have been associated with reduced risk of cardiovascular disease in several cross-sectional and prospective population studies. A variety of possible mechanisms have been investigated. The focus of the present review is on the mounting evidence that tea flavonoids can improve endothelial function and lower blood pressure.

3. In vitro studies using isolated vessels have shown that tea flavonoids possess vasodilator activity. Results of human intervention trials have shown that increased flavonoid intake from tea, as well as other dietary sources, can improve endothelial function. Emerging data also suggest that the degree of benefit may be related to flavonoid metabolism.

4. The effects of tea flavonoids on blood pressure are less consistent. Results of animal studies and population studies are consistent with a blood pressure-lowering effect of tea. However, short-term intervention trials, mainly in normotensive individuals, have not demonstrated any blood pressure reduction with tea.

5. Overall, the available data suggest that the effects of tea flavonoids on endothelial function and, perhaps, blood pressure may be responsible, at least in part, for any benefits of drinking tea on the risk of cardiovascular disease.

Key words: blood pressure, cardiovascular disease, endothelial function, flavonoids, tea.

INTRODUCTION

The results of population studies suggest that drinking tea may protect against the development of cardiovascular disease. The antioxidant polyphenolic compounds found in tea, primarily flavonoids, are suggested to be the main components responsible. The effect of tea or of flavonoids from another source on primary or secondary prevention of cardiovascular disease has not been assessed in an intervention study. Thus, in order to estimate the likely impact of dietary flavonoids on cardiovascular health, we must rely on data from less-rigorous sources.

The effects of tea and flavonoids found in tea on a wide range of cardiovascular disease-related end-points have been investigated. A number of possible mechanisms for cardiovascular benefit have been implicated. The present review will focus on the potential for tea and tea flavonoids to reverse endothelial dysfunction and to lower blood pressure in humans.

WHAT IS TEA?

The term ‘tea’ refers to the plant *Camellia sinensis*, its leaves and infusions derived from them. Worldwide, the consumption of tea is second only to water and, therefore, any physiological effects of tea could be important. Tea can be classified as green and black. Black teas are produced by promoting the enzymatic oxidation of tea flavonoids. Enzymes involved in flavonoid oxidation are inactivated to produce green tea.

Both black and green teas can be major contributors to total flavonoid intake. Approximately 35–40% of the weight of the tea leaf, both black and green, is flavonoids. The processing of tea to black tea results in many changes to the chemical composition of the tea leaf. Perhaps the most notable is oxidation of the catechins, the main class of flavonoids found in tea, resulting in significant reduction in catechin concentration. This is often reduced to less than 10% in the black tea leaf. However, black tea is rich in flavonoid oxidation products derived from the enzymatic oxidation of catechins. Monomeric catechins undergo enzymatic polymerization, which leads to the formation of condensation compounds such as theaflavins and thearubigens. These differences in flavonoid composition between black and green tea may result in differences in physiological effects.

Tea is an ideal vehicle to investigate the effects of dietary flavonoids on cardiovascular disease-related end-points in intervention...
The effect of tea and dietary flavonoids on endothelial function in humans has been a mechanism of major interest in recent years. Several studies have now investigated the effect of tea on endothelial function. 11-14 Duffy et al. 11 assessed the acute and chronic effects of tea consumption on flow-mediated dilatation of the brachial artery in individuals with pre-existing coronary artery disease. Both acute and chronic consumption of black tea over 4 weeks resulted in significant improvements in flow-mediated dilatation. There was no improvement in endothelium-independent nitroglycerine-mediated dilatation, suggesting that tea alters endothelial rather than smooth muscle cell function. 13 In a similar study, we examined the effect of chronic tea consumption, over 4 weeks, on flow-mediated dilatation of the brachial artery in individuals with mild dyslipidaemia. Regular ingestion of five cups per day of black tea resulted in a significant increase in flow-mediated dilatation. 12 However, in contrast with the study of Duffy et al., 16 we also found improvement in endothelium-independent glyceryltrinitrate-mediated dilatation. This suggests that the benefits of tea on vasodilation may be both endothelium and NO dependent and vascular smooth muscle related. In a subsequent study, we investigated the acute effects of black tea on brachial artery vasodilator function in fasting and post-prandial states in individuals with pre-existing coronary artery disease. Flow-mediated dilatation was significantly improved, but only when the tea was consumed with a meal. In that study, the endothelium-independent glyceryltrinitrate-mediated dilatation was not significantly altered. 17 The few data that are available for green tea and endothelial function suggest improvement in endothelium-dependent vasodilation. 14

More recently, we have investigated whether improvement in endothelial function with tea is related to flavonoid metabolism. Absorbed flavonoids can be rapidly metabolised and this may alter their activity. Using data from our previous trials, 12,13 we investigated whether the endothelial function response to tea was related to flavonoid O-methylation, a major pathway of flavonoid metabolism. In both studies, we found that the greater the O-methylation, the less the improvement in endothelial function. 15 These results suggest that metabolism of flavonoids may alter vasodilator activity and their effects on endothelial function. Further trials are needed to investigate this hypothesis.

**Blood Pressure**

Tea contains caffeine at approximately 3% dry weight or approximately 30–50 mg per standard cup. Caffeine results in a transient increase in blood pressure in subjects who have avoided caffeine for 12 h or more. 16 Tea containing caffeine also induces a transient increase in blood pressure. 17 However, tea contains high levels of flavonoids, which may influence blood pressure via effects on vasodilation.

The effects of tea and flavonoids derived from tea on blood pressure have been studied in several rat models. The results of these studies suggest that tea flavonoids can reduce blood pressure, but are not entirely consistent. In spontaneously hypertensive rats, both black and green tea polyphenols were found to attenuate blood pressure increases. 18 However, in the same rat model, green tea flavonoids did not alter blood pressure, despite a prolonged lifespan. 19 In addition, green tea has been shown to reduce blood pressure in fructose-fed Sprague-Dawley rats, 20 but not in Dahl salt-sensitive rats. 21

Results of population studies suggest that long-term regular ingestion of tea may lower blood pressure. 22,23 In a cohort of Norwegian

ENDOTHELIAL FUNCTION

Endothelial dysfunction is characterized by the loss of normal endothelium-dependent vasodilation. The development of endothelial dysfunction may contribute to the pathogenesis of cardiovascular disease. 9 Thus, any improvement in endothelial function could reduce the risk of coronary events.

The results of in vitro studies provide evidence for direct effects of flavonoids present in tea on endothelial function. Flavonoids found in tea 17 and extracts of black tea 9 have been shown to cause vasorelaxation of rat aortic rings. The results of several of these studies indicate involvement of nitric oxide (NO) in endothelium-dependent vasorelaxation. 7,9 Endothelium- and NO-independent mechanisms have also been described. 10 The relative importance of these mechanisms is uncertain.
men and women, higher consumption of black tea was associated with lower systolic blood pressure. We found a similar association for both tea intake and a marker of exposure to tea-derived flavonoids with systolic and diastolic blood pressure in a cross-sectional study of older women. In a population of men and women greater than 20 years of age, Yang et al. found that, compared with non-tea drinkers, the risk of hypertension was reduced by 46% and 65% in those drinking approximately two to three cups per day or more than two to three cups per day, respectively. The results of these studies suggest that tea may lower blood pressure or prevent increases in blood pressure over time. However, because tea intake is generally associated with a range of lifestyle factors that are related to cardiovascular disease risk, controlled trials are needed to address the question.

There have been no controlled trials investigating the longer-term (more than 4 weeks) effects of regular ingestion of tea. Short-term regular ingestion of tea for up to 4 weeks in intervention trials has not been found to alter blood pressure in largely normotensive individuals. It is possible that longer-term effects on vasodilator function may be required to alter vascular tone and blood pressure.

The acute effects of tea on blood pressure have been inconsistent with the reported effects of regular ingestion. This may be due, in part, to the presence of caffeine in tea and the design of the studies, which have mainly assessed effects in the fasting state. The flavonoids found in tea may also be responsible for an acute, rapid-onset and short-lived, pressor response, which is additive to the effects of caffeine. We have shown previously that a single dose of tea, containing 180 mg caffeine, caused a transient (at 30 min) increase in blood pressure approximately threefold that of caffeine alone (180 mg dose) in people who had fasted and avoided caffeine for more than 12 h. Rapid-onset changes in blood pressure may be mediated by sensory properties of the tea resulting in general activation of the sympathetic nervous system. In a more recent study, we have found that ingestion of food appears to negate, or at least blunt, this acute pressor response to flavonoids. The relevance of these acute effects to any longer-term effects of regular consumption is uncertain. However, this elevation in blood pressure may be clinically important if it leads to an incorrect diagnosis of sustained hypertension or poor blood pressure control. In addition, these acute effects may be relevant to reducing post-prandial hypertension in older individuals.

The potential link between tea and blood pressure has been investigated in a range of studies. Although there is some support for the idea that tea and tea flavonoids can attenuate the development of hypertension and reduce blood pressure, further trials are needed. In particular, the longer-term effects of regular ingestion of tea on blood pressure have yet to be investigated.

CONCLUSIONS

The evidence from cross-sectional and prospective cohort studies that a higher intake of black tea and flavonoids derived from green and black tea is associated with lower risk of cardiovascular disease is quite consistent, but not yet conclusive. Further evidence for the benefits of tea on cardiovascular risk comes from studies where effects on factors involved in the development of cardiovascular disease have been examined. Results of in vitro studies, studies using animal models, population studies and human intervention trials suggest that tea flavonoids can improve endothelial function and may also lower blood pressure. However, the effects of long-term increased tea intake on both endothelial function and blood pressure remain uncertain. Further studies are also needed to determine whether the observed effects are due primarily to specific flavonoids or class of flavonoids, or whether the effects are more generalized. In addition, the significance of flavonoid metabolism in relation to observed effects requires further investigation.

REFERENCES


