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Review

All teas are not created equal
The Chinese green tea and cardiovascular health

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Abstract

Tea is one of the most widely consumed beverages in the world, next only to water. It can be categorized into three types, depending on the level of fermentation, i.e., green (unfermented), oolong (partially fermented) and black (fermented) tea. In general, green tea has been found to be superior to black tea in terms of antioxidant activity owing to the higher content of (−)-epigallocatechin gallate. The processes used in the manufacture of black tea are known to decrease levels of the monometric catechins to a much greater extent than the less severe conditions applied to other teas. The cardioprotective effect of flavonoids from green tea can be attributed to not only antioxidant, antithrombogenic and anti-inflammatory properties but also improvement of coronary flow velocity reserve. In this article, I will discuss the effects of green tea on atherosclerosis, coronary heart disease, hypertension, diabetes, metabolic syndrome and obesity, and, finally, its comparison with black tea.

Keywords: Tea; Green tea; Chinese green tea; Cardiovascular health

1. Introduction

Tea is one of the most widely consumed beverages in the world, next only to water [1,2] and well ahead of coffee, beer, wine and carbonated soft drinks [3]. It can be categorized into three types, depending on the level of fermentation, i.e., green (unfermented), oolong (partially fermented) and black (fermented) tea. Although this process is often assumed, incorrectly, to be fermentation which usually implies additives, the more correct term should be oxidation which means exposure to air while drying [4]. In general, green tea has been found to be superior to black tea in terms of antioxidant activity owing to the higher content of (−)-epigallocatechin gallate [5–7]. The processes used in the manufacture of black tea are known to decrease levels of the monometric catechins to a much greater extent than the less severe conditions applied to other teas [5,6]. The production and consumption of the partially fermented oolong tea are confined to China [1].

The cardioprotective effect of flavonoids from green tea can be attributed to not only antioxidant [5], antithrombogenic [8,9] and anti-inflammatory [10] properties but also improvement of coronary flow velocity reserve [1,11]. In this article, I will discuss the effects of green tea on atherosclerosis, coronary heart disease, hypertension, diabetes, metabolic syndrome and obesity, and, finally, its comparison with black tea.

2. Atherosclerotic coronary heart disease

2.1. Antioxidant effect

The protective effect of tea (*Camellia sinensis*) against atherosclerosis has been attributed to the antioxidant activity of the flavonoids [3,5,12]. Over 4000 different flavonoids have been described, and they are categorized into flavonols, flavones, catechins, flavanones, anthocyanidins and isoflavonoids [13]. Green tea has been shown to retard atherosclerosis in both experimental animals [14–19] and humans [20,21]. However, although the results in animals [14–19] were very promising, clinical

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benefits were less consistent. The work of Chyu et al. [17] seemed to suggest that antioxidant epigallocatechin gallate differentially reduces evolving atherosclerotic lesions without influencing established atherosclerosis in the apoliporotein E-null mice. Therefore, failure of antioxidants in some clinical trials may be partly because such therapy is started after atherosclerosis is already well established, whereas the benefits in animal models may be results from early initiation of antioxidants while atherosclerosis is still evolving [17].

2.2. Anti-endothelial dysfunction effect

Endothelial dysfunction is an early marker for atherosclerosis; many of the risk factors that predispose to atherosclerosis can also cause endothelial dysfunction [22]. In addition to the antioxidant properties, green tea catechins have also been shown to reverse endothelial dysfunction [23,24], even in cigarette smokers [25,26]. A constituent of green tea, epigallocatechin-3-gallate, activates endothelial nitric oxide synthase by a phosphatidylinositol-3-OH-kinase-, cAMP-dependent protein kinase-, and Akt-dependent pathway and leads to endothelial-dependent vasorelaxation [27]. In a rat carotid artery balloon injury model, both Cheng et al. [28] and Kim et al. [29] showed that green tea catechins inhibit neointimal hyperplasia and suppress proliferation of vascular smooth muscle cells. These findings have obvious clinical implications, because vascular smooth muscle cell proliferation is one of the major mechanisms of restenosis following percutaneous coronary interventions.

Lung Chen Tea (Dragon Well Tea) is a well known Chinese green tea and has been shown to significantly prevent endothelial-cell induced LDL oxidation and suppress lipoxygenase activity [30]. Because LDL oxidation is a characteristic feature of atherogenesis and lipoxygenase is involved in the disease process, the consumption of Lung Chen Tea, therefore, may lower the risk of coronary heart disease. In addition, Lung Chen Tea has been shown to lower plasma cholesterol by increasing fecal bile acids and cholesterol excretion in diet-induced hypercholesterolemic Sprague–Dawley rats [31]

2.3. Antithrombogenic effect

Another mechanism by which flavonoids may confer reduction of atherosclerotic risk is by reducing thrombosis [8,9,32]. A potent thromboxane formation inhibitor is found in green tea leaves [33]. In rats taking unprocessed green tea extract, a significant reduction in thromboxane level was observed [33]. However, no appreciable changes in the thromboxane levels were noticed in the serum of rats taking processed tea extracts. This might be due to the presence of a labile component which is destroyed during the processing of green tea leaves. Of interest is the observation of a decreased cholesterol level in rats consuming unprocessed tea extract. This decrease could be linked to the decrease in thromboxane levels as observed.

The mode of antithrombogenesis of green tea catechins is interesting. They did not change the coagulation parameters such as activated partial thromboplastin time, prothrombin time, and thrombin time using human citrated plasma [34]. Therefore, the modes of antithrombotic action may be due to the antiplatelet activities, rather than to anticoagulant activities [34].

2.4. Anti-inflammatory effect

Green tea also has an anti-inflammatory effect [10]. Among various biological effects of green tea, Sueoka et al. [35] focused on its inhibitory effect on TNF-alpha gene expression mediated through inhibition of NF-kappaB and AP-1 activation. Because TNF-alpha is known to be a central mediator in chronic inflammatory diseases such as rheumatoid arthritis and multiple sclerosis, Sueoka et al. [35] therefore hypothesized that green tea might be a preventive agent for chronic inflammatory diseases. To test this hypothesis, they examined TNF-alpha transgenic mice which overexpress TNF-alpha only in the lungs. The TNF-alpha transgenic mouse is an animal model of human idiopathic pulmonary fibrosis which also frequently develops lung cancer. They found that expressions of TNF-alpha and IL-6 were inhibited in the lungs of these mice after treatment with green tea in drinking water for 4 months. Inhibition of the NF-κB and AP-1 pathway by epigallocatechin-3-gallate has also been reported more recently for the treatment of reperfusion-induced myocardial damage [36]. Therefore, these data suggest that green tea has preventive effects on chronic inflammatory diseases, including neurological disorders [37,38].

In view of the recent interest in C-reactive protein as a marker of inflammation that has been shown to be associated with an increased risk of myocardial infarction [39–42], these Japanese studies render strong support to the latest findings that the C-reactive protein level is a stronger predictor of cardiovascular events than the low-density lipoprotein cholesterol level [43]. The recent report by Hirano et al. [44] that they did not find any inverse association between green tea intake and coronary artery disease in Japanese patients but did find an inverse association between green tea intake and myocardial infarction lends further strength to the inflammatory theory of the pathogenesis of atherosclerosis and coronary artery disease [10,45,46]. Of course, the Chinese discovered thousands of years ago that green tea also warded off infections [47], although the infection theory of coronary heart disease that was recently revived was subsequently disproven [48,49].

3. Hypertension

In ancient Chinese medicine, tea has long been believed to possess hypotensive effects [50]. However, conflicting results have been shown among human trials as well as animal studies on the relation between tea consumption and blood pressure. The controversy, which is partly due to the fact that tea contains caffeine that can transiently increase blood pressure, has largely been resolved by the recent studies of Hodgson and Puddey [51]. They found that in population studies people generally drink tea with and between meals, whereas subjects in acute studies drink tea in a fasting state, and that the capacity for food to negate the pressor effect of tea in the fasting state explains a lack of any longer-term effects of tea to raise blood pressure [51].

In a recently reported study on the risk of newly diagnosed hypertension in 1507 Taiwanese subjects who were previously normotensive, Yang et al. [50] found that habitual moderate strength green or oolong tea consumption significantly reduces the risk of developing hypertension. They further noted that, compared with nonhabitual tea drinkers, the risk of developing hypertension decreased by 46% for those who drank 120–599 ml/d and was further reduced by 65% for those who drank $\geq$600 ml/d, after carefully adjusting for age, sex, socioeconomic status, family history of hypertension, body mass index, waist–hip ratio, lifestyle factors (total physical activity, sodium intake, smoking, alcohol consumption and coffee drinking), and dietary factors (vegetable, fruit, unrefined grain, fish, milk, visible-fat food, and deep fried food).

Green tea prevents the development of left ventricular hypertrophy in animal model of chronic renal failure [52]. This effect was related to the attenuation of hypertension, although a direct effect on cardiac myocyte reactive oxygen species production and growth was also identified.

Green tea polyphenols have also been shown to attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats [53]. However, earlier reports showed that green tea inhibited the incidence of stroke and prolonged the life span of stroke-prone spontaneously hypertensive rat, but did not affect the blood pressure [54]. Similar findings were reported in Japanese women: less stroke among those who drank more green tea, although no relation with tea drinking was observed for history of hypertension [55]. In a 14212-subjects, 12-provinces study in China [56], a strong inverse correlation between tea drinking and stroke was found after adjusting other risk factors of stroke ($p<0.05$). The odds ratio (OR) of stroke was 0.60 [95% confidence interval (CI): 0.42–0.85] for subjects who drank tea compared to those who did not. The OR value was 0.24 (95% CI: 0.06–1.01) for black tea ($p=0.05$) and 0.35 (95% CI: 0.18–0.72) for green tea ($p<0.01$) [56]. Thus green tea may prevent stroke due to the radical scavenger action and lipid peroxidation [54].

Nitric oxide (NO) produced by the endothelium of cerebral arterioles is an important mediator of endothelium-dependent vasodilatation, and also helps to prevent thrombosis and vascular remodeling [57]. Hypertension is associated with impaired endothelium-dependent vasodilatation, and this defect is usually at least partially attributable to a decrease in the production and/or stability of NO. Protection afforded by green tea polyphenols may reflect increased expression of the endothelial NO synthase. IGF-I activity stimulates endothelial NO production, and conceivably is a mediator of the protection associated with higher-protein diets in Japanese population and in hypertensive rats [57]. These considerations prompt the conclusion that modulation of NO availability is a crucial determinant of risk for ischemic stroke [57].

4. Diabetes

Atherosclerosis accounts for some 80 % of all diabetic mortality; about three-quarters of the cardiovascular deaths from diabetes result from coronary artery disease [58]. Plants containing flavonoids have been used to treat diabetes in Indian medicine [59]. The green tea flavonoid has been shown to have insulin-like activities [59] as well as insulin-enhancing activity [60]. However, epigallocatechin gallate, which is the principal catechin in green tea, differs from insulin in that it affects several insulin-activated kinases with slower kinetics [59]. Furthermore, epigallocatechin regulates genes that encode gluconeogenic enzymes and protein-tyrosine-phosphorylation by modulating the redox state of the cell [59]. Thus epigallocatechin gallate may be an antidiabetic agent.

Mouse experiment by Japanese investigators [61], in fact, documented for the first time that a certain serum protein may be involved in the antihyperglycemic effect of green tea. Taiwanese investigators [62] demonstrated recently that green tea increases insulin sensitivity in Sprague–Dawley rats and that the green tea polyphenol is one of the active components. In a fructose-fed rat model, the same Taiwanese investigators [63] found that green tea ameliorates insulin resistance and increases glucose transporter IV content of adipocytes isolated from the epididymal fat pads. In Japan [64] and Taiwan [65], oolong tea was shown to be an effective adjunct to oral hypoglycemic agents in the treatment of patients with type 2 diabetes.

Obviously, more research is needed to see if tea drinking should be a standard recommendation for those who have diabetes or are at risk for developing diabetes [66]. However, if one is a diabetic and likes tea, this is another good reason to keep drinking it. However, one should refrain from using added milk, soy milk, or nondairy creamer, because they may reduce the positive effect of tea on insulin activity [66].

5. Metabolic syndrome

The metabolic syndrome, formerly called metabolic 'syndrome X' [67], has reached an epidemic proportion [68] since its original description in 1988 [69]. A cluster of abnormalities defines the metabolic syndrome, including insulin resistance, hypertension, obesity, hypertriglyceridemia, low HDL cholesterol and inflammation [70].

Green tea has been shown recently to be a promising tool against the metabolic syndrome in China [66]. According to Campbell [66], Chinese researchers have experimented with using an extract from green tea called Tegreen, which contains polyphenols. In their study, rats were divided into 4 groups: one group (the control group) was fed a normal rat diet, another group was fed a high-calorie diet, and the remaining two groups were fed high-calorie diets and received Tegreen at different doses. After 8 weeks, the rats whose diets had been supplemented with Tegreen had lowered their fasting blood glucose and insulin levels, increased their insulin sensitivity, decreased their fasting triglyceride levels, and had a decrease in abdominal fat. Of course, rat and humans are very different, but using green tea in the form of a concentrated supplement could one day prove to be a weapon in the fight against the metabolic syndrome [66].

6. Obesity

Obesity has increased at an alarming rate in recent years and is now a worldwide health problem [71], including China [71,72]. It has been known for some time that tea helps to control obesity, and this is common knowledge in China. A Chinese classical pharmaceutical book called the Bencao Shiyi (The Conpendium of Materia Medica) states: "Drinking tea for a long time will make one live long to stay in good shape without becoming too fat and too heavy" [73].

The mechanisms of action of tea in obesity are:

(1) stimulation of hepatic lipid metabolism [74];
(2) inhibition of lipases [75];
(3) stimulation of thermogenesis [75–77];
(4) modulation of appetite [78]; and
(5) synergism with caffeine [79,80].

Oolong tea has been shown recently to be effective in the treatment of obesity by increasing plasma adiponectin levels [64], enhancing the effect of caffeine in oolong tea on noradrenaline-induced lipolysis in adipose tissue [81], and inhibiting pancreatic lipase activity [81].

Simple tea drinking may have easier acceptance by the patients than prescription drugs, exercise and bariatric surgery. There are 5 main attractions of this approach:(1) more natural; (2) safer; (3) no need for professional supervision; (4) readily accessible and affordable; and (5) attractive alternatives to failed attempts at weight reduction by other more conventional approaches [82].

7. Green tea vs. black tea

While there are hundred varieties of teas, most can be categorized into 3 types, depending on the level of fermentation or oxidation, i.e., green (unfermented), oolong (partially fermented) and black (fermented) tea. Green teas are not fermented during processing and thus retain the original color of the tea leaves; the most famous green tea is the Lung Chen Tea (Dragon Well Tea), grown in the hillside of Hangzhou, Zhejiang Province, China. Black teas are made from fermented leaves which account for their darker color. Oolong teas (Black Dragon Teas) are partially fermented, resulting in a black-green tea. (There is also a fourth category known as "scented teas", made by mixing various flowers and petals with green or oolong teas; the best known among these is jasmine tea).

Of all the teas studied, green tea produces the highest level of antioxidant activity and black tea the lowest (Fig. 1) [2]. Lee et al. [83] also found the antioxidant capacity per serving of green tea (436 mg vitamin C equivalents) to be much higher than that of black tea (239 mg). Thus green tea possesses the strongest cardioprotective effects [84–86]. The total catechin concentration in blood after ingestion of black tea is less than one third that following green tea: 0.17 μmol/L vs. 0.55 μmol/L [87]. The main flavonoids in green tea are catechins, whereas during production of black tea a major part of the catechins is transformed into theaflavins and thearubigens which impart the characteristic properties and taste of black tea [88]. The ratio of catechin content in green tea and black tea when based on spectrophotometric analysis is 3.1 to 1 [87]. Contrary to a common misconception, there is no tannic acid in tea [88].

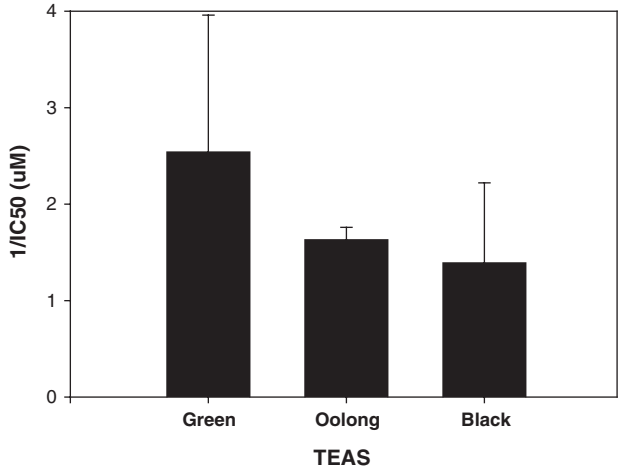

Fig. 1. Comparison of polyphenol antioxidant quality of green tea, oolong tea and black tea as measured by a dose–response inhibition of LDL+VLDL oxidation. Data are expressed as the mean±S.D. The higher the value of 1/IC50, the better the quality of antioxidants. 1/IC50=Concentration to inhibit oxidation 50%; LDL=low density lipoprotein; VLDL=Very low density lipoprotein. Reproduced from Ref. [2] with permission.

Although the health benefits of teas have largely been attributed to their antioxidant activities, flavonoids have also been shown to have significant effects on the fecal flora and fecal metabolic activities [89]. Mulder et al. [90] reported recently that the ingestion of either green tea or black tea results in a major increase in the excretion of hippuric acid into urine, slightly greater following green tea than black tea consumption. Therefore, flavonoids may exert a major influence on the colonic flora and thus confer a type of prebiotic effect [90]. Both green tea consumption and black tea consumption result in similar amounts of microbial degradation products that are absorbed by the body. These microbial metabolites, and not the native tea flavonoids, may be responsible for at least some of the health benefits attributed to tea consumption [90].

Black tea represents approximately 78% of total consumed tea in the world, whereas green tea accounts for approximately 20% of tea consumed [91]; less than 2% is oolong tea [88]. Whereas green tea is consumed mainly in China, black tea is preferred in continental Europe and the United States [92,93]. Although there is general agreement as to the protective effect of green tea against atherosclerotic coronary heart disease, the association between consumption of black tea and reduced risk of coronary heart disease is more controversial. Consumption of black tea has been found to be associated with a reduced risk of coronary heart disease in the Netherlands [94] and in men and women in the United States [95], but not in the United Kingdom [94,96] where milk is customarily taken with tea (unlike in the other two western countries) [93]. A suggestion that the milk prevents absorption of the antioxidants [94] has been disproven [87,97]. Segall [93] raised the possibility that the lactose in the milk may have an atherogenic potential [98] which counteracts the protective effect of the tea antioxidants.

In late 1990s there were more than 100 clinical trials conducted in hospitals in various parts of China to test the antihyperlipidemic effect of Chinese green tea [99]. All showed very promising results; the papers were published in China as a monograph in Chinese in 1998 [100]. A more recent comparative study of different teas from Taiwan reveals some more important findings [101]: the level of caffeine in different teas is in the order of black tea > oolong tea > green tea > fresh tea leaf; the levels of (−)-epigallocatechin-3-gallate and total catechins are in the order of green tea > oolong tea > fresh tea leaf > black tea; the nitric oxide suppressing effect is in the order of black tea > green tea > oolong tea; the induction of apoptosis is in the order of green tea > oolong tea > black tea. Green tea is more effective than black tea in improving the lipid profile [2,84,102]; another study from Taiwan shows that green tea exerts greater and faster antihyperlipidemic effect than oolong tea [103].

Finally, although clinical evidence is still sparse, epidemiologic and laboratory data suggest that drinking green tea may reduce incidence of several types of cancer [104]. Assessment of urinary 8-hydroxydeoxyguanosine (8-OHdG) as an indicator of oxidative DNA damage revealed a highly significant decrease in urinary 8-OHdG (−31%) after 4 months of drinking green tea ($p = 0.002$), but no change in urinary 8-OHdG among smokers assigned to the black tea group [105]. Therefore, regular drinking of green tea but not black tea might protect smokers from oxidative damages and could reduce cancer risk or other diseases caused by free radicals associated with smoking [105].

8. Conclusion

According to Chinese legends, tea was discovered by the Emperor Shen Nong in about 2700 BC, when a gust of wind blew tea leaves into a kettle of boiling water [92]. Emperor Shen Nong reputedly said in 2737 BC that tea can provide "vigor of body, contentment of mind, and determination of purpose" [106]. Since then green tea has been a staple product and the main beverage in China [12,92]. It is the Chinese national drink served at all meals of the day to everyone from the president to the poorest farmer. In the world, tea is also one of the most widely consumed beverage next only to water [1]. In China tea has been considered a crude medicine for over 4000 years [6,12,92]. Its beneficial effect on the cardiovascular health has been amply demonstrated in recent years. Thus, another ancient Chinese wisdom about green tea is certainly more than just a tempest in a teapot.

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